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Original article

# Prevalence of and factors associated with sarcopenia in elderly patients with end-stage renal disease

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SUMMARY

*Background & aims:* We investigated the prevalence of sarcopenia in elderly patients with end-stage renal disease (ESRD) and its relationship with various markers of nutrition, cognitive function, depressive symptoms, inflammation and β2-microglobulin.
*Methods:* A cross-sectional study was conducted with 95 patients having ESRD aged over 50 years. Sarcopenia was defined as a decline in both muscle mass and strength.
*Results:* The mean age was 63.9 ± 10.0 years; 56.8% were men and 52.6% had diabetes. Sarcopenia was highly prevalent in elderly patients with ESRD (37.0% in men and 29.3% in women). Subjective Global Assessment (SGA), inflammatory markers and β2-microglobulin levels were significantly associated with sarcopenia, even after adjustment for age, gender, diabetes, and body mass index. Additionally, patients with depressive symptoms showed a higher risk of sarcopenia relative to those without depressive symptoms (odds ratio, OR = 6.87, 95% confidence interval, CI = 2.06–22.96) and sarcopenia was more likely to be present in patients with mild cognitive dysfunction (OR = 6.35, 95% CI = 1.62–34.96).
*Conclusions:* Sarcopenia is highly prevalent in elderly patients with ESRD and is closely associated with SGA, inflammatory markers, β2-microglobulin, depression and cognitive dysfunction.


## 1. Introduction

Although obesity is associated with an increased risk of mortality in the general population, several observational reports in patients with end-stage renal disease (ESRD) have suggested the opposite.[1] At the ESRD stage, being overweight or obese is associated with improved survival whereas being underweight is associated with increased mortality, presumably because a high body mass index (BMI) is usually linked to improved nutrition.[2] However, because being overweight is also linked to inflammation, this could be a contributing factor in protein-energy wasting (PEW) and increased mortality in overweight patients with ESRD.[3] Moreover, obesity in patients with ESRD cannot be estimated simply by a high BMI because this does not differentiate muscle mass from adipose tissue mass. Indeed, several studies have demonstrated that the protective effect conferred by a high BMI seems to be limited to high muscle mass, not high fat mass.[1]

Skeletal muscle protein, represented by lean body mass (LBM), is of particular concern in morbidity and mortality. Reduced muscle mass, as a common feature of PEW, is an important predictor of poor outcome in patients with ESRD.[4] Additionally, the strength of skeletal muscle is important. Handgrip strength (HGS) is the most common method for estimating upper extremity muscle strength. It may be more useful for patients whose anthropometric measurements fail to distinguish undernourished from underweight persons, such as those with ESRD. A decline in HGS is closely associated with an increased length of hospitalization and all-cause mortality in patients undergoing dialysis.[5]

Sarcopenia refers to the gradual decline in both muscle quantity and quality. Initially, it was used to describe the age-related loss of muscle mass and power. However, recently, it has been recognized as a syndrome related to various medical conditions because catabolic inflammatory processes often found in chronic diseases

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can enhance the process.[6,7] Numerous previous studies have reported the facilitative interaction between pro-inflammatory cytokines and PEW in this patient group, and PEW is regarded as an important predictor of survival.[8] Particularly in patients with ESRD, uremia-induced anorexia, acidosis, anemia, and hormonal derangements can result in impaired protein assimilation and aggravated muscle wasting. However, due to a lack of consensus on the diagnostic criteria of sarcopenia, various methods have been used to define sarcopenia in patients with ESRD.

In present study, we assessed muscle mass and strength in patients undergoing hemodialysis, and sarcopenia was defined as a decline in both muscle mass and strength. We expected sarcopenia to be more common in elderly patients with ESRD and hypothesized that inflammation, uremic toxins, cognitive dysfunction, and depression may be associated with sarcopenia. The purpose of this study was to determine the prevalence of sarcopenia in elderly patients with ESRD and to evaluate its relationship with various markers of nutrition, such as BMI, Subjective Global Assessment (SGA), serum albumin, cognitive function, depressive symptoms, and β2-microglobulin.

## 2. Materials and methods

### 2.1. Study subjects

This observational cross-sectional study was performed in three dialysis units of Hallym University Sacred Heart Hospital, Korea, between April 2011 and August 2011. The subjects were 95 elderly hemodialyis patients who had been maintained for at least 3 months. Elderly patients were defined as aged over 50 years. Patients were excluded if they met the following criteria: younger than 50 years, active infection or bleeding within 3 months before enrollment, a history of malignancy or other chronic inflammatory disease, and insufficient visual and hearing acuity to complete the tests. Demographic data, such as age, gender, education, and financial status, were obtained through patient interviews and later confirmed from medical records. Baseline comorbid conditions were scored using the Charlson comorbidity index (CCI). Blood samples were collected for biochemical determinations immediately before a mid-week hemodialysis session and plasma was separated and stored at −80 °C until the analysis.

