ORIGINAL ARTICLE

Relationship between sarcopenia, anemia and adequacy of chronic hemodialysis

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ABSTRACT

Introduction: Chronic kidney disease (CKD) patients experience complications stemming from advanced disease and its treatment, including anemia and musculoskeletal alterations. These conditions may interrelate and contribute to adverse outcomes. **Objective:** This study aimed to evaluate the association between anemia and sarcopenia and its components—muscle strength and muscle mass—in patients with CKD undergoing hemodialysis (HD). **Methods:** This was a cross-sectional study involving chronic HD patients of both sexes. Data collection included sociodemographic, laboratory, clinical, and anthropometric variables, along with handgrip strength measurements. Sarcopenia was diagnosed based on the criteria established by the European Working Group on Sarcopenia in Older People 2. Patients were compared according to the presence or absence of anemia, and categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test. We applied a multivariate logistic regression model, using the presence of anemia as the dependent variable. **Results:** The sample included 116 patients with a mean age of 58 ± 12.2 years, of whom 68.1% were male. Among the patients, 66.4% did not present sarcopenia, 18.1% were diagnosed with probable sarcopenia, and 15.5% with sarcopenia. Sarcopenia was associated with age, comorbidities, body mass index, and hemoglobin levels. Anemia was diagnosed in 84.5% of participants and was associated with sarcopenia ($p < 0.05$), though not with its components. Probable sarcopenia (OR 6.1; 95% CI: 1.4–26.3; $p = 0.015$) and confirmed sarcopenia (OR 12.9; 95% CI: 1.3–130.9; $p = 0.030$) increased the likelihood of anemia. **Conclusions:** Our findings confirmed the relationship between anemia and sarcopenia in chronic HD patients, suggesting that sarcopenia may be associated with the occurrence of anemia.

Keywords: Erythrocytes, Dialysis, Iron, Skeletal muscle, Hemoglobin.

INTRODUCTION

Chronic kidney disease (CKD) is a global public health concern with a growing prevalence over the years. In Brazil, it is estimated that between 3 and 6 million individuals are affected by CKD, with approximately 100,000 undergoing dialysis[1]. With significant health implications, *CKD* is broadly defined as a term encompassing heterogeneous disorders that impair renal structure and function. This condition follows a prolonged course, varying in severity from mild stages to end-stage renal disease (ESRD), characterized by kidney failure[2,3]. As renal function declines, nutritional disturbances become prevalent, ranging from obesity to malnutrition and nutrient deficiencies[3–5].

The impact of CKD extends beyond renal dysfunction, as these patients experience hormonal imbalances, metabolic disturbances such as inflammation, electrolyte and fluid disorders, and impaired iron metabolism. These alterations contribute to various complications and adverse outcomes, including increased morbidity and mortality risks[3,6].

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Anemia is a condition marked by abnormalities in red blood cells, caused by factors such as iron and vitamin deficiencies, blood loss, hormonal disturbances, and chronic or genetic diseases[7]. In ESRD, anemia prevalence can reach up to 90%, stemming from several CKD-associated changes. These alterations include reduced renal erythropoietin production, shortened red blood cell lifespan, hepcidin-mediated reduced iron absorption, blood loss during hemodialysis, and inflammatory processes[3]. Despite adherence to clinical treatment protocols involving iron supplementation and erythropoietin replacement, anemia remains highly prevalent, and its treatment has shown limited efficacy[8–10].

In CKD patients, anemia is linked to fatigue, weakness, reduced cognitive ability, drowsiness, and diminished physical endurance. Although the mechanisms are not fully understood, they are likely related to the primary role of hemoglobin (Hb) in oxygen transport to tissues. Lower Hb levels impair aerobic respiration, triggering anaerobic processes, which negatively affect muscle function[11].

Another common condition in chronic diseases is sarcopenia, a musculoskeletal disorder with diverse etiologies. The primary factors contributing to sarcopenia include reduced muscle mass and strength due to aging (primary sarcopenia) or secondary factors such as hormonal changes, chronic inflammation, oxidative stress, motor neuron loss, insulin resistance, impaired muscle recovery, and myocyte apoptosis. Secondary sarcopenia is often associated with chronic diseases, physical inactivity, and malnutrition[12–15]. CKD patients are particularly susceptible to sarcopenia due to factors such as chronic inflammation, protein loss during dialysis, protein catabolism, hormonal imbalances, and lifestyle changes, including reduced nutritional intake and physical inactivity.

