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Skeletal Muscle Changes Assessed by Preoperative Computed Tomography Images Can Predict the Long-Term Prognosis of Stage III Colorectal Cancer

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Abstract

Background: Myopenia and myosteatosis are reported to be long-term prognostic factors in patients with colorectal cancer (CRC). However, the established parameters are unsuitable for the Japanese population because their body composition is different from that of the Western population.

Objective: We aimed to elucidate the effect of skeletal muscle changes among Japanese adults, measured using preoperative computed tomography (CT) as a prognostic factor in patients with stage III CRC.

Patients: We retrospectively analyzed 341 patients diagnosed with stage III CRC. The cross-sectional area (skeletal muscle index: SMI) and mean radiodensity of skeletal muscle (skeletal muscle radiodensity: SMR) were measured using preoperative CT. The optimal sex-specific cutoff value, which was used to divide the patients according to the risk of recurrence, was set for SMI and SMR. Univariate and multivariate analysis were performed to determine the prognostic factors for recurrence-free survival (RFS).

Results: The cutoff values of SMI for men and women were set as 48.5 and 41.4, respectively, and those of SMR were 35.0 and 21.7, respectively. Univariate analysis identified low SMI and SMR in men and low SMR in women as the worst prognostic factors for RFS. Multivariate analysis identified low SMI in men and low SMR in women as independent poor prognostic factors for RFS (hazard ratio [HR] = 1.87, 95% confidence interval [CI], 1.08–3.47, $P = .03$ and HR = 2.49, CI, 1.21–4.95, $P = .01$).

Conclusion: Low SMI in men and low SMR in women were the independent prognostic factors for patients with stage III CRC.

KEYWORDS
colorectal cancer, long term prognosis, myopenia, myosteatosis, skeletal muscle

1 | INTRODUCTION

The overall survival (OS) of radically resected stage IIIa/IIIb colorectal cancer (CRC) in Japanese patients was reported to be 80.4%/63.8% for colon cancer and 73.0%/53.5% for rectal cancer, respectively.[1] According to the guidelines for CRC treatment in Japan, an oxaliplatin-containing regimen (CAPOX or FOLFOX regimen) is the recommended adjuvant chemotherapy for patients with stage III CRC.[1] However, the adverse effects of oxaliplatin, such as sensory peripheral neuropathy, often occur during chemotherapy. Therefore, being able to select patients who have a higher risk of recurrence among those who are pathologically diagnosed with stage III CRC, before the introduction of adjuvant chemotherapy, would be highly beneficial. However, to date this risk factor for tumor recurrence has not been well established in stage III CRC.

Myocopenia is defined as a loss of skeletal muscle mass.[2] To measure the amount of skeletal muscle, several methods have been attempted in the research field, such as body imaging techniques, bioimpedance analysis, and anthropometric measures. Body imaging techniques for the measurement of skeletal muscle mass can be performed using computed tomography (CT), magnetic resonance imaging, and dual-energy X-ray absorptiometry. Among them, a CT scan can precisely distinguish the muscle from fat tissues; therefore, this technique is the gold standard in the research field. Myopenia is thought to be a prognostic factor for lung and gastrointestinal cancers.[3,4] Several studies reporting myopenia as a prognostic factor for resectable CRC have been published during the last decade.[5-14] Furthermore, myosteatosis was also featured as a prognostic factor in addition to myopenia.[7,12,13] Some studies have reported myosteatosis as a long-term prognostic factor.[15-18] Myosteatosis is usually diagnosed when measuring the skeletal muscle volume using CT because it can be simultaneously evaluated as the mean skeletal muscle radio density (SMR). In most studies evaluating the influence of myopenia on survival, patients are divided into two groups (myopenia group and nonmyopenia group) using the specific cutoff values reported by Prado et al or Martin et al[3,4] for univariate or multivariate analysis for survival. However, we did not consider these cutoff values to be suitable for the Japanese population because their basic body shape is quite different from that of the Western population. The mean skeletal muscle mass is lower in the Japanese population than in the Western population. In addition, the cutoff value used in the study by Prado et al was set for obese patients (body mass index [BMI] <30). Therefore, the optimal cutoff values for Japanese patients are required.

In this retrospective study we aimed to investigate whether changes in the skeletal muscle (myopenia and myosteatosis) calculated using preoperative CT could be prognostic factors for stage III CRC.

2 | PATIENTS AND METHODS

2.1 | Patients

We performed a retrospective analysis of 341 patients with CRC who underwent primary tumor resection at the Kitasato University Hospital and Kitasato University East Hospital (Sagamihara, Japan) between January 2012 and December 2017. The inclusion criteria of patients were as follows: patients with histologically confirmed colorectal adenocarcinoma, patients who underwent curative resection and pathologically diagnosed as stage III CRC, and those with perioperative abdominal CT scans available for review. Cancer staging was performed according to the Japanese classification.[19] This study was approved by the Kitasato University Medical Ethics Organization (KMEO B20-167). All individuals gave written informed consent for the use of clinical data.

