Factors Associated With the Development of Sarcopenia in Kidney Transplant Recipients

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ABSTRACT

Introduction. Sarcopenia is characterized by an involuntary loss of skeletal muscle mass, strength, and function. Previous studies suggest that it is generally associated with aging and chronic kidney diseases. The focus of this study was on the association between sarcopenia and pre-sarcopenia in kidney transplant recipients.

Methods. Fifty-one patients who underwent kidney transplantation at Kansai Medical University Hospital were enrolled, and their sarcopenia status was evaluated between April and July 2016. Sarcopenia was defined according to the criteria for the Asia Working Group for Sarcopenia. Skeletal muscle mass index was measured by using dual-energy radiograph absorptiometry; the cutoff points were <7.0 kg/m^2 for male subjects and <5.4 kg/m^2 for female subjects. For hand grip strength, values <26 kg (male subjects) and <17 kg (female subjects) was judged as sarcopenia. In both sexes, the cutoff point for walking speed was <0.8 m/s.

Results. Fifty-one recipients (36 men and 15 women) who met the inclusion criteria were enrolled in the study. The mean age of the recipients was 46.2 ± 12.8 years, and the mean duration of dialysis was 2.72 ± 3.61 years. Overall, 6 recipients (11.8%) had sarcopenia, and 25 recipients (49.0%) had pre-sarcopenia; 20 (39.2%) did not have sarcopenia. There were significant differences in age, duration of dialysis, body mass index, and triglyceride levels between the subgroups of recipients with and without sarcopenia. Multivariate regression analysis showed that age and duration of dialysis were independent variables for sarcopenic status.

Conclusions. Our observations indicate that age and duration of dialysis before transplantation were independent determinants of sarcopenia and pre-sarcopenia in these kidney transplant recipients.

SARCOPENIA is defined as an involuntary loss of skeletal muscle mass (SMM), strength, and function. The prevalence of sarcopenia generally increases with aging and the occurrence of chronic kidney disease (CKD) [1]. A physiological decrease in muscle mass in aging populations has been found to increase the risk of a predisposition to physical disability [2]. Sarcopenia leads not only to a simple decline and restriction in the functional abilities of daily life but is also related to the development of numerous adverse medical manifestations. Reduced muscle mass has been frequently observed in patients with protein-energy wasting and those with CKD [3,4]. Moreover, sarcopenia in patients with end-stage renal disease is significantly associated with higher cardiovascular morbidity and mortality rates.

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Co-existing CKD has been shown to contribute to sarcopenia, and sarcopenia may prematurely develop at a younger age in kidney transplant recipients [5]. Few studies to date, however, have investigated the factors associated with sarcopenia in kidney transplant recipients. The goal of the present study, therefore, was to evaluate the clinical determinants of sarcopenia and pre-sarcopenia in kidney transplant recipients.

PATIENTS AND METHODS

Patient Characteristics

The study population consisted of 51 patients who underwent kidney transplantation at Kansai Medical University Hospital and were evaluated from April to July 2016. Patients were included if they were aged >20 years, had undergone renal transplantation at least 1 year before the study, and had an estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2. Because the following situations may impede accurate measurement of hand grip strength (HGS) and bioimpedance, patients who had difficulty in communicating with the researchers and individuals who had malignancy, arthritis, or neuromuscular diseases involving both hands, congestive heart failure/nephrotic syndrome with severe edema, a pacemaker or prosthesis, or severe electrolyte imbalance were excluded from the study.

The study protocol was approved by the institutional review board of Kansai Medical University and was performed in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Study Procedures

Height was measured to the nearest 0.5 cm via a stadiometer with patients barefoot. Body composition was measured by bioelectrical impedance analysis using an InBody S720 scanner (Biospace Co, Tokyo, Japan) while dressed in light clothing. Bioelectrical impedance analysis was also used to determine weight, basal metabolic rate, body fat mass, and SMM. Body mass index (BMI) was calculated as body weight divided by height squared. Body composition was determined by using whole-body dual-energy radiograph absorptiometry (QDR 4500A, Hologic Inc., Bedford, Mass, United States). Bone mineral content, fat mass, and lean soft tissue mass were measured separately for each part of the body, including the arms and legs. The lean soft tissue masses of the arms and legs were almost equal to SMM. The arm and leg SMM index (SMI) were defined as the lean mass, in kilograms, of the arms and legs, respectively, divided by height in meters squared. Appendicular SMI was defined as the sum of arm and leg SMIs.

