Original Article
Özgün Araştırma

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Relationship of Muscle Mass Based on Psoas Muscle Index and Skeletal Muscle Index with Recurrence and Mortality Risk in Localized Renal Cell Carcinoma: A Comprehensive Retrospective Analysis

Lokalize Renal Hücreli Karsinomu Olan Hastalarda Psoas Kas İndeksi ve İskelet Kas İndeksine Dayalı Kas Kütlesinin Nüks ve Mortalite Riski ile İlişkisi: Kapsamlı Bir Retrospektif Analiz

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ABSTRACT

Objective: We aimed to determine the relationship between the Psoas Muscle Index (PMI) and Skeletal Muscle Index (SMI) and the risk of recurrence and mortality in patients with localized Renal Cell Carcinoma (RCC).

Material and Methods: SMI and PMI values were obtained from non-contrast computed tomography (NCCT) measurements on slices at the L3 level, normalized by height. Available survival data, including overall survival (OS) and recurrence-free survival (RFS), were collected at postoperative follow-up. Disease recurrence was defined as radiological evidence of disease on computed tomography (CT), magnetic resonance imaging, or bone scan.

Results: In the ROC analysis, the optimal cut-off value for PMI was ≤ 5.1 cm^2/m^2 and ≤ 3.1 cm^2/m^2 in male and female patients, while the cut-off value for SMI was ≤ 44 cm^2/m^2 and ≤ 30 cm^2/m^2 in male and female patients. In multivariate analyses, female gender, recurrence, clinical T stage ≥ T3b, pathological T stage ≥T3b, and sarcopenia according to PMI and SMI were independent predictors of worse OS and RFS ($p < 0.001$). In Kaplan-Meier analysis, OS in patients with and without sarcopenia was 74 vs 85 months ($p < 0.001$), respectively. RFS were shorter in patients with sarcopenia (PMI: 76 vs 84, SMI: 74 vs 85 months, both $p < 0.001$)

Conclusion: In patients with localized RCC, sarcopenia was associated with earlier recurrence, shorter OS, and RFS. Patients with sarcopenia had a worse prognosis in preoperative staging.

Keywords: psoas muscle index, renal cell carcinoma, sarcopenia, skeletal muscle index

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ÖZET

Amaç: Lokalize Renal Hücreli Karsinomlu (RHK) hastalarda Psoas Kas İndeksi (PMI) ve İskelet Kas İndeksi (SMI) ile nüks ve mortalite riski arasındaki ilişkiyi belirlemeyi amaçladık.

Gereç ve Yöntemler: SMI ve PMI değerleri, L3 seviyesindeki kesitlerde kontrastsız bilgisayarlı tomografi (BT) ölçümlerinden elde edildi ve yüksekliğe göre normalize edildi. Genel sağkalım (OS) ve nükssüz sağkalım (RFS) dahil olmak üzere mevcut sağkalım verileri ameliyat sonrası takipte toplandı. Hastalık nüksü BT, manyetik rezonans görüntüleme veya kemik taramasında hastalığın radyografik kanıtı olarak tanımlanmıştır.

Bulgular: ROC analizinde, PMI için optimal kesim değeri sırasıyla erkek ve kadın hastalarda ≤ 5,1 cm^2/m^2 ve ≤ 3,1 cm^2/m^2 iken, SMI için kesim değeri erkek ve kadın hastalarda ≤ 44 cm^2/m^2 ve ≤ 30 cm^2/m^2 idi. Çok değişkenli analizlerde, kadın cinsiyet, nüks, klinik T evresi ≥ T3b, patolojik T evresi ≥T3b ve PMI ve SMI'ye göre sarkopeni daha kötü OS ve RFS'nin bağımsız belirleyicileriydi (p<0,001). Kaplan-Meier analizinde, sarkopenisi olan ve olmayan hastalarda OS sırasıyla 74 vs 85 ay saptandı (p<0,001). RFS sarkopenisi olan hastalarda daha kısaydı (PMI: 76 vs 84, SMI: 74 vs 85 ay, her ikisi de p<0,001)

Sonuç: Lokalize RHK'li hastalarda sarkopeni daha erken nüks, daha kısa OS ve RFS ile ilişkiliydi. Sarkopenisi olan hastalar preoperatif evrelemede daha kötü prognoza sahipti.

Anahtar Kelimeler: iskelet kası indeksi, psoas kas indeksi, renal hücreli karsinom, sarkopeni

INTRODUCTION

Partial nephrectomy (PN) or radical nephrectomy (RN) is a common surgical procedure for the treatment of localized renal cell carcinoma (RCC) (1). Despite its clinical efficacy, the presence of sarcopenia in patients with localized RCC has garnered increasing attention due to its potential influence on postoperative outcomes and long-term prognosis (2). Sarcopenia, defined by the progressive and generalized loss of skeletal muscle mass and strength, transcends the mere process of aging and is frequently concurrent with various chronic conditions, including malignancies (3).

Emerging evidence underscores the detrimental impact of sarcopenia on surgical outcomes, leading to a higher incidence of postoperative complications, prolonged hospitalization, and increased mortality (4). The association between sarcopenia and cancer recurrence further emphasizes the need for a comprehensive understanding and proactive management. Quantitative measures such as the Psoas Muscle Index (PMI) and the Skeletal Muscle Index (SMI) are used to assess sarcopenia (5).