All clinical and pathological data were revalidated based on the medical and pathology records. Age, sex, height, weight, date of surgery, serum carcinoembryonic antigen (CEA) level, serum carbohydrate antigen 19-9 (CA19-9) level, cancer stage, tumor site, depth of invasion, degree of lymph node metastasis, administration of adjuvant chemotherapy, and survival data were collected.

Neoadjuvant chemoradiotherapy was performed for the rectal cancer patients if the T factor was diagnosed as higher than T3 (28% of the rectal cancer patients).

The adjuvant chemotherapy begins in 4–8 wk after first discharge of the operation for the primary tumors, and we did not perform adjuvant chemotherapy for the following patients: (a) patients who had severe systemic diseases; (b) patients who rejected chemotherapy; and (c) patients whose drug compliance was not guaranteed due to psychological disease, including dementia. The recommended regimens of chemotherapy were Capecitabine, UFT/LV, TS-1, CAPOX, and FOLFOX. The duration of chemotherapy was 6 mo, and the chemotherapy was stopped or changed to other regimens when the patient could not continue the chemotherapy due to moderate to severe adverse effects or patient rejection. After curative resection, surveillance for recurrence was conducted based on the clinical guidelines issued by the Japanese Society of Cancer of the Colon and Rectum.[1]

2.2 | Endpoints

The primary endpoint of this study was recurrence-free survival (RFS), defined as the time (in months) from the date of surgery to the date of the diagnosis of CRC recurrence or any cause of death. The secondary endpoint was OS, defined as the time (in months) from the date of surgery to the date of death from any cause.

2.3 | Measurement of skeletal muscle area

The skeletal muscle area was retrospectively measured based on CT scans performed prior to surgery. The measurement of the patients who received chemoradiotherapy was performed by using the CT images before chemoradiotherapy. All measurements were performed from a single image taken at the level of the third lumbar vertebra (L3). We used a freely available image processing software for the measurement of CT images (ImageJ, NIH, Bethesda, MD).[20]

Hounsfield unit (HU) thresholds of −30 to 150 were used for the skeletal muscle. The skeletal muscle cross-sectional area (cm^2) was normalized by the square of the height (m^2), and reported as the skeletal muscle index (SMI). The mean skeletal muscle radio density (SMR) was defined as the mean HU of all skeletal muscles at the L3 level. Therefore, in our study a low SMI indicates myopenia and a low SMR indicates myosteatosis.

2.4 | Statistical analysis

The chi-squared test was used for the analysis of categorical variables, whereas the Mann–Whitney U-test or analysis of variance (ANOVA) was used for continuous variables. The SMI and SMR were divided into four groups (Q1–Q4) according to the numbers in each sex for the analysis of general tendencies of SMI and SMR. RFS and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate analyses for RFS were conducted using Cox's proportional hazards model. The following variables were included in the analysis: age, tumor location, pathological stage, administration of adjuvant chemotherapy, and skeletal muscle changes (SMI or SMR). Variables that showed statistically significant results in univariate analysis were selected for further multivariate analysis. For univariate and multivariate analyses, patients were divided into two groups according to the cutoff values of SMI or SMR. The cutoff value was set using a receiver operating characteristic (ROC) curve. Hazard ratios (HRs) with their 95% confidence intervals (CIs) were computed from the multivariate analysis. $P < .05$ was considered statistically significant. All statistical analyses were conducted using the SAS software package JMP, v. 11.0 (SAS Institute, Cary, NC).

3 | RESULTS

3.1 | Patients' baseline parameters

The clinicopathological parameters of all patients are shown in Table 1. The median follow-up period was 44 mo (range 0–99 mo). The ratio of the patients who completed adjuvant chemotherapy was 70.0%, and the ratio of the patients who were failed to complete due to adverse effect was 15.7%. Ninety-nine patients developed recurrence and 62 patients died during the follow-up period; 10 of 62 patients died from other diseases. There were no differences in clinicopathological parameters according to sex.

