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ORIGINAL SCIENTIFIC REPORT

Impact of Preoperative Skeletal Muscle Quality Measurement on Long-Term Survival After Curative Gastrectomy for Locally Advanced Gastric Cancer

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Abstract

Background Skeletal muscle quality is a prognostic factor in various cancers. However, similar studies on curatively resected gastric cancer are lacking. We evaluated skeletal muscle quality using intramuscular adipose tissue content (IMAC) to clarify its impact on survival in patients with locally advanced gastric cancer.

Methods We reviewed 370 patients who underwent curative resection for stage II/III gastric cancer. IMAC was calculated using preoperative computed tomography images. IMAC cutoff values were determined for each sex and were set at the 75th percentile. The patients were classified into normal and high IMAC groups according to the cutoff values. Clinicopathological factors and survival outcomes were compared between the two groups. Multivariate Cox regression analysis was used to identify independent prognostic factors for overall survival (OS) and cancer-specific survival (CSS).

Results In all, 277 patients were classified into the normal IMAC group and 93 were classified into the high IMAC group. The patients in the high IMAC group were older, more obese, and had more comorbidities and poor Eastern Cooperative Oncology Group performance status than those in the normal IMAC group. Although no significant differences were observed in the pathological findings between the two groups, a high IMAC was significantly associated with poor OS and CSS. Multivariate analysis identified high IMAC as an independent prognostic factor for both OS and CSS ($p = 0.046$ and $p = 0.035$, respectively).

Conclusions High IMAC was significantly associated with poor survival, suggesting that skeletal muscle quality has oncological implications in patients with locally advanced gastric cancer.

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Introduction

Although surgical resection is the most effective treatment and provides the only hope for long-term survival in patients with locally advanced gastric cancer (LAGC), the incidence of postoperative complications after curative gastrectomy remains high [1]. Recently, sarcopenia has been reported as a prognostic factor for surgical and survival outcomes in gastric cancer [2–6]. According to the European Working Group on Sarcopenia in Older People, sarcopenia is defined as a progressive and generalized syndrome characterized by the loss of skeletal muscle mass and function, which is associated with poor physical ability and quality of life [7]. Patients with LAGC can easily

experience a decrease in skeletal muscle mass due to a loss of oral intake or cancer progression; therefore, sarcopenia is a potential therapeutic target for improving survival in LAGC [2].

Deterioration of skeletal muscle quality caused by an increase in intramuscular adipose tissue contributes to decreased muscle function, defined by muscle strength or physical performance [8–10]. Skeletal muscle quality has recently attracted attention as another factor associated with survival in various cancers [11–17]. In general, skeletal muscle quality has been reported to be affected by intramuscular adipose tissue as evaluated by computed tomography (CT).[14, 17]. Nevertheless, the simple approach of using the CT value has a critical drawback, as the CT value is greatly affected by the imaging system and scanning conditions. Therefore, it is very difficult to use the CT value as a comprehensive evaluation tool for skeletal muscle quality [18].

Intramuscular adipose tissue content (IMAC) assessment, calculated by normalizing a patient's CT values for skeletal muscle to those of subcutaneous fat, has been proposed as a novel indicator of muscle steatosis [18, 19]. Several studies have demonstrated the usefulness of IMAC in predicting survival in patients with hepatopancreatobiliary cancer and in liver transplantation recipients [11–13, 20, 21]. Recently, Lu et al. evaluated the clinical impact of skeletal muscle quality assessed using CT values on survival in gastric cancer [17]. However, no reports have used IMAC as an indicator of muscle quality in gastric cancer.

Therefore, we aimed to investigate the impact of preoperative skeletal muscle quality evaluated by IMAC on survival in patients with LAGC.

Materials and methods

Patients

This retrospective study analyzed data from patients with pathological stage II/III gastric cancer who underwent gastrectomy at our institution from January 2009 to December 2013. Eligibility criteria were histologically proven gastric cancer and R0 resection with adequate lymph node dissection, according to the Japanese gastric cancer treatment guidelines [22]. Exclusion criteria were carcinoma of the remnant stomach, other active malignant diseases, prior chemotherapy or radiotherapy for gastric cancer, special histological type, Siewert type I/II esophagogastric junction cancer, combined organ resection other than the gallbladder and spleen, and missing preoperative cross-sectional CT images of the third lumbar vertebra (L3). All patients were followed up based on the protocol provided by the Japanese gastric cancer treatment guidelines [22]. This study was approved by the institutional review board of Shizuoka Cancer Center (approval no. 29-J163-29-1-3).

