

Prevalence of Sarcopenia and Dynapenia and Their Determinants in Iranian Peritoneal Dialysis Patients

Atefeh As'habi,¹ Iraj Najafi,² Hadi Tabibi,³ Mehdi Hedayati⁴

¹Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²Department of Nephrology, Tehran University of Medical Sciences, Tehran, Iran

³Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴Cellular and Molecular Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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INTRODUCTION

Patients with chronic kidney disease (CKD) frequently suffer from *uremic sarcopenia*, the presence of low skeletal muscle mass plus low muscle strength, low physical performance, or both, and *dynapenia*, the presence of low muscle strength.¹⁻⁷ Uremic sarcopenia and dynapenia are the consequences of increased catabolism due to high production of inflammatory cytokines, metabolic acidosis, hormonal changes, physical inactivity, dietary restrictions, amino acid and protein losses during dialysis, aging, muscle composition changes, and comorbid conditions such as diabetes mellitus,

Introduction. Uremic sarcopenia and dynapenia are prevalent in chronic kidney disease patients, including dialysis patients. The present study was designed to determine the prevalence of sarcopenia and dynapenia and their determinants in peritoneal dialysis (PD) patients in Tehran, Iran.

Materials and Methods. All eligible PD patients at the peritoneal dialysis centers of Tehran were included in this cross-sectional study. Skeletal muscle mass and muscle strength were assessed using bioelectrical impedance analysis and hand grip strength, respectively. Physical performance was determined by a 4-m walk gait speed test.

Results. The prevalence rates of dynapenia and sarcopenia were 43.0% and 11.5% in the PD patients, respectively. There were significant associations between the prevalence of dynapenia and the age of patients ($P = .03$), physical activity level ($P = .04$), and the presence of diabetes mellitus ($P = .005$). In addition, a significant association was found between the prevalence of sarcopenia and sex ($P = .009$).

Conclusions. This study indicates that uremic sarcopenia and dynapenia are prevalent in PD patients in Tehran, Iran. These conditions may contribute to physical disability, decreased the quality of life, increased morbidity, and a high mortality rate. Therefore, prevention and treatment of uremic sarcopenia and dynapenia are necessary for Iranian PD patients.

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infections, and neurodegenerative conditions.^{1-3,9-13} Sarcopenia and dynapenia result in physical disability, increased risk of falls and fractures, decreased the quality of life, increased morbidity (especially cardiovascular disease), and high mortality rates.^{1,4,14-19}

Few studies have been conducted to assess the prevalence of sarcopenia and dynapenia in CKD patients, and in particular, dialysis patients. Some studies showed that the prevalence of sarcopenia ranged between 5.9% and 60.0% in nondialysis-CKD patients^{6,12,20} and 3.9% and 63.0% in hemodialysis patients.^{5,8,15,21,22} In addition, some studies reported

the prevalence of dynapenia in hemodialysis patients to range between 44.9% and 88.3%.^{7,8,22}

To our knowledge, although peritoneal dialysis (PD) services are mostly in Tehran (the capital city of Iran), no comprehensive study has yet documented the prevalence of sarcopenia and dynapenia in Iranian PD patients. In addition, according to the available literature, no investigation worldwide has reported the prevalence of sarcopenia and dynapenia in PD patients. The present study was designed to determine the prevalence of sarcopenia and dynapenia, and their determinants in PD patients in Tehran, Iran.

MATERIALS AND METHODS

Participants

All eligible PD patients ($n = 79$) in peritoneal dialysis centers of Tehran were included in this cross-sectional study between November 2015 and January 2016. The inclusion criteria were age of 18 years and greater and being on continuous ambulatory PD for at least 6 months. The exclusion criteria were the presence of edema, based on physical examination, and peritonitis; after the treatment of edema and peritonitis, these PD patients would be enrolled in our study. The study protocol was approved by the Ethics Committee of the National Nutrition and Food Technology Research Institute of Iran, and all of the patients provided written informed consent.