TABLE 1 The clinicopathological factors of all analyzed patients

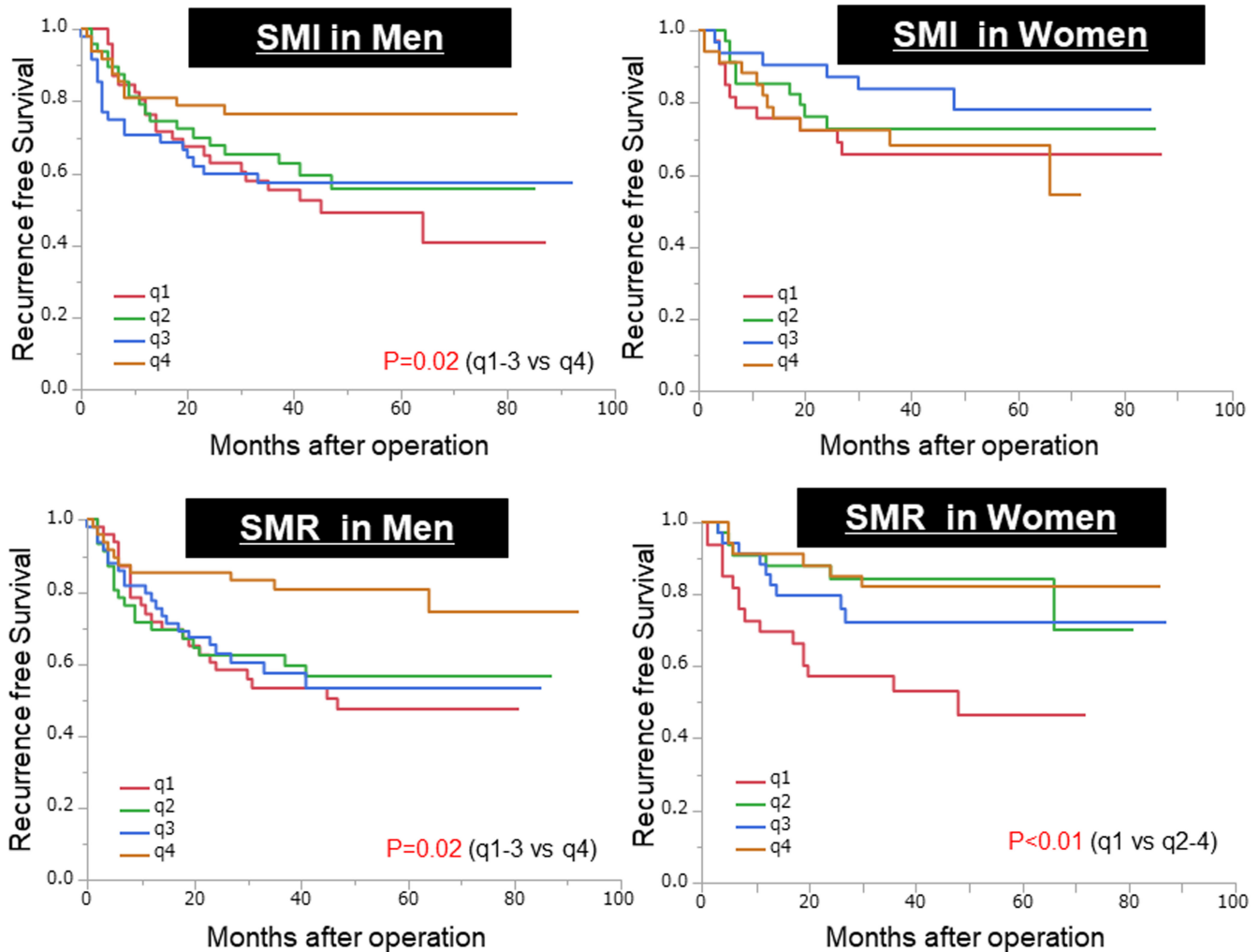|		Total	Men	Women	P value
Sex	Men	200 (58.7%)			
	Women	141 (41.3%)			
Age	70<	188 (55.1%)	109 (54.5%)	79 (56.0%)	.83
	70≧	153 (44.9%)	91 (45.5%)	62 (44.0%)	
CEA	Low	208 (62.3%)	121 (61.7%)	87 (63.0%)	.67
	High	126 (37.7%)	75 (38.3%)	51 (37.0%)	
CA19-9	Low	257 (77.2%)	158 (80.6%)	99 (72.3%)	.11
	High	76 (22.8%)	38 (19.4%)	38 (27.7%)	
Tumor location	Colon	258 (75.7%)	147 (73.5%)	111 (78.7%)	.25
	Rectum	83 (24.3%)	53 (26.5%)	30 (21.3%)	
T factor	T1	31 (9.1%)	17 (8.6%)	14 (9.9%)	.72
	T2	36 (10.6%)	19 (9.6%)	17 (12.1%)	
	T3	164 (48.4%)	101 (51.0%)	63 (44.7%)	
	T4	108 (31.9%)	61 (30.8%)	47 (33.3%)	
N factor	N1	234 (68.6%)	140 (70.0%)	94 (66.7%)	.82
	N2	95 (27.9%)	53 (26.5%)	42 (29.8%)	
	N3	12 (3.5%)	7 (3.5%)	5 (3.5%)	
Stage	3a	58 (17.0%)	35 (17.5%)	23 (16.3%)	.74
	3b	210 (61.6%)	120 (60.0%)	90 (63.8%)	
	3c	73 (21.4%)	45 (22.5%)	28 (19.9%)	
Adjuvant chemotherapy	Yes	236 (69.2%)	140 (70.0%)	96 (68.1%)	.74
	No	105 (30.8%)	60 (30.0%)	45 (31.9%)	
Recurrence	Yes	99 (29.4%)	63 (31.8%)	36 (25.9%)	.22
	No	238 (70.6%)	135 (68.2%)	103 (74.1%)	

FIGURE 1 Kaplan–Meier curves for recurrence-free survival according to quartiles (Q1–Q4) of skeletal muscle index (SMI) or skeletal muscle radiodensity (SMR) in men and women patients. Q1 shows the lowest SMI or SMR and Q4 shows the highest SMI or SMR

3.2 | Distribution of SMI and SMR in men and women

The distribution of SMI and SMR in men and women is shown in Figure S1. The median SMI in men and women were 46.2 and 36.1, respectively, and the median SMRs were 32.4 and 26.7, respectively. The SMI and SMR were significantly different between sexes (P < .0001).