Sarcopenia is a significant predictor of adverse health outcomes, including functional decline, falls, fractures, hospitalizations, prolonged hospital stays, increased surgical complications, cardiovascular risk, and mortality. Therefore, early screening and proper management of sarcopenia are crucial[12,14,16].

In recent years, sarcopenia has become a focus of research in CKD. However, understanding the relationship between musculoskeletal health and anemia remains a significant gap. Reduced oxygen availability, caused by decreased Hb levels, may compromise muscle function and mass, as observed in other populations[17]. Theoretically, these musculoskeletal changes could result from chronic oxygen restriction—whether at low or high levels—combined with other CKD-associated conditions, leading to muscle catabolism. At the same time, tissue recovery is limited by the metabolic dysfunctions inherent to this population[17,18].

Conversely, anemia in CKD predominantly arises from erythropoietin deficiency, highlighting its unique characteristics. Other factors, such as malnutrition and inflammation, exacerbate anemia. Evidence suggests that increased muscle mass and strength improve Hb levels, while low Hb concentrations impair muscle mass gain[19–21].

Thus, these two conditions appear to be interconnected and may influence the clinical outcomes of CKD[18,20,22,23]. Considering the relevance of this topic, our study aimed to evaluate the association between anemia and sarcopenia, including its components—muscle strength and mass—in CKD patients undergoing hemodialysis.

METHODS

We conducted this cross-sectional study at the Nephrology Center of Dourados (CENED), located in Dourados, state of Mato Grosso do Sul, Brazil. Data collection took place between January 2021 and May 2022. Eligible participants included individuals aged 20 years or older, of both sexes, diagnosed with CKD and undergoing hemodialysis (HD) for at least two months. During the data collection period, 145 patients aged 20 (23-87 years) underwent HD at the center.

Exclusion criteria, assessed through medical records prior to enrollment, included any restrictions preventing the performance of handgrip strength and gait speed assessments (e.g., neurodegenerative diseases or severe psychiatric disorders) and the inclusion of Indigenous populations for ethical reasons. The final sample comprised 116 patients (80% of eligible individuals)—all providing written informed consent by signing the Informed Consent Form (ICF).

This study adhered to ethical guidelines for research involving human subjects, and the Research Ethics Committee approved it under protocol number 4.461.685 and Certificate of Ethical Appreciation Presentation (CAAE) number 39989820.2.0000.5160.

We collected data using a study-specific form that included demographic, socioeconomic, clinical, anthropometric, and laboratory variables. Sociodemographic data were obtained through personal interviews during HD sessions, while clinical variables were retrieved from patients' medical records.

Data collected included sex (male, female); race (White/Hispanic, Black/Afro-descendant, Asian); marital status (never married, married, widowed, separated/divorced); employment status (employed, unemployed); and socioeconomic status based on the Economic Classification Criteria of Brazil (CCEB) developed by the Brazilian Association of Research Companies (ABEP), categorized as follows: Level A (R$ 22,749.24), Level B (R$ 5,721.72–10,788.56), Level C (R$ 1,894.95–3,194.33), and Levels D/E (R$ 862.41)[24].

Anthropometry included post-dialysis or dry weight (kg) using a Toledo® electronic scale (model 2003/26-218), height (m), and calf circumference (CC, cm) following Lohman's (1988) criteria. We measured CC using a flexible, non-elastic tape measure (Essencial®, 1.5 m, graduated in cm). Body mass index (BMI) was classified according to the World Health Organization (WHO) criteria for adults[20] and Lipschitz's (1994) classification for older adults[25,26]. *Muscle mass reduction* was defined as CC ≤33 cm for women and ≤34 cm for men[27].

Sarcopenia was diagnosed using the criteria of the European Working Group on Sarcopenia in Older People 2 (EWGSOP2)[28]. Muscle strength was assessed through handgrip strength (HGS) using a Saehan® hydraulic dynamometer, following the American Society of Hand Therapists (ASHT) guidelines. Measurements involved three repetitions per arm with a 60-second interval between attempts, recording the highest value. *Low muscle strength* was defined as <27 kg for men and <16 kg for women[28,29].

We assessed sarcopenia severity through gait speed (GS), measured using an electronic stopwatch and a 4-meter tape as a distance marker. Patients were instructed to walk the marked path at their usual pace for three trials, with a one-minute rest between each trial. The shortest time was recorded for analysis. We used a cutoff point of ≤0.8 m/s, applicable to both sexes, to indicate low physical performance[28]. Both CC and HGS were measured before the hemodialysis session.

