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The impact of nutritional status and changes of body composition on the prognosis of metastatic renal cell carcinoma patients

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Abstract : Purpose : This study aimed to analyze the impact of patients' nutritional status and changes in body composition on the prognosis of metastatic renal cell carcinoma (mRCC) patients who received systemic therapy with tyrosine kinase inhibitors (TKIs). Methods : A total of 57 mRCC patients who received systemic therapy with TKIs as first-line therapy at our facility between November 2004 and October 2018 were included. The Prognostic Nutritional Index (PNI) was used to evaluate their nutritional status. The volumes of skeletal muscle mass and fat tissue were calculated using the SYNAPSE VINCENT system. The effects of nutritional status and body composition of mRCC patients on progression-free survival (PFS) and overall survival (OS) were analyzed using Cox regression methods. Results : Low PNI at the start of systemic therapy was a significant prognostic predictor for OS (HR 3.807 [95% CI 1.205-12.027], P=0.046), and it was related to loss of muscle mass three months after systemic therapy. Although the loss of muscle mass at the start of systemic therapy was not associated with OS, loss of muscle mass during treatment predicted worse OS. Conclusions : Nutritional status of mRCC patients may predict changes in body composition and be associated with their prognosis. J. Med. Invest. 70 : 80-87, February, 2023

Keywords **:** *Renal cell carcinoma, Nutritional status, Body composition, Tyrosine kinase inhibitor*

INTRODUCTION

Systemic therapy for metastatic renal cell carcinoma (mRCC) has changed dramatically in recent years. Cancer immunotherapies targeting programmed death-1 (PD-1), programmed death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) are revolutionizing systemic therapy in mRCC (1-3). Tyrosine kinase inhibitors (TKIs) have long played a central role in sequential therapy for mRCC. TKIs still play important roles in first-line therapy as combination therapy with immune checkpoint inhibitors and in post-secondary treatment. It is crucial to select the systemic therapy not only based on oncological evaluation, but also with consideration of the patient's general status at the start of treatment. The International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk model has been widely accepted as a prognostic tool and used for treatment decisions when performing systemic therapy in mRCC (4), but it does not directly take into account factors related to nutritional status.

Assessment of nutritional status has been reported to be an important predictor of prognosis in a variety of cancer types (5). The Prognostic Nutritional Index (PNI), calculated based on the total lymphocyte count in peripheral blood and the serum albumin concentration, was initially proposed to estimate the perioperative nutritional status and surgical risk of patients undergoing gastrointestinal surgery (6). In fact, the PNI has been shown to be associated with the prognosis of various cancers (7, 8). The clinical significance and prognostic value of the PNI have also been reported in patients with mRCC treated with TKIs (9, 10).

In addition to nutritional status, the volume of patient skeletal muscle mass has also been thought to be associated with the prognosis of cancer patients. For instance, sarcopenia, loss of skeletal muscle mass, has been reported to have a negative impact on the prognosis of patients with advanced or metastatic cancers (11-15), including RCC (16, 17). In the treatment of mRCC, some reports have shown that sarcopenia was associated with increased adverse events (AEs) (18, 19) and decreased relative dose intensity (RDI) of TKIs (19). However, there are also several reports that muscle volume loss is not related to the incidence of AEs or RDI changes (16).

Thus, it has been shown that both nutritional indicators and loss of muscle mass may be involved in the prognosis of renal cancer, but the relationship between the two is unclear. It would be helpful for the selection of proper support during treatment if the mechanism by which poor nutritional status leads to a poor prognosis in mRCC patients could be clarified. In the present study, the associations between nutritional status and changes in body composition were examined, and the impacts of these factors on the prognosis of mRCC patients were assessed.

PATIENTS AND METHODS

Study Design and Patient Selection

A total of 63 mRCC patients received sunitinib or pazopanib therapy as first-line therapy without prior cytokine therapy at our hospital between November 2004 and October 2018. One patient was excluded due to lack of clinical data, and 5 patients

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were excluded due to immunotherapy in the subsequent treatment. Finally, 57 patients were analyzed retrospectively. Several variables at the time of diagnosis of mRCC were reviewed, including age, sex, body mass index (BMI), histopathology, prior nephrectomy, IMDC risk classification, skeletal muscle mass, albumin (Alb), C-reactive protein (CRP), and PNI. Other variables after 3 months of first-line therapy were also examined separately, including the tumor shrinkage rate, AEs, and changes of patient body composition parameters on computed tomography (CT). The Ethics Committee of Tokushima University Hospital approved this retrospective study (ID : 3867), which was performed in accordance with the tenets of the Declaration of Helsinki. The study was granted an exemption from requiring written, informed consent by the Ethics Committee.