3.3 | Analysis of SMI and SMR as prognostic factors

Patients were divided into quartiles based on the SMI (Q1 [men: 31.7-41.6, n = 50; women: 24.8-33.3, n = 36], Q2 [men: 41.6–46.1, n = 50; women: 33.4–36.1, n = 35], Q3 [men: 46.1-51.6, n = 50; women: 36.1–40.0, n = 35], and Q4 [men: 51.6-71.8, n = 50; women: 40.0–52.9, n = 35]) and SMR (Q1 [men: 6.95–27.5, n = 50; women: 1.4–21.9, n = 36], Q2 [men; 27.5–32.4, n = 50; women: 22.0–26.7, n = 35], Q3 [men: 32.4–35.9, n = 50; women: 26.7–32.1, n = 35], and Q4 [men: 35.9–44.7, n = 50; women: 32.1–42.5, n = 35]).

Kaplan–Meier curves for RFS according to SMI or SMR in both sexes are shown in Figure 1. In men, the Q4 SMI and Q4 SMR groups showed significantly improved RFS than Q1–3 SMI and SMR (P = .03 and .005, respectively). In women, the Q2-4 SMR group showed significantly better RFS than the Q1 SMR group (P = .0009). There seemed to be no association between SMI and RFS in women. Kaplan–Meier curves for OS according to SMI and SMR are shown in Figure 2. Similar to RFS, the men Q4 group in SMI and SMR and the Women Q2–4 group in SMR showed better prognosis.

3.4 | Univariate and multivariate analyses for the determination of independent prognostic factors for RFS

We then determined the cutoff value of SMI and SMR for recurrence using an ROC curve. The cutoff values of SMI in men and women were 48.5 and 41.4, respectively, and the area under the curve (AUC) was 0.61 and 0.49, respectively. Similarly, the cutoff values of SMR in men and women were 35.0 and 21.7, respectively (AUC was 0.62
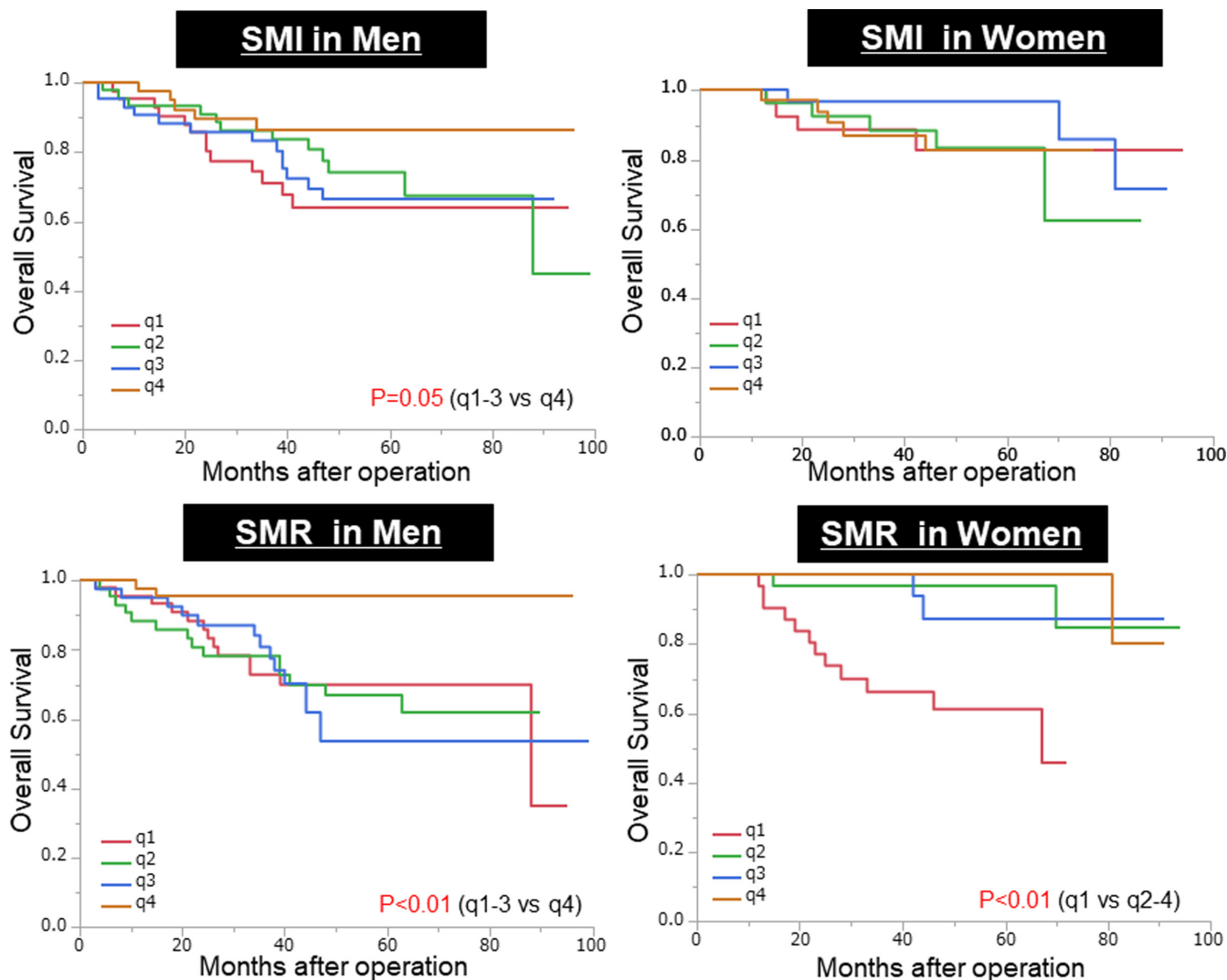
FIGURE 2 Kaplan–Meier curves for overall survival according to quartiles (Q1–Q4) of skeletal muscle index (SMI) or skeletal muscle radiodensity (SMR) in men and women patients. Q1 shows the lowest SMI or SMR and Q4 shows the highest SMI or SMR

