# Computed Tomography-Assessed Sarcopenia Predicts Mortality in Kidney Transplant Candidates

*Harun Coban,[1] Dilek Barutcu Atas,[1] Murat Tugcu,[1] Meltem Kursun,[2] Canan Cimsit,[2] Ebru Asicioglu,[1] Hakki Arikan,[1] Serhan Tuglular,[1] Arzu Velioglu[1]*

## Abstract

***Objectives:*** **Sarcopenia is common in chronic kidney disease and associated with increased mortality. We investigated the prevalence of sarcopenia, defined as low muscle mass by the psoas muscle index, in end-stage renal disease patients on waiting lists for kidney transplant and determined its association with prognostic nutritional index, C-reactive protein-to-albumin ratio, cardiovascular events, and mortality.**

***Materials and Methods:*** **Our study included 162 patients with end-stage renal disease and 87 age-matched healthy controls. We calculated nutritional status as follows: prognostic nutritional index = (10 × albumin [g/dL]) + (0.005 × total lymphocyte count (×10³/μL]) and C-reactive protein-to-albumin ratio. We gathered demographic and laboratory data from medical records.**

***Results:*** **Patients with end-stage renal disease had a mean age of 44.7 ± 14.2 years; follow-up time was 3.37 years (range, 0.35-9.60 y). Although patients with end-stage renal disease versus controls had higher prevalence of sarcopenia (16.7% vs 3.4%; *P* = .002) and C-reactive protein-to-albumin ratio (1.47 [range, 0.12-37.10] vs 0.74 [range, 0.21-10.20]; *P* < .001), prognostic nutritional index was lower (40 [range, 20.4-52.2] vs 44 [range, 36.1-53.0]; *P* < .001). In patients with end-stage renal disease with and without sarcopenia, prognostic nutritional index (*P* = .005) was lower and C-reactive protein-to-albumin ratio (*P* = .041) was higher in those with versus those without sarcopenia. Among 67 patients on waiting lists who received kidney transplants, those without sarcopenia had better 5-year patient survival posttransplant than those with sarcopenia (*P* = .001). Multivariate regression analysis showed sarcopenia and low prognostic nutritional index were independent risk factors for mortality among patients with end-stage renal disease.**

***Conclusions:*** **Sarcopenia was ~5 times more frequent in patients with end-stage renal disease than in healthy controls and was positively correlated with the prognostic nutritional index. Sarcopenia was an independent risk factor for mortality in patients on transplant waiting lists.**

**Key words:** *C-reactive protein-to-albumin ratio, Prognostic nutritional index, Psoas muscle index, Renal transplantation*

## Introduction

Sarcopenia was first defined in the literature by Rosenberg and associates in 1989 as an age-related decrease in muscle mass.[1] Apart from aging, it can also occur during the course of chronic diseases, such as cancer, cardiovascular diseases, malnutrition, physical inactivity, chronic liver disease, and chronic kidney disease (CKD).[2] About 10% of the CKD patients have sarcopenia; this rate increases to 33.7% in patients on hemodialysis.[3,4]

Sarcopenia has been defined as a combination of low muscle mass, low muscle strength, and low physical activity according to a recent consensus.[5] Nevertheless, the presence of low muscle mass is also generally referred to as sarcopenia.[6] Measurement of midarm circumference, bioimpedance analysis (BIA), or muscle mass with dual energy X-ray absorptiometry (DEXA) are commonly used methods for determining muscle mass. Recently, skeletal muscle mass measured by abdominal computed tomography (CT) was used for diagnosis of sarcopenia. Psoas muscle index (PMI), a total area of the bilateral psoas muscle area at the level of L3 vertebrae adjusted by patient's height, is a method for muscle mass quantification by CT and is well correlated to whole

*From the [1]Department of Internal Medicine, Division of Nephrology, and the [2]Department of Radiology, Marmara University School of Medicine, Istanbul, Turkey*

***Acknowledgements:*** *The authors have not received any funding or grants in support of the presented research or for the preparation of this work and have no declarations of potential conflicts of interest.*

***Corresponding author:*** *Dilek Barutcu Atas, Fevzi Çakmak Mah. Muhsin Yazıcıoğlu Cad. No: 10 Üst Kaynarca Postal code: 34899, Pendik-Istanbul, Turkey*
***E-mail:*** *drdilekb@gmail.com*

***Experimental and Clinical Transplantation (2024) 3: 214-222***



**DOI: 10.6002/ect.2023.0050**

body skeletal muscle mass.[7] Although studies in patients with cancer, liver transplant recipients, and patients on hemodialysis have been previously published, data on the use of PMI to determine sarcopenia in end-stage renal disease (ESRD) patients on transplant waiting lists, who differ from the general hemodialysis population, are scarce.

Poor nutritional status and inflammation are the major determinants of sarcopenia.[8] Studies suggest that increased inflammatory status inhibits appetite, causes increased protein catabolism, and negatively affects the nutritional status, physical inactivity, and metabolic acidosis, resulting in sarcopenia in ESRD patients.[9] C-reactive protein (CRP) is an acute-phase reactant, which is produced in response to cytokines induced by the dialysis procedure itself, comorbidities, ischemia, genetic factors, and diet. Studies have shown that the CRP-to-albumin ratio (CAR), which is the combination of systemic inflammation and nutritional status markers, is an independent prognostic marker in intensive care and peritoneal dialysis patients.[10,11] Another inflammation and nutritional status marker is the prognostic nutritional index (PNI). Relationships between PNI and patient survival in patients with malignancy and in liver transplant recipients have been previously investigated.[12,13] A study conducted at our center found a significant association between PNI and mortality in elderly patients with stage 3/4 CKD.[14] However, limited data are available on the use of these indices in ESRD and renal transplant candidates and their relationship with sarcopenia.

Sarcopenia is common in CKD and is associated with increased mortality. The use of special rehabilitation programs, nutritional support, and exercise interventions to improve sarcopenia may lead to an increase in survival among patients with ESRD.

In the present study, we aimed to investigate the frequency of CT-assessed sarcopenia and its relationship with PNI and CAR in ESRD patients on waiting lists for transplant. Associations between CT-assessed sarcopenia, major cardiovascular events (CVEs), and mortality were also evaluated.

