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REVIEW

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Handgrip strength in end stage of renal disease—a narrative review

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Abstract

Background: Handgrip strength (HS) measures have been associated with nutritional status, morbidity, and mortality in end stage of renal disease (ESRD).

Objective: We aimed to present and discuss the HS method in ESRD patients, by reviewing published studies on the subject.

Methods: PUBMED, MEDLINE, and LILACS databases were consulted, with no filters regarding the date of publication or age of population.

Results: The terms "handgrip strength," "end stage of renal disease," and "nutrition status" were used, and 32 articles with publication dates from 1983 to 2017 were included. Handgrip strength is considered a simple and rapid method of assessing muscle function in chronic kidney disease and is an important predictor of nutritional status depletion, development of comorbidities, and early mortality.

Conclusion: There is a lack of studies that analyzed associations between HS and clinical and nutritional outcomes in ESRD. The establishment of HS protocols and reference values in ESRD are necessary, to assist preventive measures of unfavorable outcomes in this population.

Keywords: Handgrip strength, Nutrition status, End stage of renal disease

Background

Nutritional and metabolic derangements are common in end stage of renal disease (ESRD), caused by hypercatabolic status, uremic toxins, malnutrition, and inflammation. These changes in nutritional status are defined as protein energy wasting (PEW) and are strongly associated with mortality in chronic diseases, including chronic kidney disease (CKD) [1, 2].

The most common consequences of PEW are important decrease of serum proteins and progressive loss of skeletal muscle, which contribute to development of frailty, sarcopenia, and impairment of muscle functioning, particularly in ESRD patients [1, 3].

The prevalence of PEW in early stages of CKD is 20 to 25% [2] and increases with progression of the disease. Methods assessing nutritional status and body composition should be able to identify important nutritional status changes and predict risk of unfavorable clinical outcomes [4, 5].

Handgrip strength (HS) is considered a simple and rapid method of assessing muscle function. Currently, it has been used as a reliable marker of clinical prognosis in several populations due to its association with nutritional status, morbidity, and mortality [3, 6].

There are comparisons in the literature of nutritional and functional parameters, such as HS, reinforcing the importance of these indicators in clinical practice as a useful nutritional assessment instrument [7].

Recent studies relate HS measured by a dynamometer with clinical conditions and adverse outcomes such as inflammation, malnutrition, overhydration status, and higher mortality in dialytic and non-dialytic ESRD population. Because of these associations, it has been suggested that a dynamometer is a valuable tool for assessing nutritional status in clinical practice in CKD [3, 8].

Despite the use of this, measure is increasing through the years; no major developments have been done in the

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past 6 years [6] to develop a standardized protocol to use HS as a tool to prevent loss of muscle mass and function in ESRD population.

Objective

This paper aimed to review the use of handgrip strength in end stages of chronic kidney disease—stages G4 and G5, pre-dialytic, and in maintenance dialysis therapy individuals, by reviewing published studies in the literature.

Methodology

This is a narrative review. PUBMED database, which contains over 26 million citations in MEDLINE biomedical literature; LILACS, the most important and comprehensive index of scientific literature in Latin America and the Caribbean; scientific journals; and online books has been consulted. Articles were searched by hand, using the terms "handgrip strength," "chronic kidney disease," and "nutritional status." There was no restriction on the basis of the language, and no filters were applied, as exclusion criteria, to the year of publication or age of the study population.

Results

There were 42 articles found with the search in databases. Thirty-one articles, published in full version, with publication between 1983 and 2017, with data about the use of HS in ESRD population, were included (Table 1). Through reading the articles, the discussion of this review was divided into four subtopics: "handgrip strength"; "sarcopenia, frailty, and chronic kidney disease"; "handgrip strength in end stage of renal disease"; and "baseline values."

Discussion

Handgrip strength

A dynamometer is a portable and practical gauging device, which generates a reliable measure of muscular strength. It has been applied in several populations and clinical situations, including CKD. Reduced measures of HS are commonly found among ESRD patients and have strong associations with morbidity and mortality [4, 9].

Nutritional assessment and muscle function evaluation enable the diagnosis of nutritional and functional impairments and, consequently, allow early interventions to avoid unfavorable outcomes, such as reduced quality of life, sarcopenia, frailty, and early death [10, 11].

Although a dynamometer is an apparatus currently used in several clinical situations, some factors may influence the measurement, such as age, gender, body mass, dominant hand, and the manipulator position [8].

Studies show that there is a predominance of higher values of muscular strength in males, in individuals aged between 30 and 45 years and in individuals who are overweight and obese, according to the body mass index (BMI). Values tend to decrease with advancing age and the presence of PEW [11].

According to Schlüssel et al., there is strength variation also between the sides of the body, which can vary between 5 and 30% [7]. Higher absolute values were obtained by measurements performed with standing individuals [12–14]. Clinical procedure and hand's dominance may influence the measurement, as described in some studies [15–17], and others only observed a significant difference between the right and left sides [18, 19]. Innes affirms that shoulder flexed at 180° yields better results when compared to 90° flexion or standard position 0° [14].

Verbal encouragement, as described more than 20 years ago by Johansson et al., results in 8% higher values of muscle contraction strength, statistically significant difference. In this study, a higher voice volume for transmitting instructions to men between 18 and 30 years was related to greater motivation and strength [20].

Besides the use of average of several HS readings, it is possible to use the measurement of only one reading, the largest between two or three, or the average of the two largest readings between three readings. According to Innes, no significant differences were observed between them, being the evaluator discretion the most appropriate method [14].