Factors analyzed

The following clinicopathological variables were collected for all patients: age, sex, Eastern Cooperative Oncology Group performance status (ECOG-PS), body mass index, comorbidities, grip strength, psoas muscle area, psoas muscle index (PMI), tumor location, macroscopic tumor type, histological classification, clinical TNM classification, pathological staging, and compliance with adjuvant chemotherapy. Surgical outcomes, including operation time, blood loss, type of resection, and extent of lymph node dissection, and postoperative outcomes, such as the postoperative hospital stay duration, postoperative complications categorized according to the Clavien–Dindo (CD) classification, recurrence rates and patterns, overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS), were also evaluated. Postoperative complications were defined as any adverse event corresponding to CD grade II or above that occurred during the postoperative hospital stay.

Image analysis and assessment of IMAC and PMI

All preoperative CT images were acquired using a multidetector scanner (Aquilion; Toshiba Medical Systems, Tochigi, Japan). To minimize measurement bias, one trained investigator (Y.W.) identified and measured subcutaneous fat and muscle areas using SYNAPSE and Volume Analyzer SYNAPSE VINCENT (Fujifilm, Tokyo, Japan).

The subfascial muscular tissue in the multifidus muscle was manually traced on plain cross-sectional CT images at the L3 level, and Hounsfield unit (HU) values were measured (Fig. 1a). Plain CT values of subcutaneous fat were also measured for regions of interest (ROIs), which comprised four circles, away from major vessels, on the back side at the L3 level. The mean of the values from the four ROIs was used to calculate the amount of subcutaneous fat (HU).

IMAC was calculated by dividing the CT value of the multifidus muscles (HU) with that of the subcutaneous fat (HU), as previously reported [18, 19]. Higher IMAC indicates greater accumulation of intramuscular adipose tissue, which may indicate lower muscle quality.

As an indicator of skeletal muscle quantity, we evaluated the PMI. The cross-sectional tissue areas of both the right and left psoas muscles were calculated automatically at the L3 level with the Volume Analyzer SYNAPSE

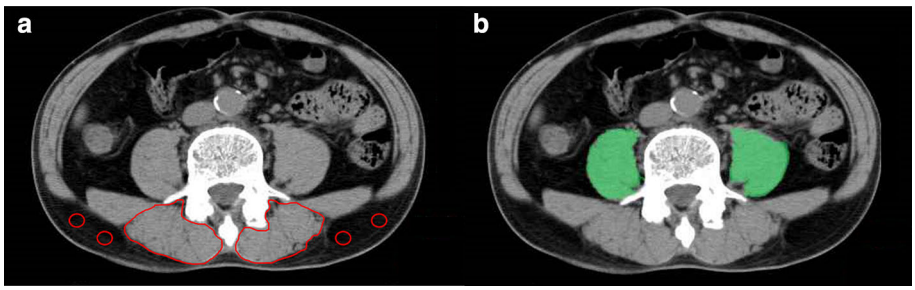

Fig. 1 Measurement of body composition parameters with cross-sectional CT images at the third lumbar level. **a** Subfascial muscular tissue in the multifidus muscle was precisely measured by manual tracing (red lines). Four small red circles were placed on subcutaneous fat tissue, away from major vessels. IMAC was calculated by dividing the mean CT value of the multifidus muscles with the mean CT value of the subcutaneous fat (four small red circles). **b** The bilateral psoas muscle areas were calculated by automatic tracing (green areas). *CT* computed tomography, *IMAC* intramuscular adipose tissue content

VINCENT (Fig. 1b). Tissue boundaries were manually corrected if necessary. PMI was calculated by normalizing the cross-sectional area of the psoas muscle to the square of the patient's height (cm^2/m^2). The PMI cutoff values for men and women were set at 6.36 cm^2/m^2 and 3.92 cm^2/m^2, respectively, based on the Japan Society of Hepatology guidelines [23].