## Materials and Methods

### Design and study participants

In this single-center, retrospective study, we included 162 patients registered on the National Organ Transplant Waiting List between January 2012 and November 2020. All patients had abdominal CT taken 3 months before or 1 month after the date of registration. As a healthy control group, we included 87 kidney donor candidates who had abdominal CT before nephrectomy. The ESRD group (n = 162) was also divided into 2 groups according to whether they had kidney transplant (from first-degree to fourth-degree living relative or spouse donors) or not during follow-up. We obtained demographic data of patients, etiology of CKD, type and duration of renal replacement therapy, previous CVE history, development of major CVE, and survival data from medical records. We also obtained complete blood count, blood urea nitrogen, creatinine, albumin, C-reactive protein, fasting blood glucose, hemoglobin A1c, total cholesterol, parathyroid hormone, and vitamin D levels at the time of registration from patient files and the hospital electronic data recording system.

We used 2 indices for the evaluation of inflammation and nutritional status: PNI and CAR. Prognostic nutritional index was calculated as follows: 10× albumin (g/dL) + (0.005 × total lymphocyte count [$\times 10^3/\mu L$]). The PNI value of controls at the fifth percentile according to sex was accepted as the limit value for ESRD patients (41.31 for men and 38.81 for women).

We also recorded number of deaths and CVEs (myocardial infarction, coronary revascularization, heart failure, and cerebrovascular events) that occurred during follow-up.

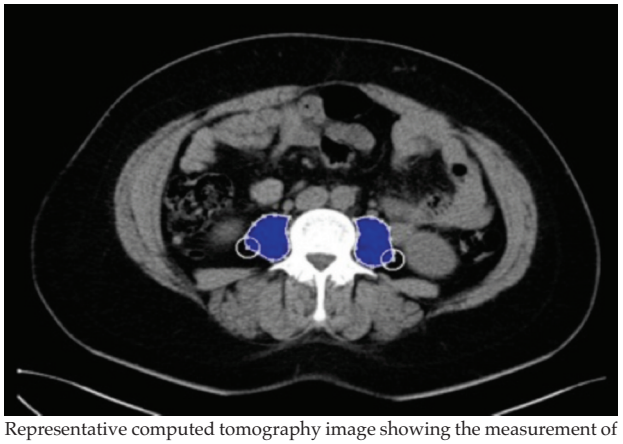
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Our study was approved by the local ethics committee (protocol number 09.2021.462). Informed consent was obtained from all individual participants included in the study.

### Radiological analysis

Abdominal CT examinations of patients and healthy controls were evaluated through digital archiving system (INFINITT PACS System, INFINITT Healthcare) by 2 experienced radiologists (MT and CC); both were blinded to clinical data and outcomes. Sarcopenia on CT images was assessed by measuring the right and left psoas muscle areas in

the abdominal sections passing through the L3 vertebra transverse process level (Figure 1). Measurements were made by manually plotting the region of interest. Images for muscle area measurements were limited to values between -29 and +150 Hounsfield units (HU) ("thresholding"). After measurements, the area and mean HU values for each of the muscle tissues were recorded. The PMI (in $cm^2/m^2$) was calculated by dividing the muscle area values by the square of the patients' heights: PMI = total psoas muscle cross-sectional area at the third lumbar vertebral level ($cm^2$)/patient height squared ($m^2$). The PMI value of controls at the fifth percentile according to sex was accepted as the limit value for defining sarcopenia (4.74 $cm^2/m^2$ for men and 3.02 $cm^2/m^2$ for women).[15]

**Figure 1.** Measurement of Psoas Muscle Area on Computed Tomography



Representative computed tomography image showing the measurement of bilateral psoas muscle area at the lower body of the L3 vertebra.

### Statistical analyses

We used the Statistical Package for the Social Science for Windows software (version 25; SPSS Inc) for statistical analysis. Continuous variables are expressed as mean ± SD or as median (with distribution range). Categorical variables are expressed as number and percentage. For comparison of clinical variables, we used the t-test for normally distributed data, the chi-square test or the Fisher exact test for categorical data, and the Mann-Whitney U test for nonnormally distributed data. To determine the conformity of continuous variables to normal distribution, we used the Kolmogorov-Smirnov and Shapiro-Wilks tests. Survival curves were constructed using the Kaplan-Meier method and compared with the log-rank test. We performed univariate and multivariate analyses using Cox regression analysis. $P < .05$ was considered significant.

## Results

### Comparison of study patients and healthy controls

The clinical and demographic characteristics of study patients and healthy controls are shown in Table 1. The mean age of patients was 44.7 ± 14.2 years, and 55.6% of patients were male. Median follow-up time was 3.37 years (range, 0.35-9.6 y) in study patients and 5.52 years (range, 1.01-9.6 y) in healthy controls ($P = .001$). Sarcopenia (assessed by CT) was more frequent (16.7% vs 3.4%; $P = .002$), CAR was higher (1.47 [range, 0.12-37.1] vs 0.74 [range, 0.21-10.2]; $P < .001$), and the PNI value was lower (40 [range, 20.4-52.2] vs 44 [range, 36.1-53]; $P < .001$) in study patients compared with healthy controls.

**Table 1.** Clinical and Laboratory Data of Patients and Healthy Controls

| | All Patients (n = 162) | Healthy Controls (n = 87) | *P* |
|---|---|---|---|
| Age, y | 44.7 ± 14.2 | 45.36 ± 11 | .665 |
| Male, No. (%) | 90 (55.6%) | 32 (36.8%) | .005 |
| Female, No. (%) | 72 (44.4%) | 55 (63.2%) | .005 |
| Smoking, No. (%) | 63 (38.9%) | 35 (40.2%) | .836 |
| Body mass index, $kg/m^2$ | 25.4 ± 4.7 | 28.2 ± 4.5 | <.001 |
| Psoas muscle index, $cm^2/m^2$ | 5.24 ± 1.71 | 5.48 ± 1.87 | .302 |
| Sarcopenia status, No. (%) | 27 (16.7%) | 3 (3.4%) | .002 |
| Albumin, g/dL | 4 (2.04-5.22) | 4.41 (3.61-5.3) | <.001 |
| Hemoglobin, g/dL | 11.2 ± 1.6 | 13.8 ± 1.6 | <.001 |
| Neutrophil count, $10^3/\mu L$ | 4.3 (0.7-13.9) | 3.7 (1.5-6.1) | .001 |
| Lymphocyte count, $10^3/\mu L$ | 1.6 (0.3-4) | 2 (0.9-4.2) | <.001 |
| Thrombocyte count, $10^3/\mu L$ | 212 (63-646) | 228 (140-380) | .093 |
| C-reactive protein, mg/L | 5.84 (0.5-115) | 3.16 (1-46.1) | <.001 |
| C-reactive protein-to-albumin ratio | 1.47 (0.12-37.1) | 0.74 (0.21-10.2) | <.001 |
| Prognostic nutritional index | 40 (20.4-52.2) | 44 (36.1-53) | <.001 |
| Total cholesterol, mg/dL | 197.4 ± 54.8 | 202.9 ± 47.9 | .434 |
| Vitamin D, µg/L | 11.95 (1.13-49) | 12.98 (4-62.61) | .278 |
| Hemoglobin A1c, % | 5.2 (3-9.6) | 5.4 (4.5-6.4) | .069 |
| Total follow-up, y | 3.37 (0.35-9.6) | 5.52 (1.01-9.6) | .001 |