This same author suggests that a period of muscular contraction of 3 s is enough to record the greatest measure of HS. A rest period between measurements is recommended and may vary from 2, 5, or 15 s to 1 min [14].

There are differences of measures performed before and after hemodialysis session: Pinto et al. showed that there was a significant reduction of HS observed after the session, when compared to the measure performed in initial minutes. The authors affirm that hemodialysis procedure affects negatively the HS [15].

Considering the possible interferences exposed, it is necessary to establish a protocol in each clinic or institution and maintain the procedure consistency to ensure reliable measurements provided by HS [7, 9, 21] (Fig. 1).

Non-dialytic ESRD individuals have several factors that contribute to the decline of muscle strength and function, such as anemia, decreased serum albumin and hemoglobin levels, presence and severity of proteinuria, decreased renal function, protein hypercatabolism, advanced age, and inflammation. These factors are more strongly contributors to decline in strength of ESRD individuals (CKD stages 4 and 5) than when compared to those of individuals in CKD stages 2 and 3 [10].

Handgrip strength in ESRD

Due to associations with morbidity and mortality, investigation of nutritional disorders in ESRD population is extremely important [6, 11]. Reduced values of HS are

Table 1 Original articles used in the narrative review

Study	Patients	Objectives	Principal results	Conclusions
Amparo et al., 2013 [3]	190 nondialysis-dependent chronic kidney disease individuals stages 2–5	It was aimed to test whether MIS is able to predict muscle strength in nondialysis-dependent chronic kidney disease individuals.	A strong negative correlation was found between HGS and MIS in univariate and multivariate analysis.	MIS shares strong links with objective measures of muscle strength in NDD-CKD patients.
Borges et al., 2017 [5]	215 patients on maintenance hemodialysis	It was aimed to evaluate if MIS is associated with mortality in patients on maintenance hemodialysis and establish a cutoff to predict mortality at different follow-up periods	> 7 points was able to predict mortality. Using this cutoff on Kaplan-Meier survival curve, MIS was associated with all-cause mortality at 18 months and 24 or more months of follow-up.	MIS is an independent predictor of mortality in hemodialysis patients.
Stenvinkel et al., 2002 [8]	206 ESRD patients, classified with regard to the presence of cardiovascular disease, diabetes mellitus, and inflammation	It was aimed to search nutritional markers that can predict outcome, regarding body composition in men and women.	The presence of cardiovascular disease, diabetes mellitus, and inflammation predicted poor outcome, with significant differences between sexes.	Sex is an important factor that must be taken into account in studies on nutrition and nutritional interventions in ESRD patients.
Hasheminejad et al., 2016 [9]	83 randomly selected hemodialysis patients	It was aimed to evaluate the handgrip strength and its relationship with the Malnutrition-Inflammation Score (MIS) among Iranian dialysis patients.	Protein energy wasting was prevalent; handgrip strength was significantly associated with nutritional assessment markers.	Handgrip strength can be incorporated as a reliable tool for assessing nutrition status in clinical practice.
Hiraki et al., 2013 [10]	120 ambulant pre-dialysis CKD stages 2 to 5	It was aimed to clarify physical function in pre-dialysis patients according to CKD stage.	All indices of physical function decreased, including handgrip strength, according to the progression of CKD.	Physical function in pre-dialysis CKD patients decreased as the disease progressed according to stage. Early intervention in CKD patients might delay the loss of physical function.
Boadella et al., 2005 [12]	56 healthy subjects voluntarily participated	It was aimed to assess with which of the maximal handgrip strength could be delivered, while sitting and while standing.	The self-selected handgrip position resulted in the highest mean maximal grip strength compared with the non-self-selected handgrip strength.	Both in sitting and in standing, participants were able to self-select the hand grip position on the hand dynamometer with which the maximal handgrip strength could be delivered.
Carrero et al. 2007 [13]	223 patients undergoing prevalent hemodialysis	It was aimed to test if appetite would be related to inflammation and outcome in hemodialysis patients, and if sex may account for differences in the symptoms associated with poor appetite.	Appetite loss was associated with worse clinical outcome even after adjustment for age, sex, inflammation, dialysis vintage, and comorbidity.	There is a close association among prevalence, malnutrition, inflammation, and outcome in patients undergoing prevalent hemodialysis
Pinto et al., 2015 [15]	156 patients on maintenance hemodialysis	It was aimed to investigate the impact of the dialysis session on the handgrip strength in patients undergoing hemodialysis.	A significant reduction of HGS was observed after the HD session, associated to the decrease in blood pressure during dialysis.	Hemodialysis procedure affects negatively the handgrip strength
Crosby et al., 1994 [16]	215 healthy subjects voluntarily participated	It was aimed to study normal hand strength and the difference between dominant and nondominant hands.	60% of patients had maximum strengths. The majority of right-handed subjects were 10% stronger in grip strength on the dominant side.	In left-handed subjects, meaning grip was the same for both hands, the nondo minant hand was stronger in 50% of left-handed subjects.
Incel et al., 2002 [17]	128 right and 21 left hand-dominant volunteers	It was aimed to evaluate the grip and pinch strength differences between sides for the right- and left-handed population.	A statistically significant difference was found between the grip and pinch strengths of dominant and nondominant hands in favor of the dominant hand.	We concluded that the dominant hand is significantly stronger in right-handed subjects but no such significant difference between sides could be documented for left-handed people.
Hanten et al., 1999 [18]	1182 healthy subjects voluntarily participated	It was aimed to develop normative maximum grip		

