Original article

Sarcopenia in hemodialysis patients from Buenos Aires, Argentina

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Abstract

Objectives: Sarcopenia is the loss of skeletal muscle mass and function that occurs with aging that can lead to greater morbidity and mortality. Chronic kidney disease and hemodialysis (HD) favors the development of sarcopenia. We studied the prevalence of sarcopenia and its components using European Working Group on Sarcopenia in Elderly People 2 proposed criteria and risk factors for its development in HD patients.

Methods: In 100 adult HD patients, we evaluated: hand grip strength (HGS), muscle mass by dual energy X-ray absorptiometry and physical performance (gait-speed and sit-stand test).

Results: Sixty patients were male and 40 were female; mean age 55.6 years. Prevalence of sarcopenia was 16% (11.1% in males and 25% in females; P = 0.05); 7% had severe sarcopenia. Prevalence of low HGS was 33% in males and 28% in females; low muscle mass was 30% in males but 70% in females and low physical performance 23% in males and 45% in females. Falls were reported by 23 patients. Patients with lower HGS had a higher prevalence of falls in the last year (40% two or more falls; P = 0.03). Only females with sarcopenia had lower bone mineral content. Neither age, body mass index, time on dialysis, or prevalence of diabetes predicted sarcopenia.

Conclusions: A significant proportion of dialysis patients had sarcopenia, more frequent in females. Low HGS was associated with a higher prevalence of falls. Only females with sarcopenia had lower bone mineral content.

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1. Introduction

Sarcopenia is the loss of muscle mass and function that occur with aging [1,2]. This geriatric syndrome can lead to mobility disorders, increased frequency of falls, fractures and immobilization, associated with increases in health costs by hospitalization [3,4]. Since 2016 the ICD (International Statistical Classification of Disease and Related Health Problems) of the World Health Organization has recognized sarcopenia as a disease (ICD-10 CM M62.84) [5]. Loss of muscle mass can be influenced by several factors, including malnutrition, disuse, drugs, and certain chronic diseases (HIV, liver disease, kidney disease etc.) [1]. There are several definitions referring to sarcopenia, each can vary according to the method used to measure each of its components [6,7]. A recent consensus published in 2019 by the European Working Group on Sarcopenia in Elderly People 2 (EWGSOP2) proposes cutoff values to assess the different parameters involved (muscle strength, mass and physical performance) [8].

Uremic state of chronic kidney disease constitutes a situation associated with hyper catabolism. Associated with this occurs the release of pro-inflammatory cytokines, metabolic acidosis, and the dialysis procedure per se, factors that can influence the progressive deterioration of muscle mass and function [9]. Several studies have found an increased mortality in hemodialyzed patients with low muscle mass [10,11].

The reported prevalence of sarcopenia in patients with chronic kidney disease (CKD) is variable. Kim et al. found a prevalence of 37% in men and 29.3% in women with terminal CKD [12]. However, in different reports the prevalence has varied from 4 to 60% depending on the different stages of chronic kidney disease [13,14].

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In hemodialysis patients, studies are inconclusive, detecting a prevalence of low muscle strength or dynapenia that can reach up to approximately 50%. Independent of muscle mass, loss of strength constitutes an important predictor of morbidity and mortality. Thus, recognizing this component of sarcopenia is cornerstone in the current nephrology practice [6,15,16].

In our country, there is little data on the loss of muscle strength mass and function in hemodialysis patients. The objectives of the present study were: 1) evaluate the prevalence of sarcopenia and its different components as muscle strength, mass and physical performance using the criteria proposed by the EWGSOP2 consensus; 2) evaluate the differences between women and men, with and without sarcopenia, and 3) find probable risk factors for the development of sarcopenia in our hemodialysis population.