### 2.2. Nutrition and inflammation status

For the assessment of nutritional status, biochemical analyses [serum albumin, prealbumin, creatinine, phosphates, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and total iron-binding capacity (TIBC)], SGA, and anthropometric measurement (height, dry weight, BMI, and triceps skin-fold thickness) were assessed. BMI was calculated using the following equation of BMI = weight/height$^2$ (kg/m$^2$), and triceps skin-fold thickness was obtained by one trained clinician using a Lange Skin-fold Caliper (Beta Technology Inc., Cambridge, MD, USA) immediately after the hemodialysis session. For SGA, five components from the medical history (weight change, dietary intake, gastrointestinal symptoms, functional capacity, comorbid conditions and its relationship to nutritional requirements) and three components of a brief physical examination (signs of fat and muscle wasting, alternations in fluid balance) were used with a seven-point scoring system.[9] High sensitivity C-reactive protein (hs-CRP) levels were checked using a BN II analyzer (Dade Behring, Newark, DE, USA) by a latex-enhanced immunonephelometric method, and serum IL-6 level was measured using with a Quantikine ELISA kit (R&D Systems, Minneapolis, MN, USA).

### 2.3. Depressive symptoms and cognitive function

The Beck Depression Inventory II (BDI-II) consists of 21 multiple-choice questions and scores for each item (range from 0 to 3), with a higher score representing a greater problem. The total score range is 0–63, in which a score of 0–13 represents minimal depression, and scores of 14–19, 20–28, and ≥29 are considered mild, moderate, and severe depression, respectively. A cutoff score of ≥16 was chosen to establish the presence of depression, as in previous studies.[10] To evaluate cognitive status, a brief neuropsychological test, the Mini-Mental State Examination (MMSE) was used. A cutoff score <24 was chosen to establish the presence of mild cognitive dysfunction.

### 2.4. Measurements of muscle mass and strength and assessment of sarcopenia

The quantification of muscle mass was assessed with a portable whole-body bioimpedance spectroscopy device (Body Composition Monitor; Fresenius Medical Care, Bad Homburg, Germany). The device could provide objective indicators of muscle mass (lean tissue mass, LTM) as well as fat mass and hydration status. LTM and fat mass were normalized to the body surface area (m$^2$) to obtain the Lean Tissue Index (LTI) and Fat Tissue Index (FTI). Low muscle mass was defined as an LTI of 2 standard deviations (SD) or more below the normal gender-specific means for young persons. For the determination of muscle strength, HGS was measured on the non-fistula hand after a dialysis session using a Jamar handheld dynamometer (JAMAR PLUS+; Sammons Preston, Inc., Bolingbrook, IL, USA), which has been established as a reliable measure in community-dwelling older adults. The subjects stood with both arms extended sideways from the body with the dynamometer facing away from the body. Three trials were performed with a rest period of at least 1 min between trials and the average value was recorded. Low muscle strength was classified as HGS less than 30 and 20 kg in men and women, respectively.[11] Sarcopenia is characterized by decreased skeletal muscle mass and strength with impaired physical performance. In this study, we adopted the European Working Group on Sarcopenia in Old People (EWGSOP) criteria.[6] Presarcopenia was defined as having low muscle mass and normal muscle strength, and sarcopenia was defined as having low muscle mass combined with low muscle strength.

### 2.5. Statistical analysis

Statistical analyses were performed using the SPSS software (ver. 18.0; SPSS Inc., Chicago, IL, USA). All data are expressed as means ± SD or median with ranges. The Kolmogorov–Smirnov test was used to analyze the normality of distribution, and for skewed data, including serum IL-6 and hs-CRP, natural log values were used. Pearson's correlation analysis was used to clarify the relationships between handgrip, LTI, FTI, BDI-II score, and various clinical and inflammatory parameters. Multiple logistic regression analysis was performed to find significant determinants of sarcopenia. $p$ Values <0.05 were deemed to indicate statistical significance.

## 3. Results

### 3.1. Patient characteristics

The subjects in the present study were 95 dialysis patients with a mean age of 63.9 ± 10.0 (range, 50–88) years; 57.2% ($n$ = 163) were men and 67.7% ($n$ = 193) had diabetes. Presarcopenia and sarcopenia were observed in 9 (9.5%) and 32 (33.7%), respectively.

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