Calculating the PNI Score

The PNI was calculated as 10 × Alb (g/dL)+0.005 × total lymphocyte count (/mm^3). The PNI was used in the present study with a cut-off value of 41 based on previous studies (6, 9).

Imaging Evaluation of Skeletal Muscle Mass Change and Defining Sarcopenia Categories

All patients underwent CT for diagnostic or follow-up purposes. Plain CT was performed at baseline (within 1 month before the start of therapy) and follow-up (after 2–3 months of treatment). For oncological evaluation, target lesions were selected based on the results of baseline imaging. Radiological response was evaluated according to the standard Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0. The early tumor shrinkage rate was assessed 3 months from the start of treatment.

The patient body composition parameters, skeletal muscle area, psoas muscle area, psoas muscle volume (PMV), subcutaneous fat area (SFA), and visceral fat area (VFA) were calculated by a single urologist using a 3-dimensional image analysis system, SYNAPSE VINCENT (FUJIFILM Healthcare Corporation, Tokyo, Japan) (Fig. 1). For skeletal muscle area, the cross-sectional area of the lumbar skeletal muscles, consisting of the rectus abdominus, internal, external, and lateral obliques, psoas, quadratus lumborum, and erector spinae on both sides, was identified. For psoas muscle area, only the psoas muscle was demarcated. To measure these parameters, the third lumbar vertebra (L3) was set as the landmark, and the mean value of three consecutive images was computed for each patient. Hounsfield unit (HU) thresholds were set for different tissues : -190 to -30 HU for subcutaneous fat tissue ; -150 to -50 HU for visceral fat tissue ; and -29 to 150 HU for skeletal muscle (16, 20).

The skeletal muscle index (SMI) and psoas muscle index (PMI) were each calculated as skeletal muscle area and psoas muscle area at the level of L3 divided by the square of the height and normalized. SMI and PMI were assessed as continuous variables and used as indicators of whole-body muscle mass, based on the finding of a previous study that the total lumbar-skeletal muscle cross-sectional area correlates linearly to whole-body muscle mass (21). Sarcopenia was defined according to the cut-off values based on SMI according to a previous study : <43 cm^2/m^2 for males with a BMI <25 kg/m^2, <53 cm^2/m^2 for males with BMI 25 kg/m^2 or greater, and <41 cm^2/m^2 for females (22). The cut-of values were also defined based on PMI : <6.36 cm^2/m^2 in males and <3.92 cm^2/m^2 in females (23). The cutoff values for PMV were determined by the median of this cohort : <120 mL/m^2 in males and <60 mL/m^2 in females.

Statistical Analysis

The data are expressed as median, minimum, and maximum values. Categorical variables are reported as frequencies and group percentages. Categorical variables were analyzed using Fisher's exact test, and continuous variables were analyzed using the Mann-Whitney U test. Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier survival curve method and compared using the log-rank test. To identify factors related to survival, univariate and multivariate analyses with Cox proportional hazards regression models were used. Furthermore, due to the limited number of cases in the study cohort, the results of the multivariate analysis were validated using the stepwise regression method. The survival risk is expressed as a hazard ratio (HR) and 95% confidence interval (CI). All analyses were performed by SPSS software, version 16.0 (SPSS, Chicago, IL, USA), and $P < 0.05$ was considered significant.

RESULTS

Patients

The patients' characteristics are shown in Table 1. The PNI was greater than 41 in 38 patients and 41 or lower in 19 patients. Patients with a low PNI had low serum Alb levels and high CRP levels. They also had a higher risk of IMDC, and cytoreductive nephrectomy tended to be avoided. Regarding skeletal muscle mass, PMV was significantly lower in low-PNI patients.