2. Methods

2.1. Study design

This was a cross-sectional study, carried out between March 2015 and February 2018. We included 100 prevalent hemodialysis patients (more than 6 months on the procedure), males and females over 18 years of age that were treated in 5 centers of the Fresenius Medical Care (FMC) Argentina in the city of Buenos Aires (FMC Caballito, FMC Fundación Favaloro, FMC Hospital Alemán, and FMC Mansilla, FMC Moron). A detailed medical history was obtained from their medical charts: cause of chronic kidney disease, start date of hemodialysis, personal and family history, and falls (more than 2 during the previous year). All body composition determinations, muscle strength and physical performance tests were performed between the 2 and 3rd weekly dialysis sessions by the same evaluator (RA). The diagnosis of sarcopenia was made according to the criteria proposed by the European working group on sarcopenia in the elderly (EWGSOP2). According to this criteria sarcopenia is defined as having a low muscle strength (< 27 Kg for males and < 16 Kg for females), and a low muscle mass: skeletal muscle index (SMI) < 70 kg/m2 for males and < 5.5 kg/m2 for females), or low appendicular muscle mass (AMM) for males < 20 kg and for females < 18 kg. The presence of low physical performance (presence of low gait speed, ≤ 0.8 m/s for both men and women or sit-stand test > 15 seconds for 5 rises) was used to define severe sarcopenia.

Among the anthropometric measurements, we determined height and weight, to calculate body mass index (BMI, kg/m²). Monthly laboratory determinations, closest to the determinations of muscle mass and strength, were registered: albumin, C-reactive protein (CRP), creatinine, total serum calcium, serum phosphate, intact parathyroid hormone (iPTH), total alkaline phosphatase, hematocrit and hemoglobin. These determinations were made by routine automated laboratory methods.

The study was conducted in accordance with declaration of Helsinki and was approved by the institutional review board of the Metabolic Research Institute (Approval number: IDIM-001-2014). Patients gave their informed consent to participate in the study.

2.2. Body composition measurements by dual-energy X-ray absorptiometry (DXA)

Body composition was measured by DXA with GE Lunar Prodigy equipment (GE Lunar, Madison, WI, USA). The whole-body composition was performed using the specific software provided by the manufacturer. Briefly, using specific anatomic landmarks, legs, arms, and trunk were isolated on the skeletal X-ray anterior view by DXA. Whole-body scans provided measurements of total and regional lean mass (kg), fat mass (kg), android gynoid (A/G) index, the percentage of fat in the different regions, and bone mineral content (g). Four-member appendicular muscle mass (AMM, kg) was recorded; this value divided by height2 was used to determine skeletal muscle mass index or SMI (AMM/m²).

2.3. Measurement of hand grip strength (HGS) and physical performance determinations

Muscle strength was assessed by HGS (Jamar Hydraulic Hand Dynamometer, JLW Instruments, Chicago, IL, USA), 3 determinations in the arm without arteriovenous fistula. The best value was released as a reference. Cutoff values, considered as reduction in muscle strength, were less than 16 kg in women and 27 kg in men. The 4-m walk gait speed was taken after a practice test and low walking speed was defined as walking speed slower than 0.8 m/s. In the sit-stand test, the time taken for 5 repetitions without hand help was recorded. Low sit-stand test was defined as > 15 s.

2.4. Statistical analysis

The means and their standard deviation of quantitative variables for both men and women are reported. The normality of the data was evaluated by test of Shapiro-Wilk. The comparison

| Etiology                      | Number |
|-------------------------------|--------|
| Glomerular disease            | 26     |
| Diabetes mellitus             | 19     |
| Polycystic kidney disease     | 17     |
| Hypertension/angio-sclerosis  | 14     |
| Renal obstructive uropathy    | 5      |
| Others                        | 6      |
| Unknown                       | 13     |
between the 2 groups was made by Wilcoxon Mann Whitney test for non-parametric variables, and Student T test for those with normal distribution. Variables with normal distribution are expressed with their mean and standard deviation (SD) and those without normal distribution are expressed with their correspond-