This article aims to highlight the association between sarcopenia, as measured by PMI and SMI, and recurrence and mortality rates in patients with localized RCC.

MATERIALS AND METHODS

We conducted a retrospective cohort study using our hospital database, identifying 487 patients diagnosed with localized RHK and operated on between January 2010 and January 2019. This study was approved by our institutional ethical review committee (Decision No: 2024/07-14 Date: 19.08.2024). It was conducted in accordance with the Declaration of Helsinki on human subjects. In our study, we extracted detailed data on variables such as age, gender, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance status, American Society of Anesthesiologists (ASA) score, type of operation, laboratory findings, tumor location, tumor size, SMI, PMI values obtained from Non-Contrast Computer Tomography (NCCT), pathological findings, recurrence and mortality status. We also collected available survival data, including overall survival (OS) and recurrence-free survival (RFS) at postoperative follow-up. All cases were staged preoperatively by Contrast-Enhanced computed tomography (CT) of the chest and abdomen. The pathological stage was re-staged according to the 2009 Tumor Node Metastasis (TNM) staging system. Exclusion criteria were absence of axial CT within 30 days after surgery, evidence of metastatic disease during surgery, lack of BMI, patients with hereditary RCC, and patients with missing data.

The psoas muscle was defined as an oval-shaped muscle adjacent to the vertebral column in axial view and measured between approximately -20 and 100 Hounsfield units on CT imaging. PMI was calculated by measuring the psoas muscle's cross-sectional area at the third lumbar vertebra (L3) level and normalized for length using Philips iSite PACS Version 3.6.96.0 Image Viewer Technology (6). Regarding SMI, the total muscle area of the psoas, paraspinal, internal oblique, external oblique, rectus abdominis, and transversus abdominis muscles on both sides was calculated at the L3 level on the same imaging system and normalized for height (6).

Disease recurrence was defined as radiological evidence of disease on CT, magnetic resonance imaging, or bone scan. Recurrence was accepted as detecting a new mass at the operation area in the radiologic imaging, but the suspicious lesion was biopsied and classified as disease recurrence after pathologic confirmation.

Statistical Analysis

The distribution of continuous variables was assessed by the Shapiro-Wilk test. Continuous variables are presented as mean and standard deviation (*SD*). Categorical variables were presented as numbers and frequencies. An independent sample t-test or Mann-Whitney U-test was used to compare the continuous variables based on the distribution. The chi-square test (Pearson Chi-Square) was used to compare the categorical variables. Data analyses were performed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA). The analysis of the receiver operating characteristic (*ROC*) curve associated with the area under the curve (*AUC*) was used to determine the optimal cutoff values of different scoring indices for mortality. Each optimal cutoff value was chosen considering the highest sensitivity, reasonably high specificity, and positive and negative predictive values. *AUC* was interpreted as good if *AUC* = 0.8–1, moderate if *AUC* = 0.7–0.8, fair if *AUC* = 0.6–0.7, and poor if *AUC* = 0.5–0.6. An area under the curve analysis of scoring systems using the MedCalc (trial *version* 22.030) program was used. Univariable and multivariable analyses (MVAs) were performed with Cox proportional hazards models to evaluate the association of sarcopenia with OS and PFS using the stepwise backward Wald method. MVA models controlled for gender, laterality, Fuhrman grade, clinical T stage, and pathological T stage. Kaplan-Meier analysis was used to evaluate OS and PFS. Kaplan Meier and Cox proportional hazards models were obtained using R software (R Foundation for Statistical Computing, Vienna, Austria), survival, sura miner, and dplyr packages. A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

ROC analysis using gender-based sensitivities and specificities revealed that the optimal cut-off values for PMI should be ≤ 5.1 cm^2/m^2 and ≤ 3.1 cm^2/m^2 in male and female patients, respectively, while the cut-off value for SMI should be ≤ 44 cm^2/m^2 and ≤ 30 cm^2/m^2 in male and female patients, respectively. The AUC value for PMI-based assessment was 0.935 in men and 0.948 in women. The SMI-based evaluation showed lower AUC values. Sensitivities and specificities according to the optimum cut-off values are given in Table 1 and Figure 1.

Table 1. Cut-off values of the applied indexes by gender

Index/ Score	Cut-off value	AUC (%95 CI)	Sensitivity	Specificity	PPV	NPV	Accuracy
PMI	≤ 5.1(cm^2/m^2)	0.790 (0.75-0.82)	97.3	58.44	16.1	99.6	0.614 (0.60-0.62)
Male	≤ 5.1(cm^2/m^2)	0.935 (0.90-0.96)	96.3	80.92	29.5	99.6	0.821 (0.80-0.83)
Female	≤ 3.1(cm^2/m^2)	0.948 (0.90-0.98)	100	76.80	25.6	100	0.785 (0.75-0.78)
SMI	≤ 44 (cm^2/m^2)	0.821 (0.78-0.85)	100	61.33	17.5	100	0.643 (0.63-0.64)
Male	≤ 44 (cm^2/m^2)	0.853 (0.81-0.89)	100	69.85	21.6	100	0.722 (0.70-0.72)
Female	≤ 30 (cm^2/m^2)	0.844 (0.77-0.90)	70	86.40	29.2	97.3	0.852 (0.81-0.88)

AUC: area under the curve, *CI:* confidence interval, *PPV:* positive predictive value, *NPV:* negative predictive value