Measurements

Height was measured to the nearest 0.5 cm, and dry body weight, to the nearest 0.1 kg. Skeletal muscle mass was assessed using bioelectrical impedance analysis (BIA) by a Body Composition Analyzer X-Contact 356 (Jawon Medical Co, Seoul, South Korea). All anthropometric and body composition measurements were performed in the fasting state, with an empty urinary bladder and gastrointestinal tract, and without dialysis solution in the peritoneal cavity. Skeletal muscle mass index was calculated as the ratio of skeletal muscle mass in kilograms to squared body height in meters.^{2,20,23} Several cutoffs have been proposed to determine low muscle mass. We considered a skeletal muscle mass index less than 10.76 kg/m^2 for men and less than 10.76 kg/m^2 for women as the cutoffs to diagnose low muscle mass.^{20,23} Two studies in CKD patients including hemodialysis

patients indicated sarcopenia based on these cutoffs were associated with mortality.^{20,23}

Muscle strength was assessed based on hand grip strength by means of a hydraulic hand dynamometer (Exacta, North Coast Medical, Giliory, USA). Hand grip strength was measured 3 times in the dominant hand with a 30-second rest interval between trials,^{24,25} and the maximum value was considered the measure of the patient's muscle strength.^{15,22,26} A low muscle strength was considered as a hand grip strength less than 26 kg for men and less than 18 kg for women.²⁷

Physical performance was determined by a 4-meter walk gait speed test.^{2,27} Each patient was asked to walk at their usual speed on a 4-meter course.^{2,26} The time was recorded by a chronometer in seconds. A gait speed lower than 0.8 m/s was an indicator of low physical performance.^{2,27} The diagnosis of sarcopenia was based on the presence of low skeletal muscle mass plus low muscle strength, low physical performance or both,² whereas dynapenia was determined on the basis of low muscle strength.²⁻⁴

The dietary intakes of the patients were assessed using a 3-day dietary recall, for 3 consecutive days,^{28,29} by a trained dietitian. Patients' diets were analyzed by the Nutritionist IV software (N Squared Computing, San Bruno, CA, USA) adjusted for some Iranian foods, especially Iranian breads and cheeses, to determine daily intakes of energy and protein. The intakes of the patients were compared with dietary guidelines for PD patients.³⁰ Physical activity level was estimated by using the long-form International Physical Activity Questionnaire.³¹ Physical activity levels based on metabolic equivalent scores (minutes per week) were classified into 3 categories of low (< 600 min/wk), moderate (600 min/wk to 2999 min/wk), and high ($\geq 3000 \text{ min/wk}$).^{31,32}

In the present study, serum concentration of high-sensitivity C-reactive protein, as an inflammation marker, was determined by enzyme-linked immunosorbent assay kits (Zellbio GmbH, Ulm, Germany). Intra-assay coefficient of variation for serum high-sensitivity C-reactive protein was 4.0%. Serum malondialdehyde concentration, as an oxidative stress marker, was assessed using a colorimetry method by commercial kits (Zellbio GmbH, Ulm, Germany), with an intra-assay coefficient of variation of 5.8 %. Serum

concentrations of creatinine and urea were measured using colorimetry methods by commercial kits (Pars Azemoon, Tehran, Iran) with the aid of a Selectra 2 Autoanalyzer (Vital Scientific, Spankeren, The Netherlands). Intra-assay coefficient of variations for serum creatinine and urea were less than 3%.

Dialysis adequacy (as total Kt/V per week) was determined for each patient by a Kt/V calculator, using information recorded in patient files, including blood urea concentration, 24-hour urine volume, urine urea concentration, 24-hour dialysis solution drain volume, dialysis solution urea concentration, weight, height, and age.³³ The peritoneal equilibration test for glucose was performed for each patient based on a 2-L 4.25% dextrose dwell with dialysate solution samples at zero and 4 hours during the dwell period. The ratio of dialysis solution glucose concentration at time 4 hours to dialysis solution glucose level at time zero was determined and then the percentage of glucose absorbed from the dialysis solution was calculated based on this ratio.^{30,34,35}

Statistical Analysis

Data were displayed as the mean \pm standard error. Statistical analysis of the data was performed using the SPSS software (Statistical Package for the Social Sciences, version 21.0, SPSS Inc, Chicago, IL, USA). The chi-square test was used to determine associations between qualitative variables. A *P* value less than .05 was considered significant.

RESULTS

Characteristics of the 79 PD patients are shown in Table 1. The underlying causes of kidney failure in the participating patients were diabetes mellitus (38%), hypertension (19%), glomerulonephritis (5%), urinary infection (5%), polycystic kidney disease (4%), nephrolithiasis (2.5%), nephrotic syndrome (5%), and other or unknown causes (21.5%).

Low muscle mass, low muscle strength, and low physical performance were observed in 18.0%, 43.0%, and 13.0% of the PD patients, respectively (Table 2). In addition, the prevalence rates of dynapenia and sarcopenia were 43.0% and 11.5%, respectively (Table 2).