Statistical analysis

All statistical analyses were performed using R version 3.4.0 software (R Foundation for Statistical Computing, Vienna, Austria). Continuous data are presented as medians (interquartile range [IQR]) and were nonparametrically analyzed using the Mann–Whitney test. Categorical variables were compared using the Chi-squared or Fisher exact test. Correlations among continuous variables were assessed using the Spearman correlation coefficient. CSS was defined as the period from the date of surgery to death due to gastric cancer. Data from patients who died from other causes or were alive at their last follow-up date were censored. OS and CSS were analyzed using Kaplan–Meier estimation, and differences in survival were evaluated using the log-rank test. Variables with $p < 0.05$ on univariate analysis were included in the subsequent multivariate Cox regression analysis. p values < 0.05 were considered statistically significant.

Results

Study population

Among the 535 patients fulfilling the eligibility criteria, 165 were excluded for various reasons. Accordingly, a total of 370 patients were enrolled in this study (Supplementary Fig. 1). The overall median IMAC value was − 0.311 (IQR − 0.3863 to − 0.2198), exhibiting a marked difference between men (− 0.330, IQR − 0.4075 to − 0.2541) and women (− 0.242, IQR − 0.3366 to − 0.1095). Therefore, separate cutoff values were used (− 0.2541 for men and − 0.1095 for women) based on the 75th percentile values, to classify patients into normal and high IMAC groups. Among the 256 male patients, 192 and 64 were classified into the normal and high IMAC groups, respectively. Likewise, among the 114 female patients, 85 and 29 were classified into the normal IMAC and high groups, respectively. In total, the normal and high IMAC groups consisted of 277 and 93 patients, respectively.

Correlation analysis

The range of IMAC values was quite different in the two sexes; therefore, we analyzed the correlations between IMAC and other factors according to sex (Fig. 2). IMAC was significantly correlated with age in both men and women. It was also weakly correlated with grip strength in both men and women. A trend toward an inverse correlation between IMAC and PMI was observed in men but not in women.

Comparison of clinicopathological factors

The clinicopathological factors were compared between the groups (Table 1). The patients in the high IMAC group were older, more obese, had more comorbidities, poorer ECOG-PS, lower grip strength, and lower PMI than did those in the normal IMAC group. The patients in the high IMAC group experienced higher intraoperative blood loss volumes, longer postoperative hospital stays, higher rates of morbidity, and lower rates of adjuvant chemotherapy than did those in the normal IMAC group. There was no significant difference in pathological findings between the two groups.