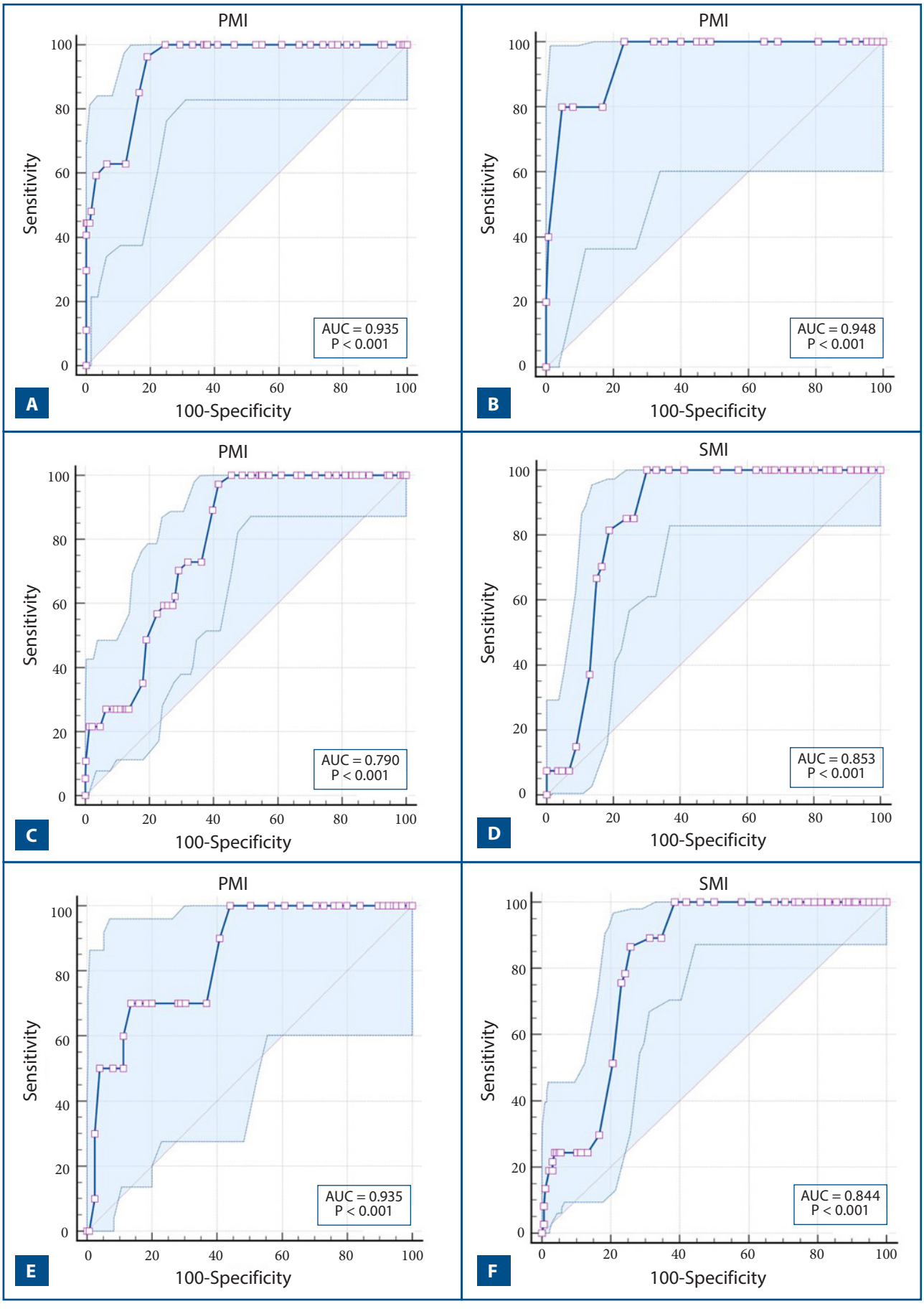

Figure 1. ROC Curve for PMI **A**-Male, **B**-Female, **C**-Total; ROC Curve for SMI **D**-Male, **E**-Female, **F**-Total

A total of 223 patients (45.7%) had sarcopenia when the PMI was used as the sarcopenia criterion, and 211 patients (43.3%) when the SMI was used. In the total cohort, the mean age of the patients was 58 years, and the gender was predominantly male (72.3%). The age of patients in the sarcopenia group was higher in both PMI- and SMI-based assessments (p<0.001). In gender distribution, the proportion of female patients was higher in patients with sarcopenia (p<0.001). ECOG performance score was higher in sarcopenic patients in PMI and SMI groups (PMI: p<0.001, SMI: p=0.035). Tumor sizes were statistically larger in sarcopenic patients, and the clinical and pathological T stages were more advanced in patients with sarcopenia (PMI: p=0.015, p=0.002; SMI: p=0.007, <0.001, respectively). Pathology findings did not show any difference between sarcopenia and histological type of tumor, but sarcopenic patients had a higher Fuhrmann Grade in both PMI and SMI groups (p<0.001). In addition, when patients were classified as lower stage (T1-2) and higher stage (T3-4), sarcopenic patients were found to have a higher T stage, and ≥T3 upstage was higher in sarcopenic patients (p<0.05). Higher recurrence and mortality rates were observed in patients with sarcopenia in PMI and SMI groups (p<0.001). No differences were observed in BMI, ASA score, laboratory parameters, laterality of the tumor, type of operation performed, and histological type of the tumor in patients with and without sarcopenia according to PMI and SMI criteria. Comparisons between sarcopenic and non-sarcopenic patients using PMI and SMI are shown in Table 2-3.