There were significant associations between the prevalence of dynapenia with the age of the patients (*P* = .03), physical activity level (*P* = .04), and the presence of diabetes mellitus (*P* = .005; Table 3).

Table 1. Characteristics of Peritoneal Dialysis Patients

Characteristic	Value (%)
Age, y	
18 to 40	17 (21.5)
41 to 64	41 (52.0)
\geq 65	21 (26.5)
Sex	
Male	35 (44.0)
Female	44 (56.0)
Dialysis vintage, y	
\leq 5	67 (85.0)
> 5	12 (12.0)
Total dialysis adequacy (Kt/V)*	
$<$ 1.7	25 (38.5)
\geq 1.7	40 (61.5)
Physical activity (metabolic equivalent scores), min/wk	
Low (< 600)	33 (42.0)
Moderate (600 to 2999)	43 (54.0)
High (\geq 3000)	3 (4.0)
Mean serum creatinine, mg/dL†	5.5 \pm 0.2
Mean serum urea, mg/dL†	95 \pm 3

*From among 79 PD patients, 65 had information regarding Kt/V index available.

†Serum creatinine and urea are presented as mean \pm standard error.

Table 2. Prevalence of Muscular and Physical Conditions

Variable	Frequency (%)
Low muscle mass	14 (18)
Low muscle strength	34 (43)
Low physical performance	10 (13)
Dynapenia	34 (43)
Sarcopenia	9 (11.5)

No significant associations, however, were found between the prevalence of dynapenia and sex, dialysis vintage, total dialysis adequacy, energy and protein intakes, inflammation, oxidative stress, and intake of calcitriol (active form of vitamin D; Table 3).

There was a significant association between the prevalence of sarcopenia with male sex (*P* = .009; Table 4). However, no significant associations were observed between the prevalence of sarcopenia and the age of the patients, dialysis vintage, total dialysis adequacy, energy and protein intakes, physical activity level, inflammation, oxidative stress, intake of calcitriol, and the presence of diabetes mellitus (Table 4).

DISCUSSION

Sarcopenia and dynapenia are mainly observed in older people, and considered as two

Table 3. Characteristics of Peritoneal Dialysis Patients With and Without Dynapenia

Parameter	Dynapenia (%)		P
	Yes	No	
Sex			
Male	13 (37)	22 (63)	
Female	21 (48)	23 (52)	> .05
Age, y			
18 to 40	5 (29)	12 (71)	
41 to 64	15 (37)	26 (63)	
≥ 65	14 (67)	7 (33)	.03
Dialysis vintage, y			
≤ 5	28 (42)	39 (58)	
> 5	6 (50)	6 (50)	> .05
Total dialysis adequacy (Kt/V)*			
< 1.7	6 (24)	19 (76)	
≥ 1.7	18 (45)	22 (55)	> .05
Energy intake, kcal/kg/d			
Inadequate†	27 (42)	37 (58)	
Adequate	7 (47)	8 (53)	> .05
Protein intake, g/kg/d			
Inadequate (< 1.2)	32 (44)	41 (56)	
Adequate (≥ 1.2)	2 (33)	4 (67)	> .05
Physical activity (metabolic equivalent), min/wk			
Low (< 600)	19 (58)	14 (42)	
Moderate (600 to 2999)	15 (35)	28 (65)	
High (≥ 3000)	0	3 (100)	.04
Microinflammation (C-reactive protein > 3 mg/L)	23 (46)	27 (54)	> .05
Oxidative stress			
≤ Median serum malondialdehyde	15 (35)	28 (65)	
> Median serum malondialdehyde	17 (53)	15 (47)	> .05
Intake of calcitriol	18 (49)	19 (51)	> .05
Diabetes mellitus	19 (63)	11 (37)	.005

*From among 79 PD patients, 65 had information regarding Kt/V index available.

†Inadequate energy intake was defined as less than 30 kcal/kg/d for an age of 60 years and greater and less than 35 kcal/kg/d for an age less than 60 years.

age-related syndromes; however, they can develop in younger adults by catabolic diseases such as CKD. In fact, CKD increases protein catabolism and results in loss of muscle mass and strength.^{2,5,20}

Our study showed that the prevalence of dynapenia (the presence of low muscle strength) was 43.0% in adult PD patients in Tehran, Iran. Few studies have assessed prevalence of dynapenia in hemodialysis patients, but according to the available literature, no study in this field has been performed yet in PD patients. In agreement with our study, Leal and colleagues, in a study conducted in Brazil, reported that the prevalence of low muscle strength was 55.8% in hemodialysis patients.³⁶ Pinto and coworkers, in another study from Brazil, showed that 44.9% of hemodialysis patients had low muscle strength.⁷ Bataille and colleagues, in a study from France, showed that