and 0.62, respectively) (Figure S2). Using these cutoff values, we divided the patients into two groups (low SMI or SMR group and high SMI or SMR group), and performed a log-rank test according to the RFS. Except for women with SMI, significant differences in RFS were observed (Figure 3). The low SMI group with men (P = .0020) and the low SMR groups with men (P = .003) and women (P = .0005) showed significantly lower RFS than the high SMI or SMR group. The SMI and SMR in men and SMR in women could be candidates for further multivariate analysis for RFS. We then performed multivariate analysis for determining independent prognostic factors for RFS using Cox's proportional hazards regression model. The candidates of prognostic factors were determined using univariate analysis for RFS. The clinicopathological parameters for univariate analysis were age, tumor location, pathological stage, administration of adjuvant chemotherapy, SMI, and SMR. The analysis was performed independently in men and women. In univariate analysis in men, age, tumor location, stage, administration of adjuvant chemotherapy, SMI, and SMR were observed to be significant factors for RFS. Multivariate analysis showed

that stage, administration of adjuvant chemotherapy, and SMI were the independent prognostic factors (Table 2). In univariate analysis in women, stage, administration of adjuvant chemotherapy, and SMR were shown to be potential prognostic factors for RFS. Multivariate analysis showed that stage and SMR were significant prognostic factors for RFS (Table 3). We also assessed the correlation between the continuation and SMI or SMR. There was no correlation between therapeutic discontinuation and SMI or SMR status (Table S1). Based on these results, the SMI in men and SMR in women were considered to be independent prognostic factors for RFS.

3.5 | Association between skeletal muscle change and clinicopathological factors

Based on the above-mentioned results, we compared the clinicopathological factors between the two groups, which were divided on the basis of a cutoff value of SMI in men or SMR in women (Table 4).
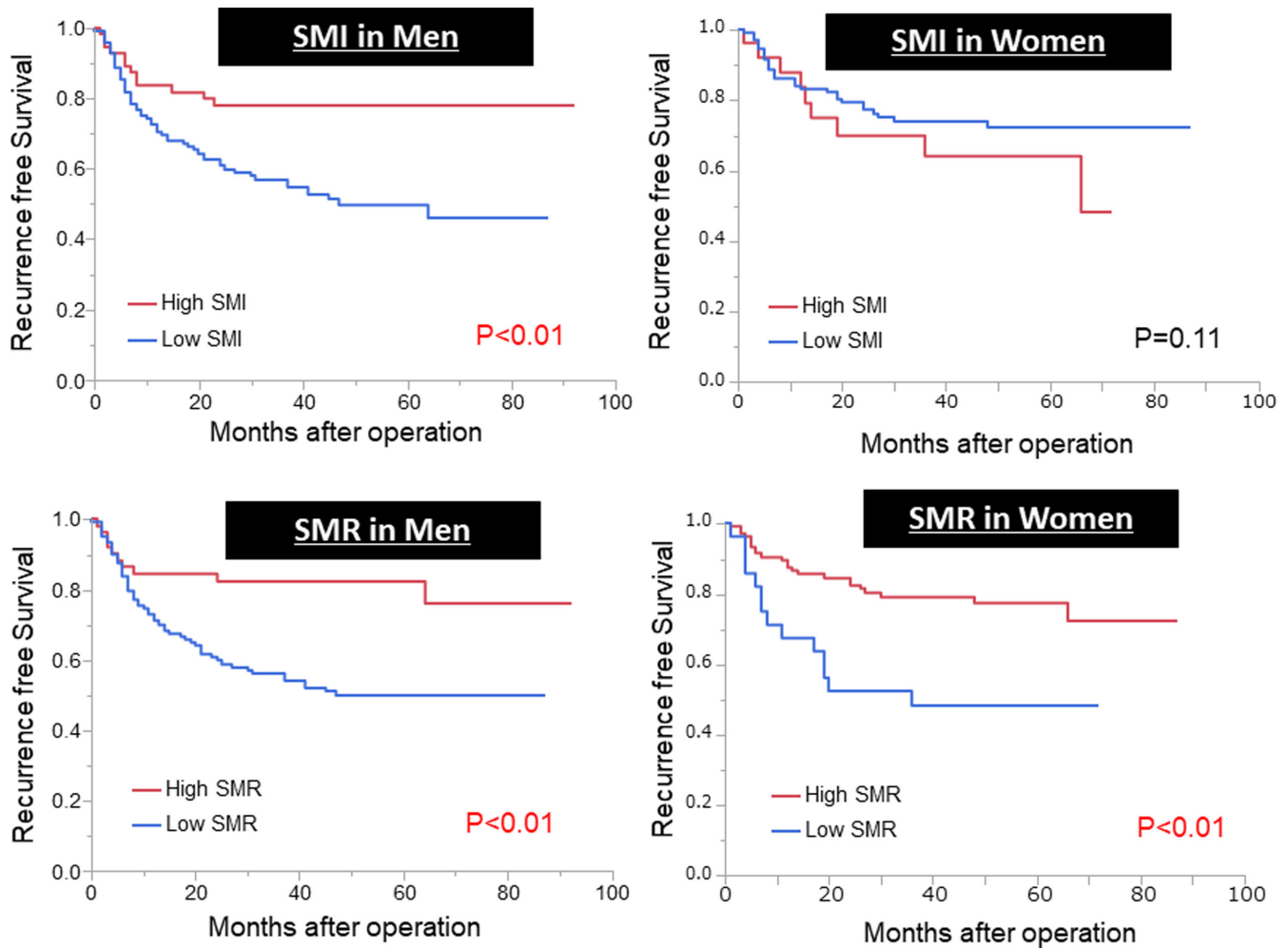
FIGURE 3 Kaplan–Meier curves for recurrence-free survival according to skeletal muscle index (SMI) or skeletal muscle radiodensity (SMR) in men and women patients divided by the optimal cutoff values