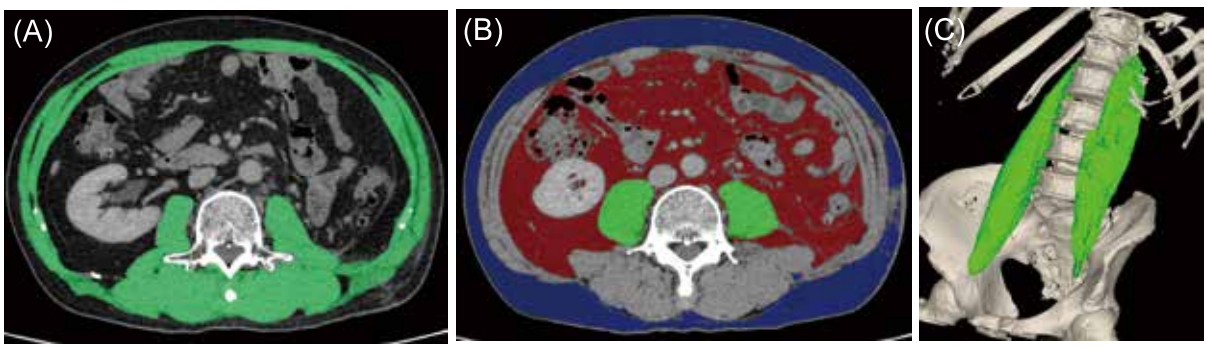

Fig 1. Three-dimensional reconstruction of computed tomography scanning images by Vincent version 4.
(A) Skeletal muscle index (SMI) at the third lumbar vertebra (L3). (B) Psoas muscle index (PMI), subcutaneous fat area (SFA), and visceral fat area (VFA) at L3. (C) Psoas muscle volume (PMV).

Table 1. Patients' characteristics according to PNI

	All	PNI		
	n = 57	>41 n = 38	≤41 n = 19	P
Age, y	67 (61-74)	67 (61-75)	65 (60-71)	0.793
Sex				
Male	43 (75.4%)	31 (81.6%)	12 (63.2%)	0.128
BMI, kg/m^2	24.1 (22.2-25.7)	24.5 (22.6-25.9)	23.1 (21.4-24.8)	0.117
Pathology				0.455
CCC	38 (66.7%)	25 (65.8%)	13 (68.4%)	
With sarcomatoid	4 (7.0%)	3 (7.9%)	1 (5.3%)	
Non-CCC	13 (22.8%)	10 (26.3%)	3 (15.8%)	
Unknown	6 (10.5%)	3 (7.9%)	3 (15.8%)	
Prior Nephrectomy				<0.001
Yes	43 (75.4%)	34 (89.5%)	9 (47.4%)	
IMDC risk classification				<0.001
Favorable	9 (15.8%)	7 (18.4%)	2 (10.5%)	
Intermediate	31 (54.4%)	26 (68.4%)	5 (26.3%)	
Poor	17 (29.8%)	5 (13.2%)	12 (63.2%)	
Skeletal muscle mass				
SMI at L3, cm^2/m^2	50.3 (43.2-55.3)	52.6 (44.8-56.2)	47.7 (40.6-52.3)	0.087
PMI at L3, cm^2/m^2	5.2 (3.7-5.9)	5.5 (3.8-6.0)	4.7 (3.0-5.8)	0.161
PMV, mL/m^2	112.3 (94.1-135.4)	120.4 (102.3-136.4)	96.6 (55.6-115.0)	0.008
Alb, g/dL	3.7 (2.9-4.1)	3.8 (3.3-4.2)	3.2 (2.4-3.5)	<0.001
CRP, mg/dL	0.8 (0.2-3.8)	0.4 (0.2-2.2)	4.2 (0.7-8.7)	0.003
TKI				1.000
Sunitinib	48 (84.2%)	32 (84.2%)	16 (84.2%)	
Pazopanib	9 (15.8%)	6 (15.8%)	3 (15.8%)	

PNI Prognostic Nutritional Index, *CCC* clear cell carcinoma, *IMDC* International Metastatic Renal Cell Carcinoma Database Consortium, *SMI* skeletal muscle index, *PMI* psoas muscle index, *PMV* psoas muscle volume, *L3* the third lumbar vertebra, *TKI* tyrosine kinase inhibitor