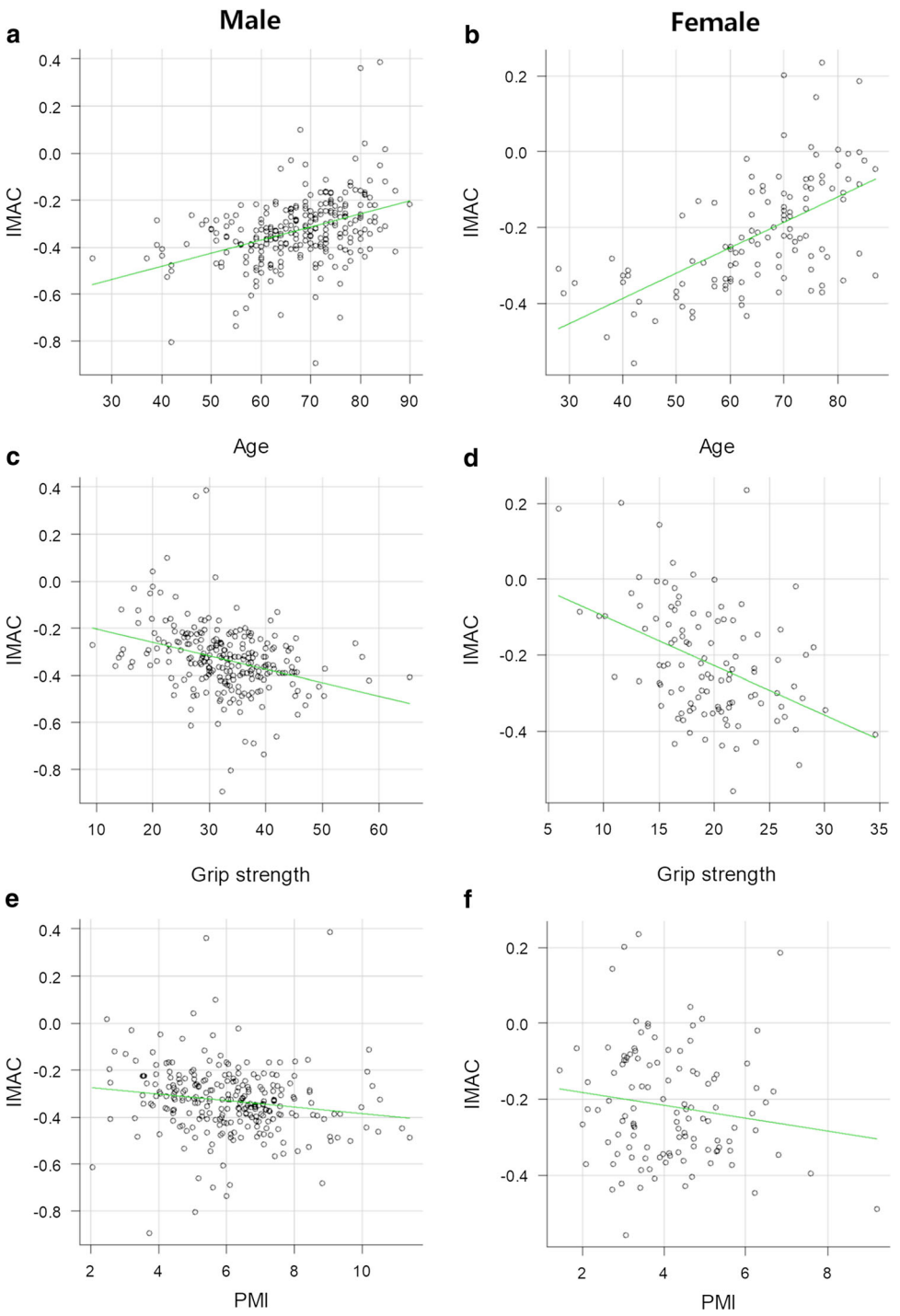

Fig. 2 Correlations between IMAC and other factors. A significant correlation was observed between IMAC and patient age in both **a** male patients ($r = 0.432$, $p < 0.001$) and **b** female patients ($r = 0.619$, $p < 0.001$). A weak inverse correlation was also observed between IMAC and grip strength in **c** male patients ($r = -0.373$, $p < 0.001$) and **d** female patients ($r = -0.400$, $p < 0.001$). A weak inverse correlation was observed between IMAC and PMI **e** in male patients ($r = -0.245$, $p < 0.001$) but not **f** in female patients ($r = -0.127$, $p = 0.176$). IMAC intramuscular adipose tissue content; PMI psoas muscle index

Survival analyses

The median follow-up period for all enrolled patients was 60 months (range 2–95; IQR 47–65). The 5-year OS was significantly poorer in the high IMAC group (60.2%) than in the normal IMAC group (79.0%). The 5-year RFS and CSS were also lower in the high IMAC group (60.1% and 77.5%) than in the normal IMAC group (75.1% and 86.5%) (Fig. 3).

Recurrence patterns and causes of death

The rate of recurrence was significantly higher in the high IMAC group ($n = 27$, 29.0%) than in the normal IMAC group ($n = 46$, 16.6%, $p = 0.026$). The recurrence patterns

Table 1 Patients' characteristics and operative outcomes

Factors	Normal IMAC (n = 277)	High IMAC (n = 93)	p value
Age [years; median (IQR)]	64 (59–72)	75 (69–80)	< 0.001*
Sex, n (%)			
Women	85 (30.7)	29 (31.2)	1.000
Men	192 (69.3)	64 (68.8)	
ECOG-PS, n (%)			
0	273 (98.6)	85 (91.4)	0.002*
1 or 2	4 (1.4)	8 (8.6)	
BMI [kg/m^2; median (IQR)]	22.13 (20.46–24.13)	23.64 (21.40–26.22)	< 0.001*
Comorbidities, yes, n (%)	115 (41.5)	63 (67.7)	< 0.001*
Grip strength [kgf; median (IQR)]	30.0 (21.6–36.3)	23.8 (17.4–30.1)	< 0.001*
Location, n (%)			
U	77 (27.8)	22 (23.7)	0.062
M	118 (42.6)	31 (33.3)	
L	82 (29.6)	40 (43.0)	
Macro type, n (%)			
0	112 (40.4)	28 (30.1)	0.105
1	9 (3.2)	8 (8.6)	
2	59 (21.3)	25 (26.9)	
3	86 (31.0)	27 (29.0)	
4	11 (4.0)	5 (5.4)	
Histological type, n (%)			
Differentiated	132 (47.7)	44 (47.3)	1.000
Undifferentiated	145 (52.3)	49 (52.7)	
Clinical T stage[a], n (%)			
cT1	64 (23.1)	13 (14.0)	0.085
cT2	52 (18.8)	16 (17.2)	
cT3	52 (18.8)	14 (15.1)	