In multivariate analyses, female gender (OS: hazard ratio [HR] 2.33, 95% confidence interval [CI] 0.41-2.27, p<0.001; RFS: HR 1.31, %95 CI 0.43-2.32, p<0.001), Fuhrmann Grade 4 (OS: HR 1.85, 95% CI 0.45-3.60, p=0.002; RFS: HR 1.12, 95% CI 0.17-2.82, p=0.002), and sarcopenia according to PMI (OS: HR 1.86, %95 CI 0.57-3.48, p<0.001; RFS: HR 1.83, 95% CI 0.94-4.73, p<0.001) and SMI (OS: HR 1.79, %95 CI 0.71-2.92, p<0.001; RFS: HR 2.19, 95% CI 0.91-3.72, p<0.001) were independent predictors of worse OS and RFS. Also, recurrence, clinical T stage ≥ T3b and pathological T stage ≥T3b had a worse effect on OS and RFS (p<0.001) Multivariate analysis results are shown in Table 4.

In Kaplan-Meier analysis, OS in patients with and without sarcopenia was 74 vs 85 months (p<0.001), respectively. RFS were shorter in patients with sarcopenia (PMI: 76 vs 84, SMI: 74 vs 85 months, both p<0.001) (Figure 2-3). Furthermore, 5-year OS rates were 82% and 91% in patients with and without sarcopenia, respectively. 10-year OS rates were 72% and 86% in patients with and without sarcopenia. In terms of RFS, 5-year survival rates were 80% and 88% in patients with and without sarcopenia, while 10-year survival rates were 69% and 80% in patients with and without sarcopenia, respectively. OS, RFS, and survival rates are shown in Table 5.

Table 2. Comparison of demographic and laboratory data of sarcopenic and non-sarcopenic patients based on PMI and SMI as evaluation criteria

Characteristic	All patient (n=487)	PMI		p value	SMI		p value
		Nonsarcopenic (n=264)	Sarcopenic (n=223)		Nonsarcopenic (n=276)	Sarcopenic (n=211)	
Age (*years*) [x]	58.04±12.77	57.02±12.86	62.24±12.59	**<0.001**[*]	56.18±13.09	60.46±11.95	**<0.001**[*]
Age categorized (*years*)				0.286[+]			**<0.001**[+]
≤60	229 (47.0)	130 (49.2)	99 (44.4)		151 (54.7)[a]	78 (37.0)[b]	
>60	258 (53.0)	134 (50.8)	124 (55.6)		125 (45.3)[a]	133 (63.0)[b]	
Gender				**<0.001**[+]			**<0.001**[+]
Male	352 (72.3)	199 (75.3)[a]	153 (68.6)[b]		227 (82.2)[a]	125 (59.2)[b]	
Female	135 (27.7)	65 (24.7)[a]	70 (31.4)[b]		49 (17.8)[a]	86 (40.8)[b]	
BMI (kg/m^2) [x]	24.97±3.49	25.23±3.61	24.67±3.33		25.25±3.60	24.62±3.31	0.057[*]

BMI categorized (kg/m^2)				0.551[+]			0.101[+]
<25	208 (42.7)	116 (43.9)	92 (41.3)		109 (39.5)	99 (46.9)	
≥25	279 (57.3)	148 (56.1)	131 (58.7)		167 (60.5)	112 (53.1)	
Surgery type				0.051[+]			0.066[+]
Open RN	147 (30.2)	93 (35.2)	54 (24.2)		84 (30.4)	63 (29.9)	
Open PN	184 (37.8)	87 (33.0)	97 (43.5)		109 (39.5)	75 (35.5)	
Laparoscopic RN	69 (14.2)	38 (14.4)	31 (13.9)		45 (16.3)	24 (11.4)	
Laparoscopic PN	42 (8.6)	20 (7.6)	22 (9.9)		17 (6.2)	25 (11.8)	
Robotic RN	10 (2.1)	4 (1.5)	6 (2.7)		3 (1.1)	7 (3.3)	
Robotic PN	35 (7.2)	22 (8.3)	13 (5.8)		18 (6.5)	17 (8.1)	
Laterality				0.423[+]			0.786[+]
Right	232 (47.6)	137 (51.9)[a]	95 (42.6)[b]		130 (47.1)	102 (48.3)	
Left	255 (52.4)	127 (48.1)[a]	128 (57.4)[b]		146 (52.9)	109 (51.7)	
ECOG performance score				**<0.001**[+]			**0.035**[+]
0	345 (70.8)	215 (81.4)	130 (58.2)		206 (74.6)[a]	139 (65.9)[b]	
>1	142 (29.2)	49 (18.6)	93 (41.8)		70 (25.4)[a]	72 (34.1)[b]	
ASA				0.451[+]			0.174[+]
1	44 (9.0)	23 (8.7)	21 (9.4)		30 (10.9)	14 (6.6)	
2	327 (67.1)	176 (66.7)	151 (67.7)		181 (65.6)	146 (69.2)	
3	113 (23.2)	62 (23.5)	51 (22.9)		62 (22.5)	51 (24.2)	
4	3 (0.6)	3 (1.1)	0 (0.0)		3 (1.1)	0 (0.0)	
Neutrophil	5.22±2.11	5.23±1.91	5.21±2.33	0.542[*]	5.15±2.11	5.30±2.12	0.430[*]
Lymphocyte	2.98±12.15	3.48±2.07	3.14±17.83	0.305[*]	3.47±16.11	2.93±1.17	0.216[*]
Platelet	270.17±83.47	268.21±78.81	272.49±88.80	0.503[*]	262.45±75.36	280.27±92.23	0.148[*]
NLR	2.69±2.35	2.41±1.70	3.02±2.91	0.111[*]	2.65±2.60	2.74±1.98	0.079[*]
PLR	143.01±147.98	130.53±141.65	157.77±154.17	0.147[*]	145.32±187.49	139.98±68.07	0.395[*]
AST	21.29±10.27	21.10±10.54	21.52±9.96	0.960[*]	20.87±10.19	21.84±10.37	0.720[*]
ALT	22.29±16.75	22.11±18.16	22.49±14.94	0.828[*]	21.82±16.41	22.89±17.19	0.923[*]
AST/ALT	1.11±0.40	1.10±0.38	1.12±0.43	0.969[*]	1.10±0.39	1.13±0.43	0.657[*]