The EWGSOP2[28] algorithm categorized patients as "no sarcopenia," "probable sarcopenia" (low muscle strength only), "confirmed sarcopenia" (low muscle strength and reduced muscle mass), or "severe sarcopenia" (confirmed sarcopenia with low GS). For statistical analyses, patients with confirmed and severe sarcopenia were grouped as "confirmed sarcopenia."

Laboratory variables included hemoglobin (Hb, g/dL), iron saturation index (ISI, %), total iron-binding capacity (TIBC, mg/dL), and ferritin (µg/dL). We retrieved these data from patients' electronic records (Dialsist Web system) as part of routine care. Fasting blood samples were analyzed in a certified laboratory. Anemia was defined based on the criteria of Kidney Disease Outcomes Quality Initiative (KDOQI): Hb <12 g/dL for women and <13 g/dL for men[4]. We used mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) values to classify anemia types[7]. *Reduced ferritin* was defined as <200 ng/mL, ISI as <20%, and TIBC as <250 µg/dL[30,31].

We used SPSS Statistics (v.22, SPSS An IBM Company, Chicago, IL) for statistical analysis. The Shapiro-Wilk test determined normality ($p>0.05$). We expressed descriptive statistics as mean ± standard deviation for continuous variables and percentages for categorical variables. We compared continuous variables using the Student's t-test. Pearson's chi-square ($\chi 2$) or Fisher's exact test assessed associations between sarcopenia, anemia, sociodemographic variables, BMI, laboratory results, and sarcopenia components. We applied a multivariate logistic regression model, adjusted for sex, age, and comorbidities, using anemia as the dependent variable.

RESULTS

We evaluated 116 patients, with a mean age of 58.0 ± 12.2 years and a median age of 28.5 years (range: 23–87). Most participants (68.1%) were male. The majority comprised adults, White/Hispanic, married individuals, and 90.5% were not employed. Socioeconomic levels A and B represented only 5.1% of the sample, whereas classes C and D/E had higher representation, at 53.5% and 22.4%, respectively. Hypertension (HTN) was the most prevalent disease, occurring alone in 42 patients (36%) or in combination with other conditions, such as diabetes and heart diseases. Diabetes was the second most prevalent condition, present alone in 5.2% of patients. Combined, heart disease and HTN co-occurred in 17 patients (14.6%), and diabetes and HTN were present in 19 patients (16.4%). Only 10% of the patients had no comorbidities. Hemodialysis treatment duration varied widely, ranging from 2 to 170 months (approximately 14 years).

We identified anemia in 84.5% of the study population. Based on mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) values in these patients (n=98), normocytic and normochromic anemia was the most prevalent type, affecting 56.0% of patients; 11.2% had microcytic and hypochromic anemia, and 32.7% exhibited macrocytic anemia.

Among the patients, 77 (66.4%) did not have sarcopenia, while 18 (15.5%) were classified as having confirmed or severe sarcopenia. Low muscle mass, assessed by CC, was present in 40.5% of patients, and low muscle strength, measured by HGS, was observed in 33.6% of cases. The association between sarcopenia, age group, comorbidities, sarcopenia components, and laboratory variables related to anemia and iron metabolism is presented in Table 1. The association between anemia, sex, age, BMI, laboratory variables related to iron metabolism, sarcopenia, and its components is detailed in Table 2. We identified an association between anemia and sarcopenia but not with the individual components of HGS, CC, and GS.

Table 1 Distribution of individuals according to sarcopenia classification and association with age, comorbidities, body mass index, laboratory variables, and sarcopenia components

Variables	**Without sarcopenia**	**Probable sarcopenia**	**With sarcopenia**	**p-value**
	n (%)	**n (%)**	**n (%)**	
Age group				**<0.001**
Adult	58 (75.3)	06 (28.6)	03 (16.7)	
Older adult	19 (24.7)	15 (71.4)	15 (83.3)	
Comorbidities				**0.025**
0–1	50 (64.9)	08 (38.1)	07 (38.9)	
2–3	27 (35.1)	13 (61.9)	11 (61.1)	
Body mass index				**<0.001**
Normal weight	39 (50.6)	06 (28.6)	08 (44.4)	
Underweight	05 (6.5)	01 (4.8)	09 (50.0)	
Overweight	26 (33.8)	12 (57.1)	01 (5.6)	
Obesity	07 (9.1)	02 (9.5)	00 (0.0)	
Laboratory variables				
Hemoglobin				**0.043**
Normal	11 (14.3)	01 (4.8)	06 (33.3)	
Anemia	66 (85.7)	20 (95.2)	12 (66.7)	
Total iron-binding capacity				**0.834**
Normal	68 (88.3)	18 (85.7)	15 (83.3)	
Reduced	09 (11.7)	03 (14.3)	03 (16.7)	
Ferritin				**0.803**
Normal	17 (22.1)	04 (19.0)	05 (27.8)	
Reduced	60 (77.9)	17 (81.0)	13 (72.2)	
Transferrin saturation				**0.945**
Normal	56 (72.7)	16 (76.2)	13 (72.2)	
Reduced	21 (27.3)	05 (23.8)	05 (27.8)	