In both men and women, low SMI or SMR in patients were significantly associated with their age ($P = .03$, $P < .0001$, respectively). In addition, the number of patients with high serum CEA levels were significantly higher in the low SMI group with men patients ($P = .02$). In women, the administration of adjuvant chemotherapy was significantly decreased in the low SMR group ($P = .0003$).

3.6 | Subanalysis regarding RFS according to the changes in the skeletal muscles and administration of adjuvant chemotherapy

To assess the effect of the SMI/SMR and adjuvant chemotherapy on prognosis, we performed a subanalysis regarding RFS, according to the SMI/SMR and adjuvant chemotherapy status. The Kaplan–Meier curve is shown in Figure 4. In women, regardless of the administration of adjuvant chemotherapy, the low SMR group showed poor prognosis. On the other hand, in men, although the statistical analysis was not done, the prognosis of patients with adjuvant chemotherapy was better than without chemotherapy. Among them (either

with or without chemotherapy), the patients with high SMI showed a better prognosis than low SMI patients.

4 | DISCUSSION

In this study, after the analysis of preoperative CT images, we demonstrated that skeletal muscle changes, such as the SMI in men and SMR in women, are important prognostic factors in patients with stage III CRC. We proceeded to conduct all the analyses independently in men and women because an obvious sex difference was seen with regard to the SMI and SMR. After the classification of all patients into quartiles based on the values of SMI and SMR, the differences in RFS and OS were clearly observed. Men in the Q1–3 SMI or SMR groups and women in the Q1 SMR group showed a significantly poor prognosis. We then hypothesized that the optimal cutoff value that could distinguish the prognosis of patients could be calculated using an ROC curve. Using these values, low SMI in men and low SMR in women were shown to be poor prognostic factors in a multivariate analysis.

TABLE 2 Univariate analysis and multivariate analysis for recurrence-free survival in men

Men		Univariate analysis		Multivariate analysis	
		HR	P value	HR	P value
Age (<70)	H	1.52 (1.05–2.22)	.03	1.15 (0.70–1.90)	.58
	L	1		1	
Tumor location	Colon	1		1	
	Rectum	1.66 (1.11–2.46)	.02	1.25 (0.49–1.33)	.38
Stage	3a	1		1	
	3b	2.81 (1.44–6.33)	< .01	2.39 (1.10–6.27)	.03
	3c	3.82 (1.84–8.96)	< .01	3.80 (1.62–10.39)	.01
Adjuvant chemotherapy	No	3.00 (2.01–4.36)	< .01	3.18 (1.93–5.25)	<.01
	Yes	1		1	
SMI	Low	2.38 (1.38–4.35)	< .01	1.87 (1.08–3.47)	.03
	High	1		1	
SMR	Low	2.37 (1.35–4.53)	< .01	1.47 (0.79–2.93)	.23
	High	1		1	

Abbreviations: SMI, skeletal muscle index; SMR: skeletal muscle radiodensity.

TABLE 3 Univariate analysis and multivariate analysis for recurrence-free survival in women

Women		Univariate analysis		Multivariate analysis	
		HR	P value	HR	P value
Age (<70)	H	1.02 (0.53–2.00)	.95		
	L	1			
Tumor location	Colon	1			
	Rectum	1.70 (0.80–3.36)	.15		
Stage	3a	1		1	
	3b	3.79 (1.13–23.52)	.03	3.89 (1.16–24.13)	.02
	3c	3.89 (1.00–25.56)	.05	4.36 (1.12–28.73)	.03
Adjuvant chemotherapy	No	2.01 (1.02–3.86)	.04	1.67 (0.81–3.33)	.16
	Yes	1		1	
SMI	Low	0.68 (0.34–1.54)	.34		
	High	1			
SMR	Low	2.87 (1.47–5.48)	< .01	2.49 (1.21–4.95)	.01
	High	1		1	

Abbreviations: SMI, skeletal muscle index; SMR, skeletal muscle radiodensity.