Patient survival according to PNI

A total of 28 (49.1%) patients died during follow-up. Median PFS and OS were 12 and 35 months, respectively. Univariate analyses showed that the significant predictors of PFS were pathological diagnosis, number of IMDC risk factors, and PNI ; the significant predictors of OS were prior nephrectomy, number of IMDC risk factors, and PNI (Fig. 2). Multivariate analysis identified PNI as the only significant and independent predictor of OS (HR 3.81 [95% CI 1.21-12.03], P = 0.046), although it was not a significant predictor of PFS (HR 2.53 [95% CI 0.88-7.25], P = 0.084). The diagnosis of the sarcopenia category by assessing SMI, PMI, or PMV was not a significant prognostic indicator of survival (Table 2). Similarly, on stepwise multivariate Cox regression analysis, PNI was the significant and independent predictor of OS, but not PFS (Table 3).

Relationship between the PNI and changes in body composition

The association of changes seen after 3 months of treatment with prognosis was investigated, including the changes in body composition, presence of AEs, and early tumor shrinkage with TKIs according to PNI (Table 4). The changes in PMV, SFA, and VFA from the initiation of treatment were means of -5.3%, -7.7%, and -0.7%, respectively, after 3 months. PMV and SFA were significantly lower in the high-PNI group than in the low-PNI group (-8.3% vs -3.3%, P = 0.010 and -14.4% vs -1.9%, P = 0.002).

Decreased PMV and SFA as predictors of OS

On multivariate analysis, the decrease in PMV (HR 3.35 [95% CI 1.04-10.82], P = 0.043) and the incidence of on-target AEs (HR 0.22 [95% CI 0.07-0.74], P = 0.014) were predictors of PFS. Furthermore, decreased PMV (HR 4.946 [95% CI 1.44-17.04], P = 0.011) and decreased SFA (HR 58.868 [95% CI 9.19-375.36], P<0.001), as well as early tumor shrinkage (HR 0.07 [95% CI 0.01-0.69], P = 0.023), were predictors of OS (Table 5). PFS and OS were significantly shorter in patients with either decreased PMV or decreased SFA (Fig. 3).

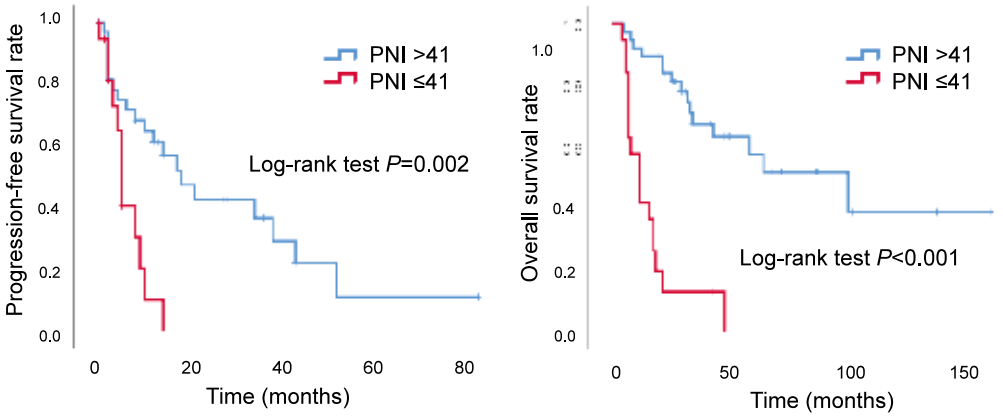

Fig 2. Progression-free survival and overall survival according to the prognostic nutritional index (PNI). The survival rate was calculated using the Kaplan-Meier method and compared using the log-rank test.

Table 2. Cox regression analyses for predicting progression-free survival and overall survival at the start of treatment