$P < .05$ was considered significant.

### Analysis of baseline characteristics according to transplant and sarcopenia status

The ESRD group (n = 162) was divided into 2 groups according to whether they had kidney transplant or not during follow-up, with 67 patients who received kidney transplant during follow-up. The initial data and analysis of patients according to transplant status are summarized in Table 2. Transplant patients were younger versus those who did not have transplant (39.4 ± 13.4 vs 48.3 ± 13.6 y; $P < .001$). Median follow-up time was 4.5 years (range, 0.5-9.6 y) in transplant patients and 3.1 years (range, 0.35-9.3 y) in patients without transplant ($P = .020$). Median follow-up time after transplant

was 4.5 years (range, 0.5-9.5 y) Although the difference did not reach statistical significance, sarcopenia seemed to be less frequent among transplant recipients (10.4% vs 21.1%; $P$ = .074). Furthermore, in ESRD patients with transplant recipients versus ESRD patients without transplant, the CAR value was lower (1 [range, 0.2-6.4] vs 3.98 [range, 0.12-37.1]; $P$ = .003) and the PNI value was higher (43 [range, 26-52.2] vs 39.31 [range, 20.4-50]; $P$ = .001).

**Table 2.** Clinical and Laboratory Data of Patients According to Transplant Status

| | Transplant Patients (n = 67) | Nontransplanted Patients (n = 95) | *P* |
|---|---|---|---|
| Age, y | 39.4 ± 13.4 | 48.3 ± 13.6 | <.001 |
| Male, No. (%) | 37 (55.2%) | 53 (55.8%) | .943 |
| Female, No. (%) | 30 (44.8%) | 42 (44.2%) | .943 |
| Duration of RRT, mo | 8 (0-284) | 6 (0-242) | .477 |
| Smoking, No. (%) | 22 (32.8%) | 41 (43.2%) | .184 |
| Body mass index, kg/m$^2$ | 24.8 ± 4.5 | 25.8 ± 4.9 | .176 |
| Psoas muscle index, cm$^2$/m$^2$ | 5.42 ± 1.65 | 5.10 ± 1.75 | .247 |
| Sarcopenia status, No. (%) | 7 (10.4%) | 20 (21.1%) | .074 |
| Albumin, g/dL | 4.3 (2.6-5.22) | 3.93 (2.04-5) | <.001 |
| Hemoglobin, g/dL | 11.4 ± 1.5 | 11 ± 1.7 | .144 |
| Lymphocyte, 10$^3$/µL | 1.6 (0.3-3.5) | 1.6 (0.4-4) | .794 |
| CRP, mg/L | 3.85 (0.9-27.6) | 8.12 (0.5-115) | .021 |
| CAR | 1 (0.2-6.4) | 3.98 (0.12-37.1) | .003 |
| Prognostic nutritional index | 43 (26-52.2) | 39.31 (20.4-50) | <.001 |
| Total cholesterol, mg/dL | 195.6 ± 53.2 | 198.7 ± 56.3 | .662 |
| Parathyroid hormone, pg/mL | 278.4 (4.4-2119) | 254.4 (11.1-1001.1) | .248 |
| Hemoglobin A1c, % | 5.1 (4-8.6) | 5.3 (3-9.6) | .044 |
| Follow-up, y | 4.5 (0.5-9.6) | 3.1 (0.35-9.3) | .020 |
| CVE, No. (%) | 5/65 (7.7%) | 11/79 (13.9%) | .236 |
| Mortality, No. (%) | 3 (4.5%) | 18 (19%) | .003 |

***Abbreviations:*** CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; CVE, cardiovascular events; RRT, renal replacement therapy
$P$ < .05 was considered significant.

When the ESRD group was divided into 2 groups according to initial sarcopenia status, PNI was lower (39 [range, 20.4-51] vs 41 [range, 23-52.2]; $P$ = .005) and CAR was higher (2.03 [range, 0.28-34.65] vs 1.28 [range, 0.12-37.1]; $P$ = .041) in the sarcopenic group (n = 27) compared with patients without sarcopenia (n = 135). Data of patients according to sarcopenia status are summarized in Table 3.

Comparisons of clinical and laboratory data of the patients according to sarcopenia and transplant status are shown in Table 4. Total follow-up time was 2.09 years (range, 1-7.93 y) in the sarcopenic transplant group, 2.47 years (range, 0.35-7.7 y) in the sarcopenic nontransplant group, 4.62 years (range, 0.5-9.6 y) in the nonsarcopenic transplant group, and 3.12 years (range, 0.61-9.29 y) in the nonsarcopenic nontransplant group ($P$ = .029).