[x]Mean±SD [*] Mann Whitney *U* test, [+] Pearson Chi-Square test. *NLR* Neutrophil Lymphocyte ratio, *PLR* Platelet Lymphocyte ratio

Table 3. Comparison of radiologic, pathologic, and follow-up results of sarcopenic and non-sarcopenic patients using PMI and SMI as evaluation criteria

Characteristic	All patient (n=487)	PMI		p value	SMI		p value
		Nonsarcopenic (n=264)	Sarcopenic (n=223)		Nonsarcopenic (n=276)	Sarcopenic (n=211)	
Clinical T-stage				**0.015**[+]			**0.007**[+]
T1a	241 (49.5)	128 (48.4)	113 (50.6)		137 (49.6)	104 (49.3)	
T1b	127 (26.1)	80 (30.3)	47 (21.1)		77 (27.9)	50 (23.7)	
T2a	59 (12.1)	30 (11.3)	29 (13)		39 (14.1)	20 (9.5)	
T2b	43 (8.8)	20 (7.5)	33 (14.7)		20 (7.2)	23 (10.9)	
T3a	13 (2.7)	6 (2.2)	7 (3.1)		3 (1.1)	10 (4.7)	
T3b	4 (0.8)	0 (0.0)	4 (1.8)		0 (0.0)	4 (1.9)	
Pathological T-stage				**0.002**[+]			**<0.001**[+]
T1a	225 (46.2)	113 (42.8)	112 (50.2)		131 (47.5)	94 (44.5)	
T1b	114 (23.4)	77 (29.2)	37 (16.6)		75 (27.2)	30 (14.2)	
T2a	42 (8.6)	27 (10.2)	15 (6.7)		34 (12.3)	12 (5.7)	
T2b	25 (5.1)	15 (5.7)	10 (4.5)		14 (5.1)	16 (7.5)	
T3a	72 (14.8)	29 (11.0)	43 (19.3)		21 (7.6)	51 (24.2)	
T3b	5 (1.0)	1 (0.4)	4 (1.8)		1 (0.4)	4 (1.9)	
T4	4 (0.8)	2 (0.8)	2 (0.9)		0 (0.0)	4 (1.9)	
Tumor size	54.29±29.38	52.51±27.13	64.40±31.77	**<0.001**[+]	50.55±25.39	59.17±33.32	**0.017**[*]
Histological type							
Clear cell	395 (81.1)	220 (83.3)	175 (78.5)		219 (79.3)	176 (83.4)	
Papillary	48 (9.9)	26 (9.8)	22 (9.9)	0.155[+]	29 (10.5)	19 (9.0)	0.663[+]
Chromophobe	24 (4.9)	12 (4.5)	12 (5.4)		16 (5.8)	8 (3.8)	
Others	20 (4.1)	6 (2.3)	14 (6.3)		12 (4.3)	8 (3.8)	
Fuhrman grade							
I	27 (5.8)	15 (5.9)	12 (5.7) [a]108		21 (8.0)	6 (3.0)	
II	252 (54.3)	144 (56.9)	(51.2)	**<0.001**[+]	159 (60.9)	93 (45.8)	**<0.001**[+]
III	97 (20.9)	63 (24.9)	34 (16.1)		54 (20.7)	43 (21.2)	
IV	88 (19.0)	31 (12.3)	57 (27.0)		27 (10.3)	61 (30.0)	
Positive Surgical Margin	37 (9.7)	20 (7.6)	17 (7.7)	0.825[+]	18 (10.9)	19 (9.1)	0.772[+]
T Stage				**0.022**[+]			**<0.001**[+]
T 1-2	403 (82.8)	228 (86.4)	175 (78.5)		248 (89.9)	155 (73.5)	
T 3-4	84 (17.2)	36 (13.6)	48 (21.5)		28 (10.1)	56 (26.5)	
≥T3 upstage	77 (15.8)	39 (14.8)	58 (26.0)	**<0.001**[+]	31 (11.2)	46 (21.8)	**0.002**[+]
Recurrence				**<0.001**[+]			**<0.001**[+]
No	421 (86.4)	244 (92.4)	177 (79.3)		262 (94.9)	159 (75.4)	
Yes	66 (13.6)	20 (7.6)	46 (20.7)		14 (5.1)	52 (24.6)	
Mortality				**<0.001**[+]			**<0.001**[+]
No	450 (92.4)	263 (99.6)	187 (83.9)		274 (99.2)	176 (83.4)	
Yes	37 (7.6)	1 (0.4)	36 (16.1)		2 (0.7)	35 (16.6)	
Recurrence time (*months*)[x]	26.12±7.80	28.73±7.40	23.94±7.54	**0.012**[++]	29.42±4.96	25.23±8.21	**0.022**[++]
Follow-up period (*months*)[x]	113.8±40.10	117.3±44.9	109.9±42.5	**0.411**	112.8±41	115.6±38.3	**0.319**