In other studies that showed SMI as a prognostic factor in CRC, Choi et al and Malietzis et al used a cutoff value of 52.4 in men and 38.5 in women.[5,8] This value was derived from the study by Prado et al,[3] which proved that myopenia was a poor prognostic factor in obese patients (BMI >30), which consisted of 15% of the patients analyzed. On the contrary, in the patient cohort of the present study, only 4.1% of the patients had a BMI >30. In addition, although the data are not shown, the ratio of obese patients (BMI >30) in our hospital who received primary tumor resection of CRC in 2010–2018 was 3.7%. The ratio of obese patients may be smaller than that of Westerners in Japan; therefore, this cutoff value was not appropriate to use. On the other hand, Charette et al and Aro et al used the cutoff value that was described in the study by Martin et al.[4,11,13] According to the report by Martin

et al, in men the threshold SMI value of patients with BMI <25 was 43 and those with BMI ≥25 was 53; however, in women it was 41, regardless of BMI. As for the SMR, the threshold value of SMR was 41 in patients with BMI <25 and 33 in patients with BMI ≥25, regardless of sex. Using this value, the ratio of patients who were classified as having low SMI or SMR was 41% and 53%, respectively. However, if we applied this cutoff value to our study cohort, patients with low SMI and SMR were 58% and 90%, respectively, of all the patients; hence, these cutoff values were too high to be set for our study cohort. This discrepancy may be due to the differences in the distribution of BMI in the patients analyzed. In the studies by Martin et al, BMI distribution was 17% in obese (BMI ≥30), 35% in overweight (30> BMI 25≥), 36% in normal weight (25 >BMI ≥20), and 12% in underweight (BMI >20). In

TABLE 4 Association between the clinicopathological factors and the patient group divided by the cutoff values

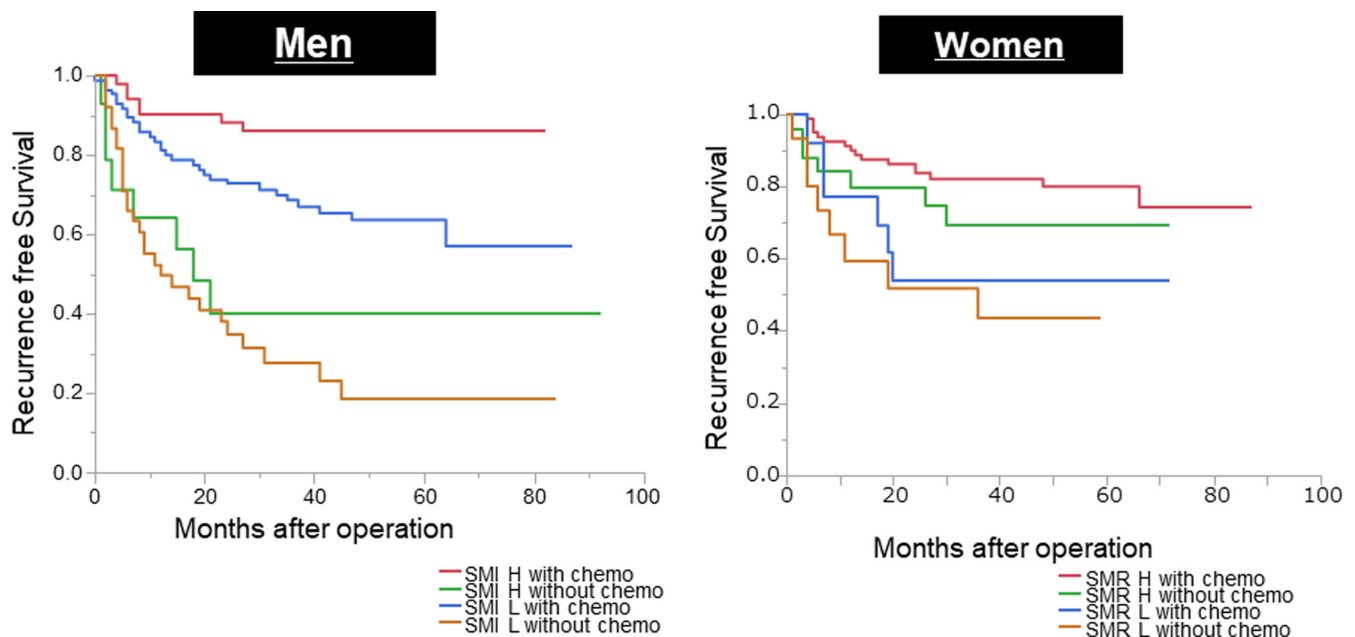|		Men			Women		
		SMI low	SMI high	P value	SMR low	SMR high	P value
Age <70	H	66 (51.2%)	25 (35.2%)	.03	28 (73.7%)	35 (33.7%)	<.01
	L	63 (48.8%)	46 (64.8%)		10 (26.3%)	69 (66.3%)	
CEA	H	56 (44.4%)	19 (27.1%)	.02	13 (35.1%)	37 (36.3%)	.90
	L	70 (55.6%)	51 (72.9%)		24 (64.9%)	65 (63.7%)	
CA19-9	H	26 (20.6%)	12 (17.1%)	.56	10 (27.0%)	27 (26.7%)	.97
	L	100 (79.4%)	58 (82.9%)		27 (73.0%)	74 (73.3%)	
Tumor location	Colon	94 (72.9%)	53 (74.7%)	.78	29 (76.3%)	83 (79.8%)	.65
	Rectum	35 (27.1%)	18 (25.3%)		9 (23.7%)	21 (20.2%)	
T factor	T1	9 (7.0%)	8 (11.4%)	.40	4 (10.5%)	10 (9.6%)	.83
	T2	11 (8.6%)	8 (11.4%)		3 (7.9%)	14 (13.5%)	
	T3	64 (50.0%)	37 (52.9%)		18 (47.4%)	46 (44.2%)	
	T4	44 (34.4%)	17 (24.3%)		13 (34.2%)	34 (32.7%)	
N factor	N1	92 (71.3%)	48 (67.6%)	.48	25 (65.8%)	70 (67.3%)	.80
	N2	34 (26.4%)	19 (26.8%)		11 (29.0%)	31 (29.8%)	
	N3	3 (2.3%)	4 (5.6%)		2 (5.2%)	3 (2.9%)	
Stage	3a	19 (14.7%)	16 (22.5%)	.39	5 (13.2%)	18 (17.3%)	.83
	3b	80 (62.0%)	40 (56.3%)		25 (65.8%)	66 (63.5%)	
	3c	30 (23.3%)	15 (21.1%)		8 (21.0%)	20 (19.2%)	
Adjuvant chemotherapy	Yes	87 (67.4%)	53 (74.6%)	.28	18 (47.4%)	79 (76.0%)	<.01
	No	42 (32.6%)	18 (25.4%)		20 (52.6%)	25 (24.0%)	