**Table 3.** Clinical and Laboratory Data of Patients According to Sarcopenia Status

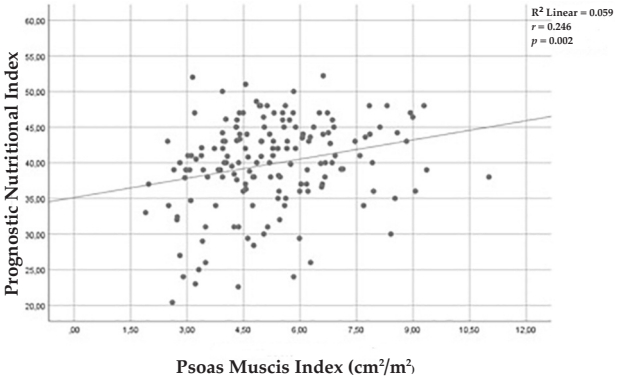
| | Patients With Sarcopenia (n = 27) | Patients Without Sarcopenia (n = 135) | *P* |
|---|---|---|---|
| Age, y | 48.1 ± 14.8 | 44 ± 14 | .166 |
| Male, No. (%) | 15 (55.6%) | 75 (55.6%) | 1.000 |
| Female, No. (%) | 12 (44.4%) | 60 (44.4%) | 1.000 |
| Duration of RRT, mo | 8 (0-168) | 6 (0-284) | .258 |
| Smoking, No. (%) | 11 (40.7%) | 52 (38.5%) | .829 |
| Body mass index, kg/m$^2$ | 24.3 ± 4.4 | 25.6 ± 4.8 | .223 |
| Psoas muscle index, cm$^2$/m$^2$ | 3.45 ± 0.9 | 5.59 ± 1.6 | <.001 |
| Albumin, g/dL | 3.9 (2.04-5.1) | 4.1 (2.3-5.22) | .005 |
| Hemoglobin, g/dL | 11.3 ± 1.6 | 11.1 ± 1.6 | .554 |
| Lymphocyte, 10$^3$/µL | 1.6 (0.3-3.1) | 1.6 (0.4-4) | .771 |
| CRP, mg/L | 7.92 (1.1-78.3) | 5.15 (0.5-115) | .133 |
| CAR | 2.03 (0.28-34.65) | 1.28 (0.12-37.1) | .041 |
| Prognostic nutritional index | 39 (20.4-51) | 41 (23-52.2) | .005 |
| Total cholesterol, mg/dL | 194.5 ± 42.7 | 198 ± 57 | .727 |
| Parathyroid hormone, pg/mL | 349.3 (72.8-1640) | 262 (4.4-2119) | .081 |
| Hemoglobin A1c, % | 5 (3-8.7) | 5.2 (4-9.6) | .097 |
| Total follow-up, y | 2.25 (0.35-7.93) | 4.1 (0.5-9.6) | .031 |
| Transplant, No. (%) | 7 (25.9%) | 60 (44.4%) | .089 |
| CVE, No. (%) | 5/20 (25%) | 11/124 (8.9%) | .049 |
| Mortality, No. (%) | 13 (48.1%) | 8 (5.9%) | <.001 |

***Abbreviations:*** CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; CVE, cardiovascular event; RRT, renal replacement therapy
$P$ < .05 was considered significant.

## Correlation between psoas muscle index, prognostic nutritional index, and C-reactive protein-to-albumin ratio

In the correlation analysis, we determined a positive correlation between PMI and PNI (r = 0.246, $P$ = .002) and a negative correlation between PNI and CAR (r = -0.356, $P$ < .001) (Figure 2 and Figure 3). We found no significant correlation between PMI and CAR (r = -0.061, $P$ = .445).

**Figure 2.** Correlation Analysis Between Psoas Muscle Index and Prognostic Nutritional Index




## Relationship between sarcopenia and mortality

Patients were divided into 4 groups according to their transplant and sarcopenia status as follows: nonsarcopenic transplant group (n = 60), sarcopenic

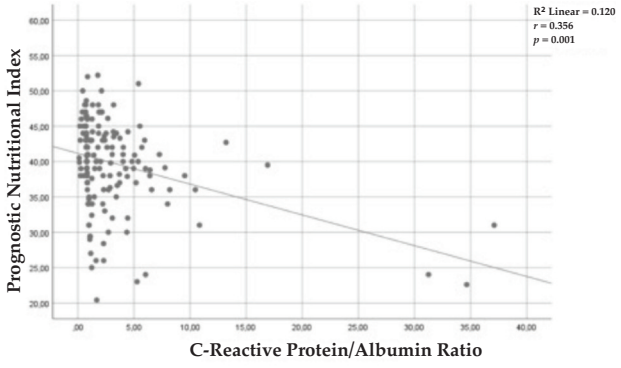
**Table 4.** Comparison of Clinical and Laboratory Data of Patients According to Sarcopenia and Transplant Status

| | Sarcopenia + Transplant (n = 7) | Sarcopenia + No Transplant (n = 20) | No Sarcopenia + Transplant (n = 60) | No Sarcopenia + No Transplant (n = 75) | *P* |
|---|---|---|---|---|---|
| Age, y | 37 (23-70) | 50 (22-78) | 38 (19-65) | 49 (19-72) | .001 |
| Male, No. (%) | 5 (71.4%) | 10 (50%) | 32 (53.3%) | 43 (57.3%) | .784 |
| Female, No. (%) | 2 (28.6%) | 10 (50%) | 28 (46.7%) | 32 (42.7%) | .784 |
| Smoking, No. (%) | 3 (42.9%) | 8 (40%) | 19 (31.7%) | 33 (44%) | .511 |
| Body mass index, kg/m$^2$ | 24.5 (18-28) | 22.9 (15.5-33.7) | 24.9 (17.3-36.1) | 26 (16.8-43.3) | .289 |
| RRT duration, mo | 4 (0-168) | 16 (1-60) | 8 (0-284) | 5 (0-242) | .166 |
| Previous CVE history, No. (%) | 0 (%0) | 2 (%10) | 7 (%11.7) | 11 (%14.7) | .873 |
| Psoas muscle index, cm$^2$/m$^2$ | 3.95 (2.48-4.61) | 2.94 (1.9-4.62) | 5.43 (3.02-11.01) | 5.43 (3.1-9.36) | <.001 |
| Albumin, g/dL | 4 (2.94-5.1) | 3.8 (2.04-4.4) | 4.33 (2.6-5.22) | 4 (2.3-5) | <.001 |
| Hemoglobin, g/dL | 11.5 (9.9-13.2) | 11.5 (7.9-14.9) | 11.4 (7.3-15.1) | 11 (6.6-16) | .404 |
| Lymphocyte count, 10$^3$/μL | 1.4 (0.3-2.5) | 1.6 (0.6-3.1) | 1.6 (0.7-3.5) | 1.6 (0.4-4) | .934 |
| CRP, mg/L | 7.53 (3.11-27.6) | 8.02 (1.1-78.3) | 3.75 (0.9-25) | 8.19 (0.5-115) | .054 |
| CAR | 1.79 (0.82-5.95) | 2.22 (0.28-34.65) | 0.9 (0.2-6.44) | 2.25 (0.12-37.1) | .005 |
| Prognostic nutritional index | 40 (29.4-51) | 38 (20.4-44) | 43.3 (26-52.2) | 40 (23-50) | <.001 |
| Total cholesterol, mg/dL | 190 (123-193) | 201 (84-310) | 187 (95-363) | 189 (71-406) | .735 |
| Parathyroid hormone, pg/mL | 434.7 (189.9-1640) | 264.1 (72.8-1001) | 272.1 (4.4-2119) | 248.8 (11.1-1001.1) | .141 |
| Hemoglobin A1c, % | 5.1 (4.5-5.9) | 4.8 (3-8.7) | 5.1 (4-8.6) | 5.3 (4-9.6) | .027 |
| Total follow-up, y | 2.09 (1-7.93) | 2.47 (0.35-7.7) | 4.62 (0.5-9.6) | 3.12 (0.61-9.29) | .029 |
| 5-y major CVE, No. (%) | 1 (14.3%) | 3 (23.1%) | 3 (4.7%) | 7 (11.9%) | .110 |
| Total major CVE, No. (%) | 1 (14.3%) | 4 (30.8%) | 4 (6.9%) | 7 (10.6%) | .071 |
| 5-y mortality, No. (%) | 2 (28.6%) | 11 (55%) | 1 (2%) | 7 (9.3%) | <.001 |
| Total mortality, No. (%) | 2 (28.6%) | 11 (55%) | 3 (5%) | 8 (10.7%) | <.001 |