Table 3

| Variable                  | Without sarcopenia (n = 54) | With sarcopenia (n = 6) | P-value |
|---------------------------|-----------------------------|-------------------------|---------|
| Age, yr                   | 55.0 (46.0–63.0)            | 64.0 (36.0–76.0)        | 0.1890  |
| Weight, kg                | 74.5 (88.5–92.0)            | 69.0 (60.0–88.5)        | 0.4322  |
| Height, m                 | 1.71 (1.65–1.75)            | 1.66 (1.60–1.79)        | 0.7158  |
| BMI, kg/m²                | 26.1 (23.0–31.0)            | 24.4 (20.5–28.3)        | 0.4668  |
| Time in HD, months        | 36.0 (21.0–60.0)            | 24.0 (9.0–36.0)         | 0.1771  |
| Fat, kg                   | 24.0 (16.4–30.5)            | 24.3 (10.6–33.2)        | 0.9253  |
| Fat, %                    | 30.6 (23.5–36.6)            | 35.3 (19.2–39.4)        | 0.8329  |
| A/G index                 | 1.22 (1.07–1.36)            | 1.09 (0.82–1.39)        | 0.4119  |
| BMC, g                    | 2643 (2249–2862)            | 2620 (2190–2692)        | 0.8329  |
| SMI, kg/m²                | 7.6 (7.1–8.2)               | 6.9 (6.6–7.1)           | 0.0106  |
| MM arms, kg               | 6.07 (5.53–6.53)            | 4.59 (4.21–5.84)        | 0.0138  |
| MM legs, kg               | 16.21 (14.82–18.93)         | 14.82 (12.65–16.35)     | 0.0748  |
| Hand grip strength, kg    | 30.0 (20.0–38.0)            | 24.0 (20.0–26.0)        | 0.0009  |
| Gait speed, m/s           | 1.0 (0.9–1.1)               | 0.90 (0.80–0.94)        | 0.3214  |
| Sit/Stand, s              | 11.17 (9.82–13.00)          | 11.00 (9.62–14.50)      | 0.8881  |
| Albumin, g/dL             | 4.1 (3.9–4.3)               | 3.9 (3.8–4.2)           | 0.1493  |
| CRP, mg/dL                | 1.0 (0.90–1.20)             | 1.2 (0.90–1.30)         | 0.5798  |
| Creatinine, mg/dL         | 10.0 (8.0–11.2)             | 8.8 (8.0–11.6)          | 0.7288  |
| Calcium, mg/dL            | 8.7 (8.2–9.1)               | 8.9 (8.0–9.1)           | 0.9999  |
| Phosphate, mg/dL          | 4.9 (4.3–5.4)               | 4.3 (4.0–6.5)           | 0.6585  |
| iPTH, pg/mL               | 556 (360–790)               | 339 (235–417)           | 0.1453  |
| ALP, IU                   | 97.0 (72–122)               | 81.0 (66–204)           | 0.6397  |
| Hematocrit, %             | 35.0 (30–37)                | 34.0 (30–36)            | 0.3139  |
| Hemoglobin, g/dL          | 11.5 (10.5–12.0)            | 11.0 (9.7–12.5)         | 0.5320  |

Median (interquartile range); HD, hemodialysis; BMI, body mass index; A/G, android/gynoid; BMC, bone mineral content; SMI, skeletal mass index; MM, muscle mass; AMM, appendicular muscle mass; CRP, C-reactive protein; PTH, parathyroid hormone; ALP, alkaline phosphatase.

used to determine the influence of independent variables on muscle strength, mass, and physical performance. We performed logistic regression analysis to evaluate if age, BMI, time on dialysis or prevalence of diabetes predicted sarcopenia in this cohort of hemodialyzed patients. Differences were considered significant if P < 0.05. Statistical analyses were performed with Statistix 7.0 (Analytical Software, Tallahassee, FL, USA).