Variable		Progression-free survival						Overall survival					
		Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
		HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Age, y	≥67 vs <67	1.71	0.83-3.55	0.149				1.26	0.63-2.54	0.515			
Sex	Male vs Female	0.80	0.37-1.75	0.575				0.71	0.33-1.53	0.376			
Pathology	CCC vs non-CCC	2.35	1.03-5.34	0.042	2.19	0.93-5.19	0.075	0.98	0.39-2.46	0.965			
Prior nephrectomy	Yes vs No	0.49	0.23-1.06	0.072				0.24	0.11-0.51	<0.001	0.40	0.15-1.06	0.074
IMDC risk factor	≥2 vs ≤1	2.60	1.24-6.66	0.014	1.41	0.54-3.70	0.484	3.88	1.76-8.58	<0.001	1.63	0.61-4.40	0.332
CRP, mg/dL	≥1.0 vs <1.0	0.79	0.38-1.66	0.535				1.37	0.67-1.66	0.384			
First-Line TKI	Sunitinib vs Pazopanib	0.83	0.29-2.40	0.732				1.23	0.47-3.22	0.670			
Sarcopenia Categories													
SMI at L3	Yes vs No	1.77	0.81-3.88	0.156				2.21	0.92-4.56	0.089			
PMI at L3	Yes vs No	0.88	0.33-2.30	0.780				1.18	0.45-3.11	0.731			
PMV	Yes vs No	1.35	0.66-2.75	0.416				1.62	0.81-3.27	0.176			
PNI	≤41 vs >41	3.44	1.51-7.86	0.003	2.53	0.88-7.25	0.084	7.11	3.25-15.55	<0.001	3.81	1.21-12.03	0.046

CCC clear cell carcinoma, *IMDC* International Metastatic Renal Cell Carcinoma Database Consortium, *TKI* tyrosine kinase inhibitor, *SMI* skeletal muscle index, *PMI* psoas muscle index, *PMV* psoas muscle volume, *PNI* prognostic nutritional index

Table 3. Stepwise multivariate Cox regression analyses for predicting progression-free survival and overall survival at the start of treatment

Variable		Progression-free survival			Overall survival		
		HR	95% CI	P	HR	95% CI	P
Age, y	≥67 vs <67				0.39	0.17-0.89	0.025
Sex	Male vs Female						
Pathology	CCC vs non-CCC	2.44	1.06-5.56	0.035			
Prior nephrectomy	Yes vs No						
IMDC risk factor	≥2 vs ≤1				6.55	2.48-17.30	<0.001
CRP, mg/dL	≥1.0 vs <1.0						
First-line TKI	Sunitinib vs Pazopanib						
Sarcopenia Categories							
SMI at L3	Yes vs No						
PMI at L3	Yes vs No						
PMV	Yes vs No						
PNI	≤41 vs >41	2.08	0.93-4.76	0.075	12.62	4.61-34.54	<0.001

CCC clear cell carcinoma, *IMDC* International Metastatic Renal Cell Carcinoma Database Consortium, *TKI* tyrosine kinase inhibitor, *SMI* skeletal muscle index, *PMI* psoas muscle index, *PMV* psoas muscle volume, *PNI* prognostic nutritional index

Table 4. Changes in parameters after 3 months of treatment according to PNI

	All	PNI		
	n = 57	>41 n = 38	≤41 n = 19	P
Early tumor shrinkage rate, %	-7.0 (-62.2 to 15.9)	-11.6 (-62.2 to 13.3)	-0.2 (-49.6 to 15.9)	0.213
Change in body composition				
PMV, %	-5.4 (-63.4 to 22.1)	-3.3 (-42.2 to 22.1)	-8.3 (-63.4 to 17.0)	0.010
SFA, %	-7.7 (-98.7 to 62.3)	-1.9 (-61.4 to 57.6)	-14.4 (-98.7 to 62.3)	0.002
VFA, %	-0.7 (-76.9 to 192.2)	-0.5 (-51.1 to 114.8)	-4.34 (-76.9 to 192.2)	0.115
AEs related to nutritional disorder (≥G2) n, %				
Anorexia	13 (22.8%)	11 (28.9%)	2 (10.5%)	0.183
Diarrhea	14 (24.6%)	8 (21.1%)	6 (31.6%)	0.516
Malaise	19 (33.3%)	13 (34.2%)	6 (31.6%)	1.000
On-target AEs (≥G2) n, %				
Hand-foot syndrome	19 (33.3%)	14 (36.8%)	5 (26.3%)	0.555
Hypertension	27 (47.4%)	18 (47.4%)	9 (47.4%)	1.000
Thyroid dysfunction	26 (45.6%)	20 (52.6%)	6 (31.6%)	0.165
Other AEs (≥G2) n, %	33 (57.9%)	22 (57.9%)	11 (57.9%)	1.000

PNI Prognostic Nutritional Index, *PMV* psoas muscle volume, *SFA* subcutaneous fat area, *VFA* visceral fat area, *AE* adverse event