[x] *Mean±SD, n* (%) [*] Mann Whitney *U* test, [+] Pearson Chi-Square test, [++] Independent samples *t* test.

Table 4. Multivariable Analysis of Sarcopenia for Overall Survival and Recurrence-Free Survival After Surgery

	Overall Survival		Recurrence Free Survival	
	HR (%95 CI)	**p value**	**HR (%95 CI)**	**p value**
Gender				
Male	1 (reference)		1 (reference)	**<0.001**
Female	1.33 (0.41-2.27)	**<0.001**	1.31 (0.43-2.32)	
Fuhrman grade				
IV	1.85 (0.45-.60)	**0.002**	1.12 (0.17-3.82)	**0.002**
Clinical T-stage				
T3b	1.45 (0.70-2.74)	**<0.001**	1.6 (0.81-3.15)	**<0.001**
T4	1.46 (0.54-2.02)	**<0.001**	1.68 (0.81-3.24)	**<0.001**
Pathological T-stage				
T3b	0.03 (0.01-0.12)	**<0.001**	0.03 (0.01-0.12)	**<0.001**
T4	0.07 (0.02-0.23)	**<0.001**	0.08 (0.02-0.23)	**<0.001**
Sarcopenia, PMI	1.86 (0.57-3.48)	**<0.001**	1.83 (0.94-4.73)	**<0.001**
Sarcopenia, SMI	1.79 (0.71-2.92)	**<0.001**	2.19 (0.91-3.72)	**<0.001**
Recurrence	2.18 (0.70-4.24)	**<0.001**	2.20 (0.6-4.41)	**<0.001**

Table 5. 5 and 10-year Overall and Recurrence Free survival rates, standard errors, and 95% confidence intervals

	Groups	**Survival Rate (*SE*)**	**(95%*CI*)**
OS	**5-year survival**		
	Nonsarcopenic	0.912 (0.012)	0.937-0.984
	Sarcopenic	0.829 (0.025)	0.797-0.895
	10-years survival		
	Nonsarcopenic	0.865 (0.019)	0.789-0.964
	Sarcopenic	0.721 (0.028)	0.658-0.817
RFS	**5-year survival**		
	Nonsarcopenic	0.888 (0.012)	0.814-0.953
	Sarcopenic	0.809 (0.026)	0.690-0.891
	10-years survival		
	Nonsarcopenic	0.801 (0.020)	0.703-0.912
	Sarcopenic	0.691 (0.031)	0.613-0.834