***Abbreviations:*** CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; CVE, cardiovascular event; RRT, renal replacement therapy
*P* < .05 was considered significant.

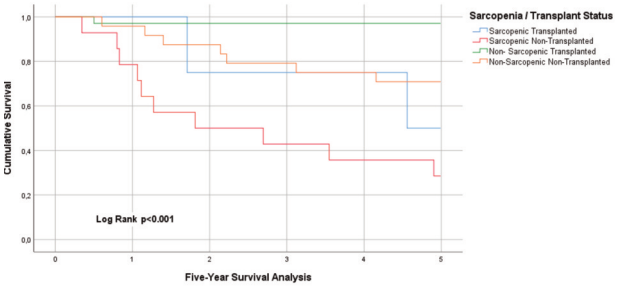
transplant group (n = 7), nonsarcopenic nontransplant group (n = 75), and sarcopenic nontransplant group (n = 20). There were 5 deaths in the transplant groups, with 2 who had sarcopenia. There were 19 deaths in the nontransplant groups, with 11 who had sarcopenia. The highest mortality rate was 55% and was observed in the sarcopenic nontransplant group.

**Figure 3.** Correlation Between Prognostic Nutritional Index and C-Reactive Protein-to-Albumin Ratio




In the 5-year Kaplan-Meier patient survival analysis, the nonsarcopenic transplant group had better survival outcomes than the nonsarcopenic nontransplant group (*P* = .005), the sarcopenic transplant group (*P* = .001), and the sarcopenic nontransplanted group (*P* < .001). The nonsarcopenic nontransplant group had a significantly better survival outcome than the sarcopenic nontransplant group (*P* = .006) (Figure 4). Survival was similar between the sarcopenic transplant group and the nonsarcopenic nontransplant group (*P* = .499).

**Figure 4.** Five-Year Patient Survival




In multivariate analysis, sarcopenia (hazard ratio [HR] = 10.277; 95% CI, 3.912-27.000; *P* < .001), not having a transplant (HR = 3.949; 95% CI, 1.301-11.993; *P* = .015), low PNI (HR = 3.532; 95% CI, 1.303-9.574; *P* = .013), and duration of renal replacement therapy (HR = 1.009; 95% CI, 1.002-1.015; *P* = .008) were significantly associated with mortality (Table 5).

## Relationship between sarcopenia and cardiovascular events

The CVE rate in our ESRD patients was 11.1%, and the CVE prevalence in sarcopenic patients was higher than in nonsarcopenic patients in follow-up

(25% vs 8.9%; $P = .049$). A total of 4 CVEs occurred in the transplant patient group, including in 1 patient with sarcopenia. In the nontransplant group, 11 CVEs were recorded, with 4 patients having sarcopenia. In the 5-year Kaplan-Meier analysis, the nonsarcopenic transplant group had significantly less CVEs than the sarcopenic nontransplant group ($P = .011$). There were no differences between the other groups regarding CVEs.

In the univariate Cox regression analysis in which we examined all ESRD patients, sarcopenia (HR = 3.635; 95% CI, 1.238-10.671; $P = 0.019$) and age (HR = 1.043; 95% CI, 1.003-1.084; $P = .033$) were significantly associated with the development of CVE. In multivariate analysis, sarcopenia (HR = 5.057; 95% CI, 1.560-16.394; $P = .007$) and male sex (HR = 5.141; 95% CI, 1.407-18.777; $P = .013$) were associated with the development of CVE (Table 5).

**Table 5.** Independent Predictors of Mortality and Cardiovascular Events

| | Hazard Ratio | 95%CI | *P* |
|---|---|---|---|
| Predictor of mortality | | | |
| Sarcopenia | 10.277 | 3.912-27.000 | <.001 |
| Not having a transplant | 3.949 | 1.301-11.993 | .015 |
| Low PNI | 3.532 | 1.303-9.574 | .013 |
| Duration of RRT | 1.009 | 1.002-1.015 | .008 |
| Predictor of CVE | | | |
| Sarcopenia | 5.057 | 1.560-16.394 | .007 |
| Male sex | 5.141 | 1.407-18.777 | .013 |

***Abbreviations:*** CVE, cardiovascular event; PNI, prognostic nutritional index; RRT, renal replacement therapy
$P < .05$ was considered significant.

## Discussion

We showed that CT-assessed sarcopenia, defined by low PMI, was almost 5 times more frequently prevalent in ESRD patients on kidney transplant waiting lists than in healthy controls (16.7% vs 3.4%; $P = .002$) and was positively correlated with PNI. In ESRD patients on waiting list, we observed a significant association among sarcopenia, mortality, and CVEs.