FIGURE 4 Kaplan–Meier curves for recurrence-free survival according to the combination of adjuvant chemotherapy and skeletal muscle index (SMI) in men or skeletal muscle radiodensity (SMR) in women

the present study the ratios were 4%, 19%, 56%, and 20%, respectively. Obviously, the ratio of obese or overweight patients was lower in our study; therefore, this cutoff value was not suitable for our cohort.

In women, the SMI was not proven to be a predictor of recurrence; however, the SMR was a powerful predictor. The exact reason why SMI could be a prognostic factor only in men was unclear; however, if we assume that men with low SMI and women with low SMR

in our study experienced the muscle-wasting effect due to cancer, this difference in the phenotype resulting from the muscle-wasting effect based on sex could be explained. Because our study cohort had a relatively narrow range of patients (consisting of only patients with stage III CRC), the difference in the phenotype of skeletal muscle change based on the sex difference was clearly revealed. In fact, skeletal muscle gene expression for genes associated with cancer cachexia in patients differs between men and women.[21] In this study, atrophy-related genes (FOXO1) and muscle growth-related genes (AKT1 and MSTN) were higher in women and the expression of apoptosis-related genes (CASP9) was higher in men. Similar to our findings, Tokunaga et al reported the difference on the impact of the preoperative body composition between men and women.[9] In that study, the prognostic factors were SMI in men and visceral fat area in women. SMR was not calculated in that study. If we hypothesized that the decrease in SMR was caused by the replacement of skeletal muscle with fat tissue, the result of our study and Tokunaga et al's study may support the fact that the increase in the fat tissues in the body composition in women has a poor effect on prognosis.

This is the first study that focused only on patients with stage III CRC. In daily clinical practice, the performable therapy after radical excision is limited to adjuvant chemotherapy, which is performed in high-risk patients with stage II or stage III CRC. Moreover, the rate of patients who received adjuvant chemotherapy in our cohort was ~70%, and we believe that this is not far from the usual rate in Japanese high-volume centers, although we cannot present this with clear evidence. Not all patients are suitable for the induction of adjuvant chemotherapy because of their low performance status or comorbidity; therefore, an optimal method of patient selection is necessary. Considering how to use the indicator of skeletal muscle changes, such as SMI or SMR, is one of the effective ways to use them as the standards for the introduction of adjuvant chemotherapy. However, most of the previous studies have shown the prognostic value of myopenia or myosteatosis in patients with stage I–III CRC,[5-18,21-24] of which the range of the studied cohort was too broad. The results of our study demonstrated more detailed information on the prognosis of patients with stage III CRC. In our study, the prognosis of patients with skeletal muscle change without adjuvant therapy was similar to those with no skeletal muscle change with adjuvant chemotherapy. This result can be used for the decision of the introduction of adjuvant chemotherapy in patients with stage III CRC who underwent curative surgery, but had factors that lead to hesitation of the induction of adjuvant chemotherapy.

The limitation of our study is that it was a retrospective study performed at a single institute.

5 | CONCLUSION

We found that skeletal muscle change measured using preoperative CT could be a prognostic factor in patients with stage III CRC. Men with low SMI and women with low SMR showed a poor prognosis.

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