SE: Standard Error, CI: Confidence Interval

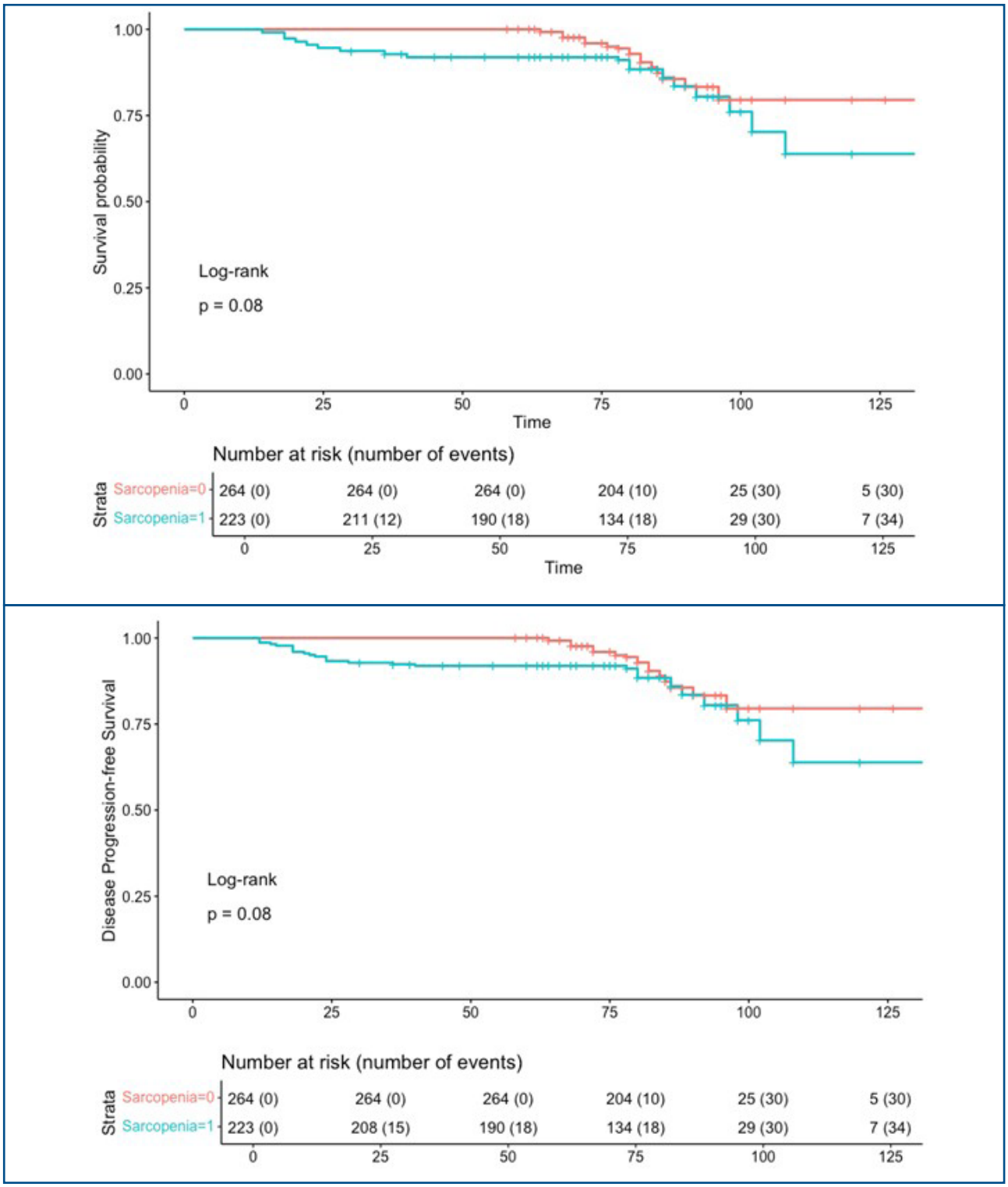

Figure 2. Kaplan-Meier analyses showing OS (A) and RFS (B) in patients with and without sarcopenia in PMI-based assessment

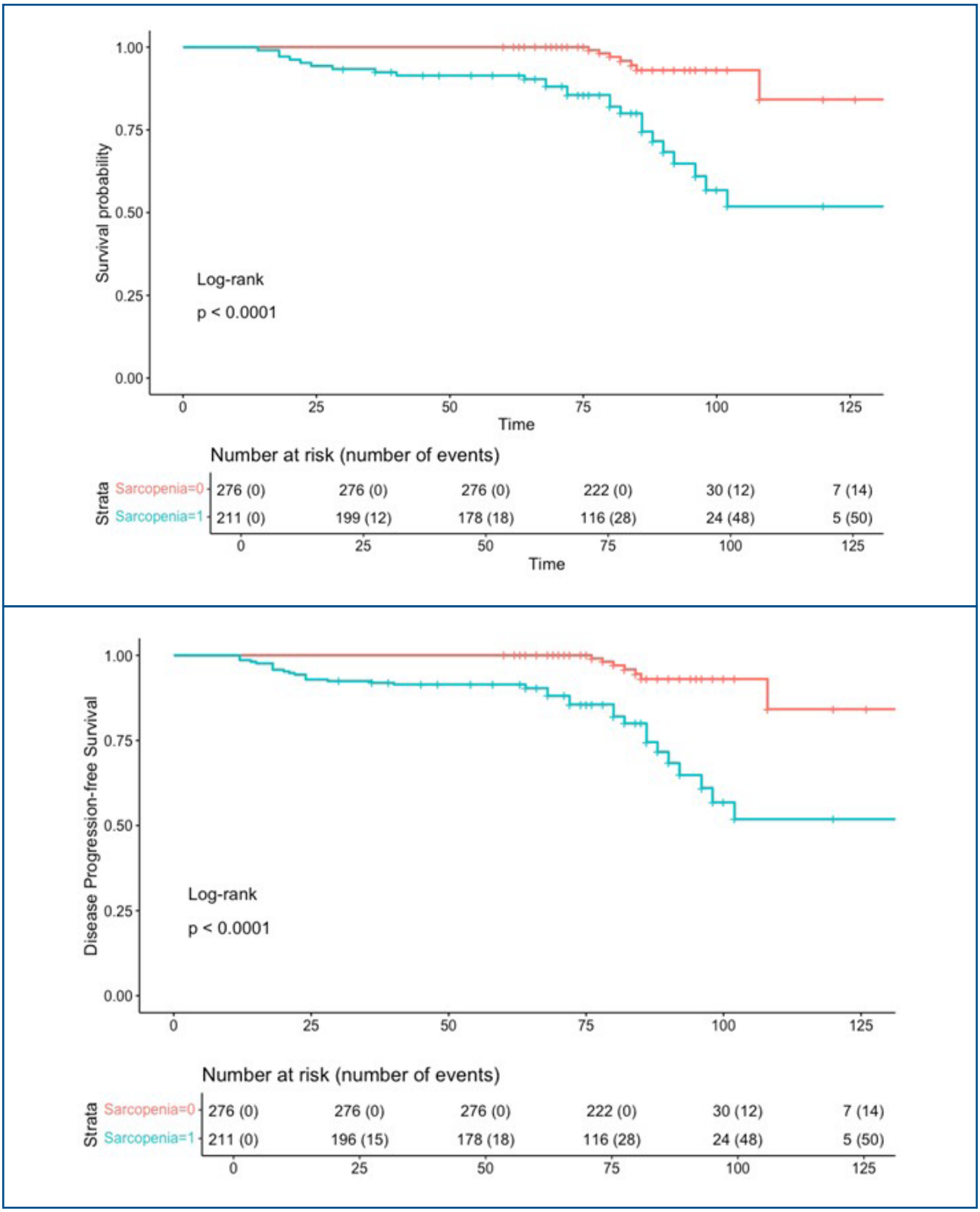

Figure 3. Kaplan-Meier analyses showing OS (A) and RFS (B) in patients with and without sarcopenia in SMI-based assessment