In CKD, chronic inflammation, uremic toxins, hormonal imbalance (insulin resistance, vitamin D deficiency, and hypogonadism), oxidative stress, metabolic acidosis, and increased ubiquitination play key roles in the increased catabolic process that results in sarcopenia.[16-18] Loss of amino acids during the dialysis process and decreased protein and calorie intake can cause negative energy and protein balance.[19] Decreased physical activity also causes loss of muscle mass and contributes to development of sarcopenia in dialysis patients.[20] In previous studies, the incidence of sarcopenia in CKD was reported to be between 12.6% and 20%, increasing as the CKD stage progresses.[21,22] According to a recently published meta-analysis, sarcopenia prevalence in dialysis patients ranged from 4% to 68%, depending on which diagnostic criteria were used, and the pooled estimated prevalence of sarcopenia was 28.5%.[6] Rate of sarcopenia also showed a wide range in studies that examined the frequency of sarcopenia evaluated only by muscle mass with BIA or DEXA (6.1%-48%).

As of yet, no gold standard method is available for determining muscle mass. Although BIA and DEXA have been extensively used, they are affected by the hydration status in dialysis patients. However, the use of CT to measure PMI is a novel method that may provide more accurate information on muscle mass and does not require the use of advanced radiologic software systems.[23] However, few data are available on CT-assessed sarcopenia prevalence of dialysis patients. The lack of relevant PMI cut-off values for assessing sarcopenia is the main reason. In our study, CT-assessed sarcopenia was found in 16.7% of ESRD patients using a fifth percentile cutoff value of healthy controls. We used this method to eliminate differences between males and females and geographical differences between the patients and to determine the most appropriate and ideal cut-off value for our study population.

Increased inflammation and malnutrition are strongly associated with the development of sarcopenia in ESRD patients.[4,24,25] Similarly, we also found lower albumin, lower PNI, and higher CAR levels in patients with sarcopenia as determined by PMI. The positive correlation of PMI and PNI and the negative correlation of PNI and CAR further confirm these findings. Thus, we may conclude that muscle mass can be used as an indicator of systemic inflammation and malnutrition.

An increased risk of mortality, morbidity, and CVEs has been reported in patients with sarcopenia.[5] The relationship between sarcopenia and mortality in ESRD patients has also been increasingly studied and reported in recent years.[26,27] In a study by Takata and colleagues, higher mortality was found in dialysis patients with low muscle mass detected

by PMI, which they determined with a similar method to the one used in our study.[28] Yajima and colleagues showed that CT-measured psoas muscle thickness predicts mortality in patients undergoing hemodialysis.[29] To date and to our knowledge, only 1 study of patients waiting for kidney transplant has used CT-assessed sarcopenia to assess the risk of mortality. Locke and colleagues highlighted that greater psoas lean muscle mass measured by abdomen CT was associated with decreased risk of mortality.[30] Similarly, in our study, the mortality rate in patients with sarcopenia waiting for transplant was significantly higher than patients without sarcopenia waiting for transplant (48.1% vs 5.9%; $P < .001$). In addition, being sarcopenic was found to be the strongest risk factor for mortality, at 5 years, in the multivariate analysis (HR = 10.277; 95% CI, 3.912-27.000; $P < .001$).

Studies examining the relationship between sarco-penia and CVE in the general population have shown that the risk of CVE increases in patients with low CT-assessed psoas muscle mass.[31] Chronic kidney disease is a well-known risk factor for CVE. In patients with CKD, low PMI was found to be an independent risk factor for major CVEs.[32] In a recent study of 244 HD patients, patients with sarcopenia had significantly higher CVEs than patients without sarcopenia.[33] In our study, the CVE rate in our ESRD patients was 11.1%, and the CVE prevalence in patients with sarcopenia was significantly higher than in patients without sarcopenia in follow-up (25% vs 8.9%; $P = .049$). Sarcopenia was also found to be the most significant risk factor for CVE in our ESRD patients (HR = 5.057; 95% CI, 1.560-16.394; $P = .007$). Nevertheless, our study should not be generalized since we only examined the patients on the waiting list. Patients with ESRD who are on the kidney transplant waiting list are in generally better condition, do not have serious comorbidities, and have a longer life expectancy, in contrast to general dialysis patients. The pathophysiology of sarcopenia in cardiovascular diseases includes hemodynamic and metabolic changes such as inflammation, neuroendocrine disorders, oxidative stress, insulin resistance, endothelial dysfunction, and low muscle blood flow, which result in impaired skeletal muscle. However, sarcopenia-related exercise intolerance also contributes to cardiovascular diseases.[34]

Kidney transplant is the best method for treatment of ESRD, with patient survival expected to be significantly improved posttransplant.[35,36] Indeed, in our study, better survival rates were found in those who received transplants than in those who did not have transplants. Moreover, the most important finding of our study is that transplant patients with sarcopenia had survival rates similar to patients without sarcopenia and who did not have transplants. This important finding shows that the presence of sarcopenia is critical for prediction of mortality even in transplant patients. Although many studies have reported the relationship between pretransplant sarcopenia and posttransplant morbidity and mortality in liver transplant recipients, the number of studies on kidney transplant recipients is limited.[12,37,38] Deliege and colleagues showed an association between pretransplant low muscle mass and increased posttransplant mortality in only older male kidney transplant recipients.[39] In a recent study, CT-assessed sarcopenia was used to show the pret-ransplant physical frailty phenotype, with the study demonstrating that frail recipients had higher risks of mortality and graft loss.[40] Furthermore, in a recent study of 484 kidney transplant patients, pretransplant sarcopenia influenced posttransplant wound healing, collection (hematoma and lymphocele), and acute rejection. For patients waiting for transplant, deter-mining whether patients have sarcopenia and providing necessary improvements (exercise and nutrition) will positively affect patient survival.[41]

We observed a significant relationship between low PNI value and mortality. The presence of sarcopenia has been previously shown to be associated with the risk of mortality and worse prognosis in patients on peritoneal dialysis.[42] Hori and colleagues also reported that low PNI levels pretransplant were an independent predictor of mortality in kidney transplant recipients.[43] Thus, we can conclude that the common indexes for inflammation and malnutrition can also be used as prognostic markers in wait-listed ESRD patients.