Sarcopenia components				
Calf circumference				**<0.001**
Normal muscle mass	48 (62.3)	21 (100)	00 (0.0)	
Low muscle mass	29 (37.7)	00 (0.0)	18 (100)	
Handgrip strength				**<0.001**
Normal muscle strength	77 (100)	00 (0.0)	00 (0.0)	
Low muscle strength	00 (0.0)	21 (100)	18 (100)	
Gait speed				**0.245**
Adequate performance	57 (74.0)	12 (57.1)	11 (61.1)	
Low physical performance	20 (26.0)	09 (42.9)	07 (38.9)	

Table 2 Distribution of individuals according to anemia status and association with sex, age, body mass index, laboratory variables, sarcopenia, and its components

Variables	**With anemia**	**Without anemia**	**p-value**
	n (%)	**n (%)**	
Sex			**>0.05**
Male	70 (71.4)	09 (50.0)	
Female	28 (28.6)	09 (50.0)	
Age group			**>0.05**
Adult	57 (58.2)	10 (55.6)	
Older adult	41 (41.8)	08 (44.8)	
Body mass index			**>0.05**
Normal weight	47 (48.0)	06 (33.3)	
Underweight	13 (13.3)	02 (11.1)	
Overweight	29 (29.6)	10 (55.6)	
Obesity	09 (9.2)	00 (0.0)	
Laboratory variables			
Total iron-binding capacity			**>0.05**
Normal	85 (86.7)	16 (88.9)	
Reduced	13 (13.3)	02 (11.1)	
Ferritin			**>0.05**
Normal	21 (21.4)	05 (27.8)	
Reduced	77 (78.6)	13 (72.2)	
Transferrin saturation			**>0.05**
Normal	72 (73.5)	13 (72.2)	
Reduced	26 (26.5)	05 (27.8)	
Sarcopenia classification			**< 0.05**
Absent	66 (67.3)	11 (61.1)	
Probable	20 (20.4)	01 (5.5)	
Confirmed	12 (12.3)	06 (33.4)	

Sarcopenia components			
Calf circumference			**>0.05**
Normal muscle mass	58 (59.2)	11 (61.1)	
Low muscle mass	40 (40.8)	07 (38.9)	
Handgrip strength			**>0.05**
Normal muscle strength	66 (67.3)	11 (61.1)	
Low muscle strength	32 (32.7)	07 (38.9)	
Gait speed			**>0.05**
Adequate performance	68 (69.4)	12 (66.7)	
Low physical performance	30 (30.6)	06 (33.3)	

The analysis of continuous variables is provided in Table 3, where no significant differences were observed concerning anemia.

Using anemia as the dependent variable in a multivariate logistic regression model adjusted for sex and age, we confirmed an association between anemia and sarcopenia. The presence of confirmed sarcopenia increased the odds of anemia by 12.9 times (Table 4).

Table 3 Comparison of continuous variables in relation to anemia among patients with chronic kidney disease undergoing hemodialysis

Variables	***Anemia***		**p***
	Absent	**Present**	
	mean±SD	**mean±SD**	
Age (years)	55.9±9.2	58.4±12.7	0.426
BMI (kg/m²)	25.7±4.7	25.0±5.0	0.888
CC (cm)	34.0±3.0	35.0±3.9	0.588
HGS (kg)	23.22±8.5	28.4±10.8	0.558
GS (m/s)	0.87±0.27	0.90±0.24	0.057
TBIC (mg/dL)	300±48.9	290±45	0.402
Ferritin (mcg/dL)	155.1±115	142±133	0.687
TSAT (%)	28.5±5.7	29.7±6.5	0.402

SD: standard deviation; t *Student* test (*); BMI: body mass index; CC: calf circumference; HGS: handgrip strength; GS: gait speed; TSAT: transferrin saturation; TIBC: total iron-binding capacity.