DISCUSSION

This study evaluates the association of preoperative PMI and SMI used to evaluate sarcopenia with recurrence and mortality in localized RCC patients undergoing PN and RN. We showed that patients with lower PMI and SMI had shorter OS and RFS. The results showed that sarcopenia is an independent risk factor for recurrence and mortality in RCC patients.

Sarcopenia, which is characterized by loss of skeletal muscle mass and function, has emerged as an important prognostic factor in oncology, including RCC patients (7). Sarcopenia is increasingly recognized as a predictor of adverse outcomes in cancer patients (8). PMI and SMI are specific measurements used to evaluate sarcopenia. Although some values have been determined for these measurements in the literature, we determined cut-off values for PMI and SMI by ROC analysis, as sarcopenia status is affected by patient age, BMI, and height. In the evaluation of sarcopenia in terms of PMI, the lowest values in the literature are 3.2 cm^2/m^2 for men and 2.6 cm^2/m^2 for females, while the highest values are 8.4 cm^2/m^2 for men and 8.04 cm^2/m^2 for females (3,9). In terms of SMI, the lowest values were 40 cm^2/m^2 for men and 30 cm^2/m^2 for females, while the highest values were 55 cm^2/m^2 for men and 41 cm^2/m^2 for females (10-11). Other studies have different values for PMI and SMI, and no standardization has been obtained yet (12-22). In our study, the cut-off value for PMI was 5.1 cm^2/m^2in males and 3.1 cm^2/m^2in females, and the cut-off value for SMI was ≤ 44 cm^2/m^2 in males and ≤ 30 cm^2/m^2 in females. In our study, 45.7% of the patients were sarcopenic according to PMI and 43.3% according to SMI.

Sarcopenic patients have been found to have higher T stages for RCC, but some studies did not find significant results (5,17,18). In addition, Fuhrman grades, which indicate more aggressive and poorly differentiated tumors, may be associated with an increased incidence of sarcopenia in patients. Mokina et al. found lower PMI values in patients with higher T stages (17). Mao et al. found a relationship between sarcopenia and higher T stage in terms of PMI, but not between SMI and T stage (5). Noguchi et al. reported that there was no relationship between PMI and T stage (18). Our study found higher T stages and higher Fuhrmann grades in patients with lower PMI and SMI. More accurate information about the prognosis can be given to patients by evaluating the T stage and sarcopenia status of the patients in the preoperative period.

The relationship between PMI and SMI and recurrence and mortality in patients with localized renal cancer is of significant clinical interest (5,7,15,16,18-22). Studies have shown increased cancer recurrence rates and decreased survival rates in renal cancer patients with low SMI, but studies on PMI are limited (5,7,15,16,18-22). In a study by Noguchi et al. with 316 male patients, they found shorter RFS in patients with low PMI but did not detect any difference in terms of OS (18). Psutka et al. reported that sarcopenia was independently associated with OS after RN regarding the prognosis of RCC localized with SMI (7). However, it was not found to be associated with RFS. Lee et al. found that low SMI was an independent risk factor for postoperative all-cause and cancer-specific mortality in patients who underwent RN between 2004 and 2014 in a series of 632 patients (15). Higgins et al. found worse OS, cancer-specific survival, and RFS in patients with low SMI and found that sarcopenia was associated with an increased likelihood of recurrence and death (16). A meta-analysis showed that patients with sarcopenia had worse OS (HR = 1.76; 95% CI, 1.35-2.31; $P < 0.001$) (19). Some studies have not found a significant relationship between sarcopenia and survival in patients with RCC, but remarkably, patients with RCC are metastatic in studies on survival (20-22). Our study investigated OS and RFS in patients with and without sarcopenia based on PMI and SMI. Patients with lower PMI and SMI had shorter OS and RFS.

This study used high-quality cancer data to provide a better understanding of the impact of PMI and SMI on recurrence and prognosis in localized RCC patients. However, limitations of the study include its retrospective design, as it was conducted in a single center, and the small number of patients included in the oncological survival analysis. This increases the risk of selection bias in our study, and therefore, we cannot comment on whether the results apply to all postoperative RCC patients.

CONCLUSION

In conclusion, PMI and SMI are valuable measures to assess sarcopenia in kidney cancer patients, but they must be standardized. Our diagnostic ROC curves provide the literature with new cut-off values for diagnosing cancer sarcopenia with PMI and SMI. In localized RCC patients, sarcopenia was associated with earlier recurrence, shorter OS, and RFS. In addition, our study showed that patients with sarcopenia have a worse prognosis with preoperative staging.

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Research involving human participants: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Experimental-Informed Consent: Written informed consent was obtained from patients who participated in this study.

Ethics Approval: The study was approved by The University of Health Sciences, Izmir Tepecik Training and Research Hospital Ethical Committee, Izmir, Türkiye (Decision No: 2024/07-14 Date: 19.08.2024).

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