Sarcopenia is known to be increased in patients with ESRD and to be associated with mortality. Major causes of sarcopenia in CKD are CKD itself, aging, CKD-related dietary restrictions, physical inactivity, and chronic inflammation. Screening ESRD patients who are at risk for sarcopenia and early and timely identification may improve patient survival. Treatment with physical therapy, in particular resis-

tance training, nutritional support, and patient education are essential in the management of sarcopenia.[44]

Our study had some limitations. First, abdominal CT was used to measure muscle mass. The use of CT imaging is not currently recommended in kidney transplant candidates for pretransplant evaluation. Second, in line with retrospective nature of our study design, only patients who had previous abdominal CT for any reason were included the analysis. Therefore, the small number of patients and radiography exposure are major limitations of the study. Third, in our study, we were unable to use the full definition of sarcopenia according to the European Working Group on Sarcopenia in Older People.[40] In this definition, in addition to the presence of low muscle mass, muscle strength should also be considered for sarcopenia. However, it is well-known that muscle function, muscle strength, and physical performance are generally low in ESRD patients. Thus, we can conclude that low muscle mass is the most important criterion in the diagnosis of sarcopenia. Furthermore, it is well known that physical inactivation, obesity, diabetes, CKD, and all other chronic diseases can also contribute to sarcopenia. Sarcopenia itself can negatively affect these diseases. Thus, it is difficult to assess the contribution of each comorbidity to sarcopenia in this particular patient group.

## Conclusions

Computed tomography-assessed sarcopenia is approximately 5 times more frequent in kidney transplant candidates than in our healthy controls. The PNI in patients, used as a common marker of inflammation and nutrition, correlated with low muscle mass. Having low muscle mass increases the risk of mortality in both transplant patients and patients without transplant. For this reason, it is necessary to detect sarcopenia with low muscle mass in a timely manner, to consequently increase physical activity, and to try to correct it appropriately with exercise programs. Further large studies are needed to investigate the relationship of low muscle mass assessed by CT with inflammation and mortality, both in ESRD patients on the kidney transplant waiting list and in kidney transplant recipients.

## References


1. Rosenberg IH. Summary comments. *Am J Clin Nutr.* 1989;50(5):1231-1233.
2. Agarwal E, Miller M, Yaxley A, Isenring E. Malnutrition in the elderly: a narrative review. *Maturitas.* 2013;76(4):296-302. doi:10.1016/j.maturitas.2013.07.013
3. Kakiya R, Shoji T, Tsujimoto Y, et al. Body fat mass and lean mass as predictors of survival in hemodialysis patients. *Kidney Int.* 2006;70(3):549-556. doi:10.1038/sj.ki.5000331
4. Kim JK, Choi SR, Choi MJ, et al. Prevalence of and factors associated with sarcopenia in elderly patients with end-stage renal disease. *Clin Nutr.* 2014;33(1):64-68. doi:10.1016/j.clnu.2013.04.002
5. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on sarcopenia in older people. *Age Ageing.* 2010;39(4):412-423. doi:10.1093/ageing/afq034
6. Shu X, Lin T, Wang H, et al. Diagnosis, prevalence, and mortality of sarcopenia in dialysis patients: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle.* 2022;13(1):145-158. doi:10.1002/jcsm.12890
7. Hamaguchi Y, Kaido T, Okumura S, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. *Nutrition.* 2016;32(11-12):1200-1205. doi:10.1016/j.nut.2016.04.003
8. Burton LA, Sumukadas D. Optimal management of sarcopenia. *Clin Interv Aging.* 2010;5:217-228. doi:10.2147/cia.s11473
9. Hanna RM, Ghobry L, Wassef O, Rhee CM, Kalantar-Zadeh K. A practical approach to nutrition, protein-energy wasting, sarcopenia, and cachexia in patients with chronic kidney disease. *Blood Purif.* 2020;49(1-2):202-211. doi:10.1159/000504240
10. Ataş DB, Aşıcıoğlu E, Tuğcu M, Arıkan İH, Velioğlu A. Long-term predictors of mortality in peritoneal dialysis patients. *J Nephrol.* 2021;30(3):1-6.
11. Ranzani OT, Zampieri FG, Forte DN, Azevedo LC, Park M. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. *PLoS One.* 2013;8(3):e59321. doi:10.1371/journal.pone.0059321
12. Hamaguchi Y, Kaido T, Okumura S, et al. Impact of skeletal muscle mass index, intramuscular adipose tissue content, and visceral to subcutaneous adipose tissue area ratio on early mortality of living donor liver transplantation. *Transplantation.* 2017;101(3):565-574. doi:10.1097/TP.0000000000001587
13. Mirili C, Yilmaz A, Demirkan S, Bilici M, Basol Tekin S. Clinical significance of prognostic nutritional index (PNI) in malignant melanoma. *Int J Clin Oncol.* 2019;24(10):1301-1310. doi:10.1007/s10147-019-01461-7
14. Barutcu Atas D, Tugcu M, Asicioglu E, et al. Prognostic nutritional index is a predictor of mortality in elderly patients with chronic kidney disease. *Int Urol Nephrol.* 2022;54(5):1155-1162. doi:10.1007/s11255-021-03002-6
15. Masuda T, Shirabe K, Ikegami T, et al. Sarcopenia is a prognostic factor in living donor liver transplantation. *Liver Transpl.* 2014;20(4):401-407. doi:10.1002/lt.23811
16. Gungor O, Ulu S, Hasbal NB, Anker SD, Kalantar-Zadeh K. Effects of hormonal changes on sarcopenia in chronic kidney disease: where are we now and what can we do? *J Cachexia Sarcopenia Muscle.* 2021;12(6):1380-1392. doi:10.1002/jcsm.12839
17. Domanski M, Ciechanowski K. Sarcopenia: a major challenge in elderly patients with end-stage renal disease. *J Aging Res.* 2012;2012:754739. doi:10.1155/2012/754739
18. Sabatino A, Cuppari L, Stenvinkel P, Lindholm B, Avesani CM. Sarcopenia in chronic kidney disease: what have we learned so far? *J Nephrol.* 2021;34(4):1347-1372. doi:10.1007/s40620-020-00840-y
19. Deleaval P, Luaire B, Laffay P, et al. Short-term effects of branched-chain amino acids-enriched dialysis fluid on branched-chain amino acids plasma level and mass balance: a randomized cross-over study. *J Ren Nutr.* 2020;30(1):61-68. doi:10.1053/j.jrn.2019.03.079