Table 1 continued

Factors	Normal IMAC (n = 277)	High IMAC (n = 93)	p value
cT4	109	50	
	(39.4)	(53.8)	
Clinical N stage[a], n (%)			
cN0	177	53	0.533
	(63.9)	(57.0)	
cN1	41	19	
	(14.8)	(20.4)	
cN2	44	15	
	(15.9)	(16.1)	
cN3	15	6	
	(5.4)	(6.5)	
Clinical stage[a], n (%)			
IA/IB	106	26	0.097
	(38.3)	(28.0)	
IIA/IIB	94	34	
	(33.9)	(36.6)	
IIIA/IIIB/IIIC	77	32	
	(27.8)	(34.4)	
IV	0 (0.0)	1	
		(1.1)	
Type of gastrectomy, n (%)			
Distal	156	64	0.072
	(56.3)	(68.8)	
Proximal	3	2	
	(1.1)	(2.2)	
Pylorus-preserving	12	1	
	(4.3)	(1.0)	
Total	106	26	
	(38.3)	(28.0)	
Lymph node dissection, n (%)			
$<$ D2	47	16	1.000
	(17.0)	(17.2)	
$\geq$ D2	230	77	
	(83.0)	(82.8)	
Operation time [min; median (IQR)]	239	242	0.379
	(204.0–271.0)	(206.0–284.0)	
Blood loss [mL; median (IQR)]	278	396	0.003*
	(164.0–488.0)	(199.0–746.0)	
Postoperative hospital stays [days; median (IQR)]	10	10	$<$ 0.001*
	(9–12)	(10–16)	
Complications (CD $\geq$ II) yes, n (%)	71	37	0.012*
	(25.6)	(39.8)	
Pathological tumor size	55	60	0.104
[mm; median (IQR)]	(38.0–75.0)	(40.0–85.0)	
Pathological stage[a], n (%)			
IIA	85	31	0.419
	(30.7)	(33.3)	

Table 1 continued

Factors	Normal IMAC (n = 277)	High IMAC (n = 93)	p value
IIB	71	26	
	(25.6)	(28.0)	
IIIA	50	11	
	(18.0)	(11.8)	
IIIB	34	16	
	(12.3)	(17.2)	
IIIC	37	9	
	(13.4)	(9.7)	
Adjuvant chemotherapy, yes, n (%)	181	49	0.035*
	(65.3)	(52.7)	
PMA [cm^2; median (IQR)]	14.7	12.3	< 0.001*
	(11.1–18.9)	(8.2–15.9)	
PMI [cm^2/m^2; median (IQR)]	5.58	4.71	< 0.001*
	(4.44–6.87)	(3.53–6.09)	

IQR interquartile range, ECOG-PS Eastern Cooperative Oncology Group performance status, BMI body mass index, CD Clavien–Dindo classification, PMA psoas muscle area, PMI psoas muscle index

[a]The 14th edition of Japanese Classification of Gastric Carcinoma

[*]Statistically significant

were not different between the groups. The most common site of recurrence in both groups was the peritoneum (high IMAC: 40.7%, normal IMAC: 45.6%, p = 0.811), followed by hematogenous sites (37.0% and 39.1%, p = 0.808), lymph nodes (22.2% and 21.7%, p = 0.552), and local recurrence (3.7% and 8.7%, p = 0.656). Death by gastric cancer was significantly more frequent in the high IMAC group than in the normal IMAC group (70.3% and 48.8%, p = 0.037), whereas the groups did not significantly differ in death by other diseases (24.1% and 41.9%, p = 0.080).