HGS was evaluated by using a hand grip dynamometer (Sammons Preston Rolyan Co, Bolingbrook, Ill, United States). The maximum strength of the dominant hand of each subject was measured 3 times, and the average value was recorded. Walking speed was measured by determining the time required to walk for a distance of 10 meters.

Sarcopenia was defined according to the criteria of the Asia Working Group for Sarcopenia [6]. The cutoff points for SMI on dual-energy radiograph absorptiometry were <7.0 kg/m^2 for men and <5.4 kg/m^2 for women. The cutoff points for HGS were <26 kg for men and <17 kg for women. In both sexes, the cutoff point for walking speed was <0.8 m/s.

The pre-sarcopenia stage was defined as low SMI, with no effects on HGS or walking speed. The sarcopenia stage was defined as low SMI, plus low HGS or low walking speed (Table 1). The 51 recipients received standard induction immunosuppression consisting of tacrolimus, mycophenolate mofetil, basiliximab (anti-CD25), and prednisone. In 8 recipients who received ABO-incompatible grafts, rituximab (200 mg/m^2 per body surface area) was additionally administered 1 week before transplantation. Complications such as diabetes mellitus and hypertension were recorded.

Laboratory Measures

Blood samples were obtained from the antecubital vein between 8:30 and 10:00 AM after fasting for ≥8 hours. A hospital autoanalyzer was used to measure the following: complete blood cell counts; neutrophil counts; hemoglobin, albumin, and fasting plasma glucose concentrations; lipid profile; 24-hour protein excretion; and tests of graft function. Graft function was evaluated based on eGFR, which was calculated from serum creatinine concentrations using the standardized conversion formula for Japanese subjects [7].

Statistical Analysis

The 51 kidney transplant recipients were categorized into 3 subgroups (6 with sarcopenia, 25 with pre-sarcopenia, and 20 with non-sarcopenia). Data are expressed as mean ± standard deviation. Nonparametric data were analyzed with the Kruskal-Wallis test; if the results of this test were significant ($P < .05$), groups were compared by using the Mann-Whitney U test with a Bonferroni correction, with statistical significance defined as $P = .05/3$ or $P = .018$. Furthermore, the data were further examined by dividing patients into 2 groups: group 1, sarcopenia + pre-sarcopenia; and group 2, nonsarcopenia. Logistic regression analysis was used to determine the effect of sarcopenia-related parameters on the development of sarcopenia and pre-sarcopenia.

All statistical analyses were performed by using StatView for Windows statistical software (Abacus Concepts Inc., Berkeley, Calif, United States).

RESULTS

The 51 kidney transplant recipients who met the inclusion criteria consisted of 36 men and 15 women (mean age, 46.2 ± 12.8 years). Their mean time from transplantation was 7.1 ± 6.5 years, and their mean duration of dialysis was 2.72 ± 3.61 years. Six patients (11.8%) had sarcopenia, 25 (49.0%) had pre-sarcopenia, and 20 (39.2%) did not

Table 1. The Criteria of Sarcopenia by the Asia Working Group for Sarcopenia (AWGS)

	Muscle Mass (Skeletal Muscle Mass Index)	Muscle Strength (Handgrip Strength)		Performance (Walking Speed)
Presarcopenia	↓			
Sarcopenia	↓	↓	or	↓
Severe sarcopenia	↓	↓	and	↓

The cutoff points for skeletal muscle mass index (SMI) on DXA were <7.0 kg/m^2 for men and <5.4 kg/m^2 for women.

The cutoff points for handgrip strength (HGS) were <26 kg for men and <17 kg for women.

The cutoff point for walking speed was <0.8 m/s in both sexes.