20. Regolisti G, Maggiore U, Sabatino A, et al. Interaction of healthcare staff's attitude with barriers to physical activity in hemodialysis patients: a quantitative assessment. *PLoS One*. 2018;13(4): e0196313. doi:10.1371/journal.pone.0196313
21. Isoyama N, Qureshi AR, Avesani CM, et al. Comparative associations of muscle mass and muscle strength with mortality in dialysis patients. *Clin J Am Soc Nephrol*. 2014;9(10):1720-1728. doi:10.2215/CJN.10261013
22. Moon SJ, Kim TH, Yoon SY, Chung JH, Hwang HJ. Relationship between stage of chronic kidney disease and sarcopenia in Korean aged 40 years and older using the Korea National Health and Nutrition Examination surveys (KNHANES IV-2, 3, and V-1, 2), 2008-2011. *PLoS One*. 2015;10(6):e0130740. doi:10.1371/journal.pone.0130740
23. Buckinx F, Landi F, Cesari M, et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. *J Cachexia Sarcopenia Muscle*. 2018;9(2):269-278. doi:10.1002/jcsm.12268
24. Fahal IH. Uraemic sarcopenia: aetiology and implications. *Nephrol Dial Transplant*. 2014;29(9):1655-1665. doi:10.1093/ndt/gft070
25. Kaizu Y, Ohkawa S, Odamaki M, et al. Association between inflammatory mediators and muscle mass in long-term hemodialysis patients. *Am J Kidney Dis*. 2003;42(2):295-302. doi:10.1016/s0272-6386(03)00654-1
26. Lin YL, Liou HH, Wang CH, et al. Impact of sarcopenia and its diagnostic criteria on hospitalization and mortality in chronic hemodialysis patients: a 3-year longitudinal study. *J Formos Med Assoc*. 2020;119(7):1219-1229. doi:10.1016/j.jfma.2019.10.020
27. Wilkinson TJ, Miksza J, Yates T, et al. Association of sarcopenia with mortality and end-stage renal disease in those with chronic kidney disease: a UK Biobank study. *J Cachexia Sarcopenia Muscle*. 2021;12(3):586-598. doi:10.1002/jcsm.12705
28. Takata T, Motoe A, Tanida K, et al. Feasibility of computed tomography-based assessment of skeletal muscle mass in hemodialysis patients. *J Nephrol*. 2021;34(2):465-471. doi:10.1007/s40620-020-00871-5
29. Yajima T, Arao M, Yajima K, Takahashi H. Usefulness of computed tomography-measured psoas muscle thickness per height for predicting mortality in patients undergoing hemodialysis. *Sci Rep*. 2021;11(1):19070. doi:10.1038/s41598-021-98613-5
30. Locke JE, Carr JJ, Nair S, et al. Abdominal lean muscle is associated with lower mortality among kidney waitlist candidates. *Clin Transplant*. 2017;31(3). doi:10.1111/ctr.12911
31. Imaizumi T, Shiga Y, Idemoto Y, et al. Associations between the psoas major muscle index and the presence and severity of coronary artery disease. *Medicine (Baltimore)*. 2020;99(28):e21086. doi:10.1097/MD.0000000000021086
32. Harada K, Suzuki S, Ishii H, et al. Impact of skeletal muscle mass on long-term adverse cardiovascular outcomes in patients with chronic kidney disease. *Am J Cardiol*. 2017;119(8):1275-1280. doi:10.1016/j.amjcard.2017.01.003
33. Hayashi H, Izumiya Y, Hayashi O, Ichii M, Tsujimoto Y, Yoshiyama M. Dynapenia is an independent predictor of cardio-cerebrovascular events in patients undergoing hemodialysis. *Heart Vessels*. 2022;37(6):1066-1074. doi:10.1007/s00380-021-02006-7
34. Zuo X, Li X, Tang K, et al. Sarcopenia and cardiovascular diseases: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2023;14(3):1183-1198. doi:10.1002/jcsm.13221
35. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*. 1999;341(23):1725-1730. doi:10.1056/NEJM199912023412303
36. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant*. 2011;11(10):2093-2109. doi:10.1111/j.1600-6143.2011.03686.x
37. Kaido T, Ogawa K, Fujimoto Y, et al. Impact of sarcopenia on survival in patients undergoing living donor liver transplantation. *Am J Transplant*. 2013;13(6):1549-1556. doi:10.1111/ajt.12221
38. van Vugt JLA, Alferink LJM, Buettner S, et al. A model including sarcopenia surpasses the MELD score in predicting waiting list mortality in cirrhotic liver transplant candidates: a competing risk analysis in a national cohort. *J Hepatol*. 2018;68(4):707-714. doi:10.1016/j.jhep.2017.11.030
39. Deliege PG, Braconnier A, Chaix F, et al. Skeletal muscle index as a prognostic marker for kidney transplantation in older patients. *J Ren Nutr*. 2021;31(3):286-295. doi:10.1053/j.jrn.2020.08.014
40. Chen X, Shafaat O, Liu Y, et al. Revision of frailty assessment in kidney transplant recipients: Replacing unintentional weight loss with CT-assessed sarcopenia in the physical frailty phenotype. *Am J Transplant*. 2022 Apr;22(4):1145-1157. doi:10.1111/ajt.16934
41. Beau M, Barbieux J, Bigot P, et al. Study of post-kidney transplantation parietal complications and presarcopenia. *Transplant Proc*. 2023;55(1):116-122. doi:10.1016/j.transproceed.2022.10.056
42. Kamijo Y, Kanda E, Ishibashi Y, Yoshida M. Sarcopenia and frailty in PD: impact on mortality, malnutrition, and inflammation. *Perit Dial Int*. 2018;38(6):447-454. doi:10.3747/pdi.2017.00271
43. Hori S, Ichikawa K, Morizawa Y, et al. Clinical significance of postoperative nutritional status as a prognostic factor in kidney transplant recipients. *Transplant Proc*. 2019;51(6):1763-1772. doi:10.1016/j.transproceed.2019.04.047
44. Zanker J, Sim M, Anderson K, et al. Consensus guidelines for sarcopenia prevention, diagnosis and management in Australia and New Zealand. *J Cachexia Sarcopenia Muscle*. 2023;14(1):142-156. doi:10.1002/jcsm.13115