Univariate and multivariate survival analyses

The results of the univariate and multivariate analyses are given in Table 2. The univariate analyses showed that age ≥ 65 years, clinical T stage 3 or 4, clinical N stage 2 or 3, low grip strength, low PMI, and high IMAC were associated with poor OS. Moreover, age ≥ 65 years, macroscopic type 3 or 4, clinical T stage 3 or 4, clinical N stage 2 or 3, undifferentiated histological type, and high IMAC were associated with poor CSS.

The multivariate analyses showed that clinical N stage 2 or 3 and high IMAC were independent predictors of poor OS, while undifferentiated histological type, clinical N stage 2 or 3, and high IMAC were independent predictors of poor CSS in patients with LAGC after curative gastrectomy.

Discussion

This study revealed that patients with high IMAC had poorer OS, RFS, and CSS after curative gastrectomy for stage II/III gastric cancer than did those with normal IMAC. In addition, high IMAC was identified as an independent predictor of worse OS and CSS.

Sarcopenia is described as an age-related decrease in skeletal muscle mass and function associated with short-term and long-term outcomes in gastric cancer [2–6]. Because of the difficulty in evaluating skeletal muscle function, several studies have defined sarcopenia based on skeletal muscle quantity alone [2, 4–6]. Only one study has evaluated skeletal muscle quality by assessing the accumulation of intramuscular adipose tissue [17].

An increase in intramuscular adipose tissue has been identified as a potential contributor to decreased muscle function [8–10]. In general, the amount of intramuscular adipose tissue is calculated using the CT values of skeletal muscle [14, 17]. Psoas muscle quality measured by the CT value was reported to be an independent prognostic factor in gastrointestinal surgery [15], but not in gastric cancer [17]. However, the CT value is greatly affected by peak kilovoltage (kV) and electric current (mA); thus, it cannot be easily generalized [18].

IMAC, a novel quantitative measure of skeletal muscle quality [18, 19], has been reported to be a prognostic factor in hepatopancreatobiliary cancers [12, 13, 24]. Since the value of IMAC is normalized to the value of subcutaneous