88.3% of hemodialysis patients had low muscle strength.⁸ In another study from Brazil, the prevalence of low muscle strength was 85.0% in hemodialysis patients.²²

Dynapenia leads to physical disability and increased risk of cardiovascular diseases and mortality.^{4,15,18,37} One of the leading causes of dynapenia is the loss of skeletal muscle mass.^{4,38} However, muscle strength decreases more rapidly than muscle mass.^{4,38} It was thought that the loss of skeletal muscle mass largely explained low muscle strength, but some studies indicated that the contribution of muscle atrophy in the development of dynapenia is modest.⁴ Therefore, all factors that affect loss of skeletal muscle mass may cause dynapenia.^{3,38} These factors include inflammation, oxidative stress, metabolic acidosis, decreased secretion of testosterone, insulin resistance,

Table 4. Characteristics of Peritoneal Dialysis Patients With and Without Sarcopenia

Parameter	Sarcopenia (%)		P
	Yes	No	
Sex			
Male	8 (23)	27 (77)	
Female	1 (2)	43 (98)	.009
Age, y			
18 to 40	3 (18)	14 (82)	
41 to 64	3 (7)	38 (93)	
≥ 65	3 (14)	18 (86)	> .05
Dialysis vintage, y			
≤ 5	8 (12)	59 (88)	
> 5	1 (8)	11 (92)	> .05
Total dialysis adequacy (Kt/V)*			
< 1.7	4 (16)	21 (84)	
≥ 1.7	4 (10)	36 (90)	> .05
Energy intake, kcal/kg/d			
Inadequate†	8 (12.5)	56 (87.5)	
Adequate	1 (7)	14 (93)	> .05
Protein intake, g/kg/d			
Inadequate (< 1.2)	9 (12)	64 (88)	
Adequate (≥ 1.2)	0	6 (100)	> .05
Physical activity (metabolic equivalent), min/wk			
Low (< 600)	4 (12)	29 (89)	
Moderate (600 to 2999)	5 (12)	38 (88)	
High (≥ 3000)	0	3 (100)	> .05
Microinflammation (C-reactive protein > 3 mg/L)	8 (16)	42 (84)	> .05
Oxidative stress			
≤ Median serum malondialdehyde	4 (9)	39 (91)	
> Median serum malondialdehyde	5 (16)	27 (84)	> .05
Intake of calcitriol	3 (8)	34 (92)	> .05
Diabetes mellitus	2 (7)	28 (93)	> .05

*From among 79 PD patients, 65 had information regarding Kt/V index available.

†Inadequate energy intake was defined as less than 30 kcal/kg/d for an age of 60 years and greater and less than 35 kcal/kg/d for an age less than 60 years.

growth hormone resistance, physical inactivity, inadequate energy and protein intakes, and vitamin D deficiency.^{1,3,38} Another cause of dynapenia is an increased muscle fat content in CKD patients.^{4,38} It has been shown that fat infiltration into muscle lower muscle strength, muscle quality, and work performance.^{2,4,38} An important contributor to dynapenia is some impairment in the nervous system's ability, such as a reduction in activating voluntary contraction of skeletal muscle and a decrease in motor neuron excitation.^{3,4,38,39}

In our study, no significant associations were found between the prevalence of dynapenia and sex, dialysis vintage, total dialysis adequacy, energy and protein intakes, inflammation, oxidative stress, or intake of calcitriol (active form of vitamin D). However, a significant association was observed between the prevalence of dynapenia and the age

of patients. Although dynapenia was prevalent at each age group in adult PD patients, the frequency of dynapenia was significantly higher in PD patients, aged 65 years and older, compared to those below the age of 65 years. It may be due to the simultaneous presence of aging and CKD, as two contributors to dynapenia, in PD patients aged 65 years and older.¹ There was a significant association between the prevalence of dynapenia with physical activity level in our study and the prevalence of dynapenia in PD patients with low, moderate, and high levels of physical activity was 65%, 35%, and zero, respectively. It has been shown that physical activity, especially resistance exercise training, is an effective strategy for preventing and managing dynapenia.^{40,41}