Table 4

| Variable                  | Without sarcopenia (n = 30) | With sarcopenia (n = 10) | P-value |
|---------------------------|-----------------------------|-------------------------|---------|
| Age, yr                   | 57.0 (49.0–65.0)            | 62.3 (56.0–68.0)        | 0.3904  |
| Weight, kg                | 59.3 (53.0–73.0)            | 55.0 (49.6–62.3)        | 0.1992  |
| Height, m                 | 1.55 (1.51–1.60)            | 1.52 (1.49–1.55)        | 0.2162  |
| BMI, kg/m²                | 25.3 (23.2–29.6)            | 22.8 (21.9–27.6)        | 0.2502  |
| Time in HD, months        | 33 (12–66)                 | 27 (6–60)               | 0.7330  |
| Fat, kg                   | 24.4 (16.3–33.8)            | 18.4 (13.3–26.4)        | 0.2245  |
| Fat, %                    | 39.8 (31.3–46.3)            | 36.1 (31.1–43.6)        | 0.6271  |
| A/G index                 | 0.94 (0.83–1.06)            | 0.93 (0.84–1.12)        | 0.6890  |
| BMC, g                    | 1918 (1675–2169)            | 1650 (1466–1773)        | 0.0039  |
| SMI, kg/m²                | 6.0 (5.5–6.5)               | 5.4 (5.3–5.6)           | 0.0046  |
| MM arms, kg               | 3.69 (3.09–4.24)            | 3.06 (2.91–3.11)        | 0.0013  |
| MM legs, kg               | 11.09 (10.11–12.61)         | 9.46 (9.11–9.63)        | 0.0008  |
| AMM, kg                   | 14.71 (13.50–16.83)         | 12.52 (11.93–12.97)     | 0.0001  |
| Hand grip strength, kg    | 19.0 (18.0–22.0)            | 14.0 (12.0–14.0)        | 0.0001  |
| Gait speed, m/s           | 1.00 (0.82–1.10)            | 0.90 (0.80–1.10)        | 0.5802  |
| Sit/Stand, s              | 12.44 (10.71–15.14)         | 11.40 (9.91–12.00)      | 0.2500  |
| Albumin, g/dL             | 4.0 (3.9–4.3)               | 4.0 (3.9–4.2)           | 0.6943  |
| CRP, mg/dL                | 1.0 (0.9–1.2)               | 1.1 (0.7–1.3)           | 0.8190  |
| Creatinine, mg/dL         | 8.4 (6.2–9.5)               | 7.1 (5.4–9.0)           | 0.3230  |
| Calcium, mg/dL            | 8.8 (8.6–9.4)               | 8.6 (8.2–9.1)           | 0.2035  |
| Phosphate, mg/dL          | 5.0 (4.3–5.7)               | 4.5 (3.8–5.2)           | 0.3148  |
| iPTH, pg/mL               | 426 (241–720)               | 417 (322–735)           | 0.6856  |
| ALP, IU                   | 97 (80–126)                | 100 (93–138)            | 0.2371  |
| Hematocrit, %             | 33 (31–36)                 | 35 (34–38)              | 0.3239  |
| Hemoglobin, g/dL          | 11.2 (10.0–11.9)            | 10.9 (10.6–11.7)        | 0.6167  |

Median (interquartile range); HD, hemodialysis; BMI, body mass index; A/G, android/gynoid; BMC, bone mineral content; SMI, skeletal mass index; MM, muscle mass; AMM, appendicular muscle mass; CRP, C-reactive protein; PTH, intact parathyroid hormone; ALP, alkaline phosphatase.
3. Results

Of the 100 patients, 60 were male and 40 were female. Their clinical characteristics of the patients are presented in Table 1. Etiology on CKD is presented in Table 2.

The prevalence of sarcopenia and severe sarcopenia was 16% and 7% in the whole group. In men the prevalence of sarcopenia was 11.1%, low muscle mass 33%, low muscle mass in 30%, and a low physical performance in 23%. In females the prevalence of sarcopenia was 25%, low muscle mass 70%, and low physical performance in 45%. A total of 23 patients reported falls. Patients with low muscle strength had more falls during the previous year (40%; P = 0.03).