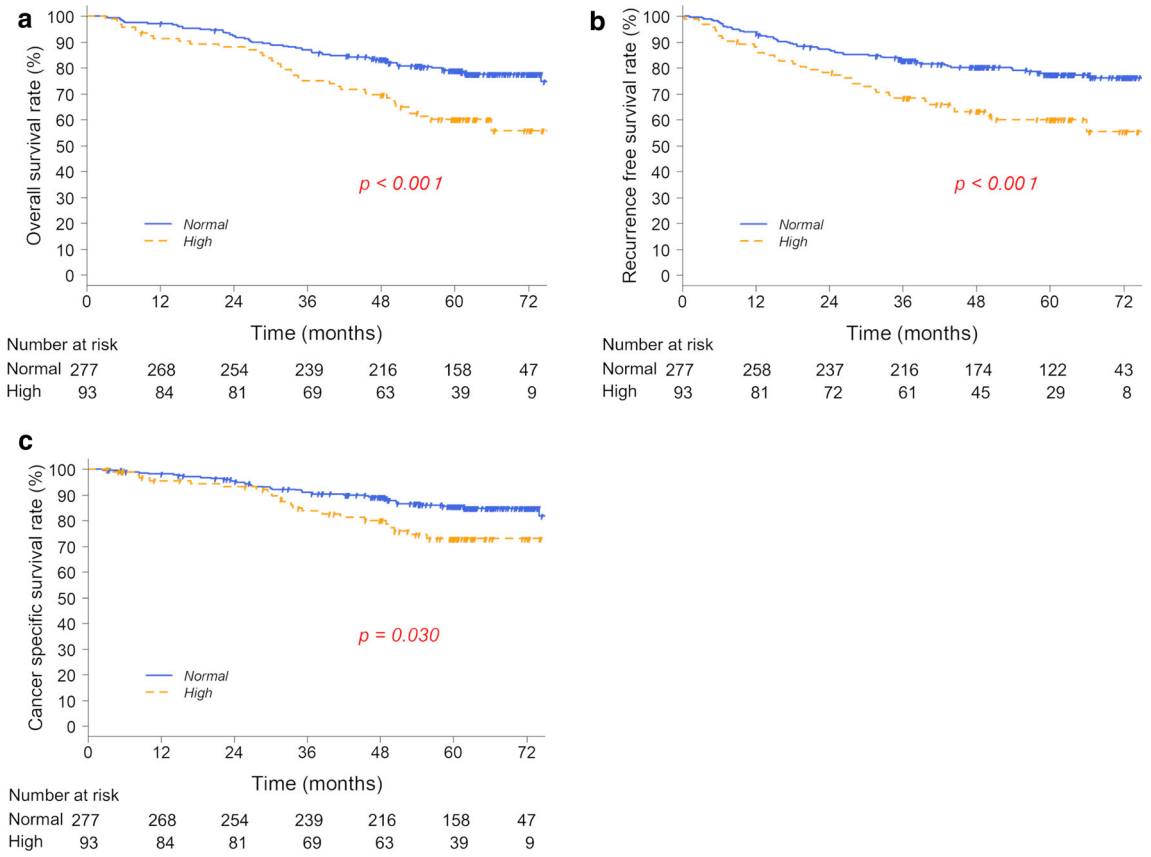

Fig. 3 Association between IMAC and overall, recurrence-free, and cancer-specific survival after radical gastrectomy. **a** OS, **b** RFS, and **c** CSS rates were significantly lower in patients with high IMAC than in patients with normal IMAC ($p < 0.001$, $p < 0.001$, $p = 0.030$, respectively). OS overall survival; RFS recurrence-free survival; CSS cancer-specific survival

fat in each patient, it is not affected by the CT system and scanning conditions [19]. Therefore, it can more sensitively reflect skeletal muscle quality. In this study, IMAC was significantly associated with OS, RFS, and CSS. Furthermore, IMAC was found to be an independent predictor of OS and CSS, suggesting that muscle quality as evaluated by IMAC is associated with an increase in gastric cancer death rather than death by other diseases.

The mechanism by which low-quality skeletal muscle leads to poor survival remains incompletely understood. Loss of muscle tissue with aging is accompanied by the infiltration of fat tissue, a condition known as myosteatosis [25]. The pathogenesis of myosteatosis is complex and consists of various factors, such as diffuse muscle atrophy, altered endocrine function, inflammation, insulin resistance, and nutritional deficiencies [26]. Recently, both adipose tissue and skeletal muscles have been acknowledged as secretory organs that release proinflammatory and anti-inflammatory cytokines and peptides, such as myokines and adipokines [27]. The interplay between adipose tissue and skeletal muscles through these cytokines leads to immune system dysfunction, which is an important mediator of the effects of low-quality skeletal muscle on cancer survival [28]. Hence, patients with high IMAC are suggested to have poor survival outcomes.

In general, skeletal muscle strength is believed to be related to muscle quantity. Although a relationship between muscle strength and IMAC has not yet been demonstrated, our study demonstrated a weak relationship between grip strength and IMAC in both men and women. However, grip strength was not identified as an independent prognostic factor. Therefore, IMAC is considered to be a more important parameter than grip strength for evaluating decreased muscle strength.

Several studies have identified the loss of skeletal muscle quantity as an independent predictor of short-term and long-term outcomes in gastric cancer [2, 4–6]. Our previous study demonstrated that skeletal muscle quantity and strength, measured by arm muscle area (AMA) and grip strength, were independent predictors of OS and CSS in patients aged ≥ 65 years who underwent curative gastrectomy [3]. In contrast, our current study showed that

Table 2 Univariate and multivariate analyses of clinicopathological factors for overall and cancer-specific survival