Table 5. Cox regression analyses for predicting progression-free survival and overall survival after 3 months of first-line treatment

Variable		Progression-free survival						Overall survival					
		Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
		HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Best overall response	≥PR vs ≤SD	0.19	0.06-0.59	0	0.50	0.12-2.05	0.34	0.06	0.01-0.44	0.006	0.07	0.01-0.69	0.023
Δ3m PMV decrease	≥10% vs <10%	3.14	1.30-7.61	0.01	3.35	1.04-10.82	0.04	3.52	1.58-7.85	0.002	4.95	1.44-17.04	0.011
Δ3m SFA decrease	≥20% vs <20%	1.90	0.79-4.57	0.15				5.45	2.37-12.52	<0.001	58.87	9.14-375.36	<0.001
Δ3m VFA decrease	≥20% vs <20%	2.31	0.96-5.02	0.06				2.59	1.21-5.55	0.014	1.21	0.39-3.81	0.742
On-target AEs	Yes vs No	0.43	0.19-0.99	0.05	0.22	0.07-0.74	0.01	0.87	0.35-2.14	0.761			
Other AEs	Yes vs No	0.56	0.28-1.14	0.11				0.77	0.38-1.57	0.466			

PMV psoas muscle volume, *SFA* subcutaneous fat area, *VFA* visceral fat area, *AE* adverse event

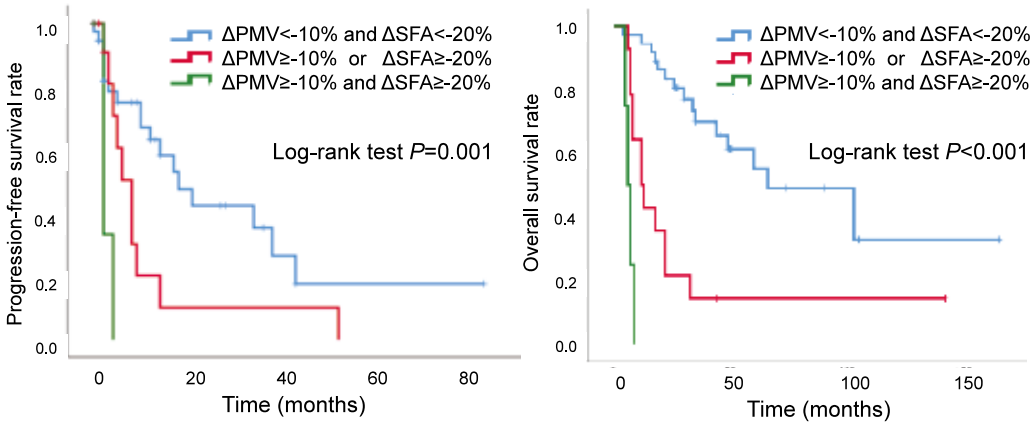

Fig 3. Progression-free survival and overall survival compared according to decreased psoas muscle volume (PMV) and subcutaneous fat area (SFA). The survival rate was calculated using the Kaplan-Meier method and compared using the log-rank test.

DISCUSSION

Prognostic models that include many factors are used in clinical practice, since the prognosis of mRCC patients cannot be explained by one factor. Nutritional status has been shown to be strongly associated with OS in patients with mRCC treated with TKIs (24). Although the IMDC risk classification is an established prognostic classification for mRCC treatment, it does not directly take factors related to nutritional status into account. The fact that some reports showed improvement of the prognosis prediction accuracy of the IMDC classification when nutritional index scores such as PNI (9, 10) and the modified Glasgow prognostic score (mGPS) (16) were included, emphasized the importance of nutritional evaluation.

Cancer cachexia is a pathological status in which deterioration of nutritional status is observed with advanced cancer. Cancer cachexia is defined by progressive loss of muscle mass, but there are no factors that clearly predict its onset (25). Cancer cachexia is classified into three stages, pre-cachexia, cachexia, and refractory cachexia, by the European Palliative Care Research Collaborative (EPCRC) (25). It is important to anticipate the onset of cachexia and provide earlier intervention, as the response to treatment may be diminished in advanced cachexia (26, 27).