Males with sarcopenia (Table 3) had a HGS (24 vs 30 kg; P < 0.001) and SMI (6.9 vs 7.6 kg/m²; P = 0.01) lower than those without sarcopenia. Females with sarcopenia (Table 4) also had a HGS (14 vs 19 kg; P = 0.001) and SMI (5.4 vs 6.0 kg/m²; P = 0.01) significantly lower than those without sarcopenia. Muscle mass in both upper and lower limbs was significantly lower among patients affected by sarcopenia. However, physical performance tests failed to show statistically significant differences among those with and without sarcopenia. Females with sarcopenia had a significantly lower total bone mineral content compared to those without sarcopenia (1650 vs 1918 g; P = 0.045).

In the whole population of dialysis patients there were very good correlations between HGS and AMM and SMI (Table 5). There were also good correlations between HGS and measurements of physical performance, gait speed and sit-stand test. In contrast, no correlation was seen between AMM and SMI with gait speed or sit-stand test. There were very good correlations between creatinine with HGS, AMM and SMI (P < 0.05). There was a very good correlation between time on dialysis with HGS but not with AMM or SMI. There was also a very good correlation between KT/Ve (a measure of dialysis dose) with HGS, AMM, SMI (P < 0.05) but not with physical performance tests.

We found that neither age, BMI, time on dialysis, or prevalence of diabetes predicted sarcopenia in this group of patients on maintenance hemodialysis.

### Table 5

| Variable       | Hand grip strength | AMM       | SMI       | Gait speed | Sit/Stand |
|----------------|--------------------|-----------|-----------|------------|-----------|
| **Hand grip strength** |                    |           |           |            |           |
| Pearson correlation | 0.731              | 0.644     | 0.251     | –0.275     | –0.275    |
| N               | 100                | 100       | 100       | 100        | 100       |
| **AMM**         |                    |           |           |            |           |
| Pearson correlation | 0.731              | 0.893     | 0.071     | 0.022      | 0.111     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **SMI**         |                    |           |           |            |           |
| Pearson correlation | 0.644              | 0.893     | 0.012     | 0.458      | 0.485     |
| N               | 100                | 100       | 100       | 89         | 100       |
| **KT/Ve**       |                    |           |           |            |           |
| Pearson correlation | –0.279             | –0.602    | 0.467     | –0.074     | –0.077    |
| N               | 99                 | 99        | 100       | 100        | 100       |
| **Gait speed**  |                    |           |           |            |           |
| Pearson correlation | 0.251              | 0.491     | 0.905     | 0.074      | 0.025     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Sit/Stand**   |                    |           |           |            |           |
| Pearson correlation | –0.275             | –0.022    | 0.112     | –0.234     | –0.234    |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Time in HD**  |                    |           |           |            |           |
| Pearson correlation | –0.275             | –0.022    | 0.111     | 0.179      | 0.081     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Albumin**     |                    |           |           |            |           |
| Pearson correlation | 0.147              | –0.057    | –0.073    | 0.107      | 0.154     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **CRP**         |                    |           |           |            |           |
| Pearson correlation | 0.084              | 0.161     | 0.042     | –0.043     | –0.006    |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Creatinine**  |                    |           |           |            |           |
| Pearson correlation | 0.321              | 0.296     | 0.317     | 0.044      | 0.055     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Calcium**     |                    |           |           |            |           |
| Pearson correlation | 0.109              | 0.117     | 0.134     | –0.158     | 0.021     |
| N               | 100                | 100       | 100       | 100        | 100       |
| **Phosphate**   |                    |           |           |            |           |
| Pearson correlation | 0.012              | –0.016    | 0.040     | –0.051     | –0.013    |
| N               | 100                | 100       | 100       | 100        | 100       |
| **iPTH**        |                    |           |           |            |           |
| Pearson correlation | 0.037              | 0.017     | 0.055     | –0.029     | –0.099    |
| N               | 100                | 100       | 100       | 100        | 100       |

AMM, appendicular muscle mass; SMI, skeletal mass index; HD, hemodialysis; CRP, C-reactive protein; iPTH, intact parathyroid hormone; KT/Ve, index of dialysis adequacy standardized; Sig: significance; N, number of patients.
4. Discussion

In this study we observed that sarcopenia was present in 16% of this group of prevalent hemodialysis patients, being higher in females than in males (25% vs 11.1%). While HGS was similarly decreased in females and males (28% vs 30%), appendicular lean mass was more decreased in females than males (70% of females and 30% in males). Patients with decreased HGS had a higher prevalence of falls the year before the study (40% two or more falls; \( P = 0.03 \)). Only sarcopenic females had a lower total bone mineral content compared to those non-sarcopenic.