Overall survival						
Age, ≥ 65 versus < 65 years	2.424	1.622–3.624	< 0.001*	1.331	0.751–0.914	0.137
Sex, men versus women	1.258	0.820–1.930	0.316			
BMI, ≥ 25 versus < 25 kg/m^2	0.819	0.510–1.316	0.435			
Comorbidity, yes versus no	1.366	0.917–2.036	0.124			
Macroscopic type, 3/4 versus 0/1/2	1.257	0.828–1.909	0.268			
Location, upper versus middle/lower	1.210	0.769–1.904	0.389			
Histological type, undifferentiated versus differentiated	1.347	0.905–2.006	0.147			
Clinical T stage [b], 3/4 versus 1/2	1.808	1.207–2.709	0.008*	1.355	0.836–2.191	0.219
Clinical N stage [b], 2/3 versus 0/1	2.088	1.267–3.440	< 0.001*	1.796	1.148–2.846	0.011*
Grip strength, low versus normal	1.710	1.138–2.570	0.007*	1.272	0.823–1.967	0.279
PMI, low versus high	1.528	1.026–2.275	0.041*	1.174	0.762–1.807	0.468
IMAC, high versus normal	2.053	1.280–3.292	< 0.001*	1.379	1.006–1.967	0.046*
Cancer-specific survival						
Age, ≥ 65 versus < 65 years	1.401	0.830–2.367	0.221			
Sex, men versus women	0.850	0.486–1.486	0.556			
BMI, ≥ 25 versus < 25 kg/m^2	0.888	0.480–1.645	0.715			
Comorbidity, yes versus no	1.185	0.704–1.994	0.520			
Macroscopic type, 3/4 versus 0/1/2	1.792	1.040–3.087	0.025*	1.354	0.765–2.397	0.299
Location, upper versus middle/lower	1.012	0.560–1.827	0.969			
Histological type, undifferentiated versus differentiated	1.900	1.130–3.194	0.020*	1.815	1.037–3.177	0.037*
Clinical T stage [b], 3/4 versus 1/2	1.952	1.152–3.309	0.023*	1.287	0.650–3.177	0.469
Clinical N stage [b], 2/3 versus 0/1	2.381	1.239–4.575	0.001*	1.999	1.115–3.585	0.020*
Grip strength, low versus normal [c]	1.599	0.940–2.722	0.073			
PMI, low versus high	1.128	0.671–1.897	0.649			
IMAC, high versus normal	1.805	0.974–3.344	0.030*	1.513	1.028–2.225	0.035*

CD Clavien–Dindo classification, BMI body mass index, PMI psoas muscle index, IMAC intramuscular adipose content

[a] Subtotal includes distal, proximal, and pylorus-preserving gastrectomy

b The 14th edition of Japanese Classification of Gastric Carcinoma

[c] Cutoff values for men and women are set at 30 kgf and 20 kgf, respectively, according to the European Working Group on Sarcopenia in Older People*statistically significant

skeletal muscle quantity measured by PMI was not associated with OS and CSS. A previous study also demonstrated similar results [17]. One possible reason for this discrepancy is that the current study used PMI as a substitute for AMA as a measure of muscle mass. In the previous study, low muscle mass was defined as a value below the 20th percentile of the AMA in the study population. In contrast, PMI has comprehensive cutoff values for low muscle mass calculated from healthy adults [20, 29]. Recently, the Asian Working Group for Sarcopenia proposed quantifying skeletal muscle mass by dual-energy X-ray absorptiometry or bioimpedance analysis with muscle strength [30]. Although PMI and AMA are both alternatives to dual-energy X-ray absorptiometry or bioimpedance analysis [29, 31], assessing both muscle quantity and strength, rather than quantity alone, could be a more accurate method for evaluating skeletal muscle mass loss.

The close association between high IMAC and survivals suggests the need for interventions to improve skeletal muscle quality, such as exercise [32, 33], an omega-3 fatty acid dietary supplement [34], melanocortin-4 receptor antagonist [35], and myostatin inhibition [36]. Further studies are required to elucidate the type of preoperative intervention that may improve skeletal muscle quality in patients with high IMAC.

The present study had several limitations. First, this was a retrospective analysis from a single institute. Second, the IMAC cutoff value may vary depending on individual characteristics, such as age, sex, and ethnicity. In this

study, cutoff values were established based on patient data from a single hospital. Different patient populations may have different cutoff values; thus, a multicenter study or studies on other patient populations are needed to determine a comprehensive cutoff value.

In conclusion, high IMAC was significantly associated with poor survival, suggesting that skeletal muscle quality has certain oncological implications in patients with LAGC.

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Compliance with ethical standards

Conflict of interest Masanori Terashima has received personal fees from Taiho, Chugai, Ono, Bristol-Myers Squibb, Yakult, Takeda, Eli Lilly, Pfizer, and Daiichi Sankyo, outside the submitted work. All other authors declare no conflict of interest.

Human and animal rights This study was approved by the institutional review board of Shizuoka Cancer Center (approval no. 29-J163-29-1-3).

Informed consent Informed consent was not obtained from the patients. Instead, all patients were previously informed of an opt-out method.

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