To evaluate nutritional status, the PNI was used as a nutritional index. The cutoff value of this index is controversial, but based on the original report, the cutoff value was set to 41 in the present study (6, 7). The present results showed that low PNI at the start of treatment in mRCC patients treated with TKIs as first-line therapy was not significantly associated with PFS. However, it was a significant predictor of OS. Consistent with the present study, a low PNI was reported to be associated with OS rather than PFS, which is strongly associated with drug responsiveness (9, 28).

As with PNI, there are several reports that showed that sarcopenia, loss of skeletal muscle mass, at the start of treatment affected the prognosis and the development of side effects in mRCC patients treated with TKIs (19). Whereas there are many reports that SMI and PMI are indices that reflect sarcopenia (29, 30), there is also a report that measurement by cross-sectional area does not reflect sarcopenia (31). Therefore, the volume of the psoas major muscle was measured in the present study and evaluated as PMV. However, unlike the previous reports (16, 17), the loss of muscle volume at the start of treatment was not a predictor of a poor prognosis in the present study. On the other hand, the progressive decreases in PMV and SFA observed 3 months after the start of treatment were prognostic factors for OS independent of early tumor shrinkage with systemic therapy, suggesting that these results were not due only to responsiveness of tumors to systemic therapy. Ishihara *et al*. showed that more than half of patients had decreased skeletal muscle mass during first-line sunitinib therapy for mRCC (32). Consistent with the present study, they also reported that progressive loss of skeletal muscle mass, regardless of the existence of sarcopenia at the start of systemic therapy, was significantly associated with PFS and OS (32). Additionally, several studies reported that decreased skeletal muscle mass during systemic therapies was negatively associated with prognosis in patients with advanced or metastatic disease (33-35).

Furthermore, it was interesting that patients with a low PNI in the present study showed significant progressive decreases in PMV and SFA 3 months after the start of treatment. Several studies have reported that loss of fat tissue can precede skeletal muscle depletion in the progression of cancer cachexia. Basic research has shown that changes in lipid metabolism induce the loss of muscle mass in cancer cachexia (36, 37). Furthermore, it has been reported that the reduction of subcutaneous fat, not visceral fat, is more important in the progression of cancer cachexia (38), supporting the present results.

Thus, the present results suggest that it is important to consider not only the antitumor effect of drug therapy, but also the general status of the patient, such as nutritional status and changes in muscle mass and/or fat tissue volume after initiating treatment. It may also be possible to improve prognosis through active interventions for malnutrition.

There are several limitations in the present study. This was a retrospective study with a small number of cases, and the lack of a sufficient number of cases for the number of variables in the multivariate analysis might lead to statistical weaknesses, which required validation using the stepwise regression method. Moreover, this was a long-term study, so to avoid any effects or bias regarding the subsequent treatment, only patients treated with TKIs or mammalian target of rapamycin inhibitors (mTORi) were selected for further treatment. Patients who received IO therapy were excluded. Next, although weight change is an important index used as a diagnostic criterion for cachexia (25), it was not measured in all cases and was excluded from the examination items.

Evaluating patients' nutritional status may help predict the prognosis of mRCC patients and improve the quality of treatment selection in the age of cancer immunotherapy, including combination therapy of immunotherapy and TKI, as well as TKI monotherapy. In patients with decreased PNI, the efficacy of TKI is expected to be limited, and careful follow-up may be required to consider early treatment switching. In the future, evaluation of the efficacy of PNI as a prognostic factor in immunotherapy and other therapies may provide useful knowledge for treatment selection. In addition, appropriate nutritional support based on nutritional evaluation should be considered in order to improve the therapeutic outcomes of mRCC patients.

CONCLUSION

The nutritional index at the start of treatment may predict the changes in the patient's general status, such as decreases in muscle mass and fat tissue volume, with systemic treatment and may be associated with the prognosis of mRCC patients. The importance of nutritional indicators should also be clarified in the era of cancer immunotherapy, and appropriate nutritional intervention will hopefully improve treatment outcomes.

ACKNOWLEDGEMENTS

Not applicable.

STATEMENT OF ETHICS

The Ethics Committee of Tokushima University Hospital approved this retrospective study (ID : 3867), which was performed in accordance with the tenets of the Declaration of Helsinki. The study was granted an exemption from requiring written, informed consent by the Ethics Committee.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

FUNDING SOURCES

None.

AUTHOR CONTRIBUTIONS

K.O. wrote the manuscript. T.F. supervised the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data analyzed during this study are included in this published article.

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