Table 4 Multivariate logistic regression analysis using anemia as the dependent variable in patients with chronic kidney disease undergoing hemodialysis (n=116)

Variables	OR	95% CI	p-value*
Sarcopenia			
Absent	1	1	
Probable	6.1	1.4-26.3	0.015
Confirmed	12.9	1.3-130.9	0.030

OR: odds ratio; 95% CI: 95% confidence interval. Model adjusted for sex (male or female) and age (adults and older adults).

DISCUSSION

This study examined the association between anemia and sarcopenia, including its muscle strength and mass components for diagnosing this musculoskeletal disorder. We identified a significant association between reduced Hb levels and sarcopenia, thereby confirming the relationship between anemia and sarcopenia in CKD. The proportion of patients with anemia and sarcopenia or probable sarcopenia was higher than in the group without anemia. However, no associations were found between sarcopenia and markers of iron metabolism, including total iron-binding capacity (p >0.10), ferritin (p >0.10), and transferrin saturation (p >0.10). This lack of association may be attributed to the low prevalence of iron-deficiency anemia, as 57% of patients had normocytic and normochromic anemia, often linked to inadequate or inefficient erythropoietin production. Although erythropoietin is part of the standard clinical protocol for anemia treatment in CKD, its effectiveness remains suboptimal[9,32,33].

Anemia prevalence was significantly high among these patients, even with adherence to clinical treatment protocols for anemia in CKD, which included intravenous iron supplementation and subcutaneous epoetin alfa administration[34]. Previous studies have demonstrated that, despite using erythropoiesis-stimulating agents (ESAs), patients with CKD often fail to achieve adequate oxygen exchange compared to healthy individuals[9,33]. This inefficiency in anemia treatment may be attributed to several factors, including the chronic inflammation characteristic of this population, frequent blood loss during hemodialysis, and hemolysis.

The relationship between reduced Hb levels and sarcopenia involves well-established physiological mechanisms observed in other populations. Reduced muscle mass and strength could result from diminished oxygen availability due to lower Hb levels, triggering various compensatory responses via negative feedback[11,17,35]. In skeletal muscle, this hypoxic response includes increased anaerobic respiration, lactic acid production, and local pH reduction. Furthermore, blood flow redistribution to more vital organs exacerbates oxygen depletion in skeletal muscle. The resulting acidosis from lactic acid production can impair muscle recovery and regeneration, while increased energy demands amplify protein catabolism, potentially causing morphological muscle changes, as demonstrated in animal models[17,18,36–39].

Given the multiple causes of anemia in CKD and the central role of erythropoietin deficiency, as highlighted in this study, characterized by predominantly normocytic and normochromic anemia, it cannot be conclusively stated whether these compensatory responses occur similarly in this population and whether additional mechanisms play equally significant roles. Because of the high prevalence of anemia in CKD and its unique characteristics, further research in diverse populations is necessary to elucidate the relationship between anemia and muscle mass and strength reduction[40]. Recent findings suggest improved Hb levels with increased muscle mass and reduced oxidative stress in hemodialysis patients participating in resistance training programs[16]. Our study further supports these findings, as multivariate logistic regression analysis identified sarcopenia as an explanatory variable for anemia, adjusted for sex and age.

The results also indicate an association between comorbidities, which may be explained by reduced physical activity and chronic inflammation that exacerbate musculoskeletal depletion[35,41]. Patients with two to three comorbidities had a higher prevalence of sarcopenia than those with none or one comorbidity. Consistent with previous research, age emerged as an important factor in sarcopenia. Among older adults (≥60 years), the number of patients with sarcopenia was comparable to those without sarcopenia and those with probable sarcopenia. Conversely, among younger adults, the disparity between the absence and presence of sarcopenia was substantial (75.3% vs. 16.7%, respectively).

It is necessary to highlight both the strengths and limitations of this study. This research is among the first to investigate the association between anemia, sarcopenia, and its components in CKD patients undergoing hemodialysis. However, limitations include its cross-sectional design, which precludes establishing causal relationships, information bias, and potential confounders. While not the first choice for diagnosing sarcopenia, the method used for muscle mass assessment holds significant practical value. CC has proven to be an accessible and effective tool, particularly in clinical studies[28,41].

The results should be interpreted cautiously, acknowledging the multitude of factors that can influence skeletal muscle mass and quality, similar to the complexities observed in anemia. Further studies are needed to explore the relationship between anemia and sarcopenia, along with skeletal muscle alterations, in CKD and other populations.

CONCLUSION

This study reinforces the association between anemia and musculoskeletal health in CKD patients undergoing hemodialysis. It suggests that the presence of sarcopenia may contribute to the occurrence of anemia in this population.

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Conflicts of interest

The authors declare no conflicts of interest related to the conduct of this study.

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