Several studies have found different prevalence of sarcopenia in dialysis patients [12–18]. Our prevalence of sarcopenia was 16%, similar to 13.7% that was found by Ren et al [14], for hemodialysis patients less than 60 years of age. For patients on dialysis with age greater than 60 years the prevalence has been shown to be greater than 30% [14–16]. Several factors may explain the wide variability of estimated prevalence, including average age of the use of different cut-off points to define sarcopenia between studies, the different guidelines used, the different methods of estimation of muscle mass (DXA or bioimpedance), the different diagnostic approximation (± 2 SD, residuals, quantiles), and the lack of consensus on whether to use square height or weight to factor muscle mass [14].

The prevalence of the different components of sarcopenia differed between males and females, especially low muscle mass, which was much higher in females. HGS was similarly decreased in both males and females, around 30%. This component of sarcopenia has been proposed as simple and useful predictor of prognosis in this dialysis population. A 4-year study has investigated the association between handgrip strength and the risk of all-cause mortality in maintenance hemodialysis. They observed that the hazard of death was significantly higher for patients with lower HGS for males (HR = 3.10; 95% CI = 1.68–5.74) and for females (HR = 2.72; 95% CI = 1.03–7.19) [19]. These results were corroborated by other studies [20,21]. Finally, in a recent meta-analysis of 9 prospective cohort studies, the comparison of patients with low HGS in relation to those with high HGS, showed that the summary risk ratio for all-cause mortality was 1.88 (95% CI 1.51–2.33; \( P < 0.001 \)) [22]. In our study we found a good correlation between HGS and gait speed. In a very recent study, patients with low gait speed and handgrip strength had the highest risks for all-cause mortality and cardiovascular events among the groups (adjusted hazard ratio of 2.72, \( P = 0.024 \)); elderly patients with low gait speed and handgrip strength were at the highest risk for poor clinical outcomes [23]. These results may provide support for the assessment of handgrip strength and gait speed in all maintenance hemodialysis patients for early identification of those who may require special care to increase survival.

Several studies have reported that both aerobic and resistance exercise training increases muscle mass and strength and therefore helps improve sarcopenia in hemodialysis patients [24–26]. A meta-analysis reported that any type of regular exercise training is effective in improving exercise capacity, physical functions, and muscle mass and strength in all CKD patients [27].

Two findings in this study were of particular interest: 1) patients with low muscle strength had a higher prevalence of falls during the previous year, and 2) sarcopenic females had lower total bone mineral content than non-sarcopenic females; although this difference was not present in males. Sarcopenia has been shown to be associated with low bone mineral density at the femoral neck and lumbar spine in both sexes, although in age-categorized gender groups, sarcopenia was an independent risk factor for low BMD only in females [28].

We could not find factors predictors of sarcopenia, probably because of the low number of patients studied. Other studies have found that age, time on dialysis, and diabetes were predictors of sarcopenia in other dialysis populations.

Our study had several limitations: 1) this study was performed in district specific-subjects that may be quite different from Asian, European, and North American countries; 2) the number of patients analyzed was quite small; and 3) we were unable to evaluate the influence of vitamin D levels on the components of sarcopenia in our patients since very few had 25(OH)D serum levels measured. In a previous study we found a high association between vitamin D deficiency with low HGS and lower physical performance (in sit/stand test) [29].

5. Conclusions

A significant proportion of our dialysis patients had sarcopenia, more frequent in females than males. Low HGS was associated with a higher prevalence of falls but only women with sarcopenia had lower bone mineral content. Recognizing sarcopenia in dialysis patients would allow us to develop strategies to prevent its development, thus preventing falls and other complications as fractures.

CRediT author statement

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Conflicts of interest

The authors declare no competing interests.

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