In addition, a significant association was found between the prevalence of dynapenia and the

presence of diabetes mellitus. In this study, the prevalence of dynapenia in PD patients with diabetes mellitus was 2-fold higher than those without diabetes mellitus. In agreement with our study, Bentes and colleagues showed that muscle strength was significantly inversely associated with serum glucose in postmenopausal women with type 2 diabetes mellitus.⁴² In diabetic patients, insulin deficiency, ketoacidosis, and oxidative stress result in muscle protein catabolism and consequently loss of muscle strength.^{1,14,43-45}

The frequency of low muscle mass, low muscle strength, and low physical performance was 18%, 43% and 13% in our PD patients, respectively. Also, our study showed that the prevalence of sarcopenia (the presence of low skeletal muscle mass plus low muscle strength, low physical performance, or both) was 11.5% in adult PD patients of Tehran. Limited studies have determined prevalence of sarcopenia in patients with CKD, including hemodialysis patients. To our knowledge, no research in this field has been done yet in PD patients. In agreement with our study, some research reported that the prevalence of sarcopenia ranged between 5.9% and 60.0% in nondialysis CKD patients.^{6,12,20} In addition, Kim and coworkers, in a study conducted in North Korea, showed that the prevalence of sarcopenia in hemodialysis patients was 37.0% in men and 29.3% in women.²¹ In Isoyama and colleagues' study, the prevalence of sarcopenia was 20.0% in dialysis patients.¹⁵ Lamarca and coworkers, in a study from Brazil, reported that the prevalence of sarcopenia ranged between 4.0% and 63.0% in elderly hemodialysis patients according to different methods and cutoff points.²² Bataille and colleagues, in a study from France, showed that 31.5% of hemodialysis patients had sarcopenia.⁸ In Ren and colleagues' study, the incidence of sarcopenia was 13.7% in total hemodialysis patients and 33.3% in hemodialysis patients over 60 years.²³ Kittikulnam and colleagues, in a study conducted in the United States, reported that the prevalence of sarcopenia was 3.9% in hemodialysis patients.⁵

Sarcopenia results in physical disability, increased risk of falls and fractures, decreased the quality of life, increased morbidity, especially cardiovascular disease, and a high mortality rate.^{1,14-17} Uremic sarcopenia may be caused by inflammation, oxidative stress, metabolic acidosis, decreased secretion of testosterone, insulin resistance, growth

hormone resistance, physical inactivity, inadequate energy and protein intakes, and vitamin D deficiency.^{1,38} These factors may mediate sarcopenia through increasing muscle protein catabolism and reducing muscle protein synthesis.^{1,38}

In our study, a significant association was found between sarcopenia and sex. The prevalence of sarcopenia in male PD patients was significantly higher as compared to their female counterparts, which may be due to decreased secretion of testosterone,¹ resulting in reduced muscle protein synthesis and increased muscle protein catabolism.¹ The present study showed that sarcopenia was prevalent at each age group in adult PD patients and no significant association was found between the prevalence of sarcopenia with the age of PD patients. In our study, there were no significant associations between the prevalence of sarcopenia with dialysis vintage, total dialysis adequacy, energy intake, oxidative stress, intake of calcitriol, and diabetes mellitus. The prevalence of sarcopenia in PD patients with low, moderate, and high levels of physical activity was 12%, 12% and zero, respectively, but no significant association was observed between the prevalence of sarcopenia and physical activity level. The prevalence of sarcopenia was 16% and 4% in PD patients with and without inflammation, respectively, but this difference was not significant. In addition, the prevalence of sarcopenia was zero in PD patients with adequate protein intake, whereas it was 12% in PD patients with inadequate protein intake; however, this difference was not significant.

Prevention and treatment strategies for uremic sarcopenia and dynapenia include an increase in physical activity especially resistance exercise training, adequate energy and protein intakes, reduction of inflammation by L-carnitine therapy,^{38,46-48} and if is needed, androgen therapy.^{38,46}

CONCLUSIONS

Uremic sarcopenia and dynapenia are prevalent in PD patients in Tehran, Iran, which may contribute to physical disability, decreased the quality of life, increased morbidity, especially cardiovascular disease, and a high mortality rate. Therefore, prevention and treatment of uremic sarcopenia and dynapenia are necessary for Iranian PD patients.

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CONFLICT OF INTEREST

None declared.

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Correspondence to:

Hadi Tabibi, PhD

Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, 46, West Arghavan St, Farahzadi Blvd, Shahrok Qods, PO Box: 19395-4741, Tehran, Iran

Tel: +98 21 2235 7483-5

Fax: +98 21 2236 0660

E-mail: hadtabibi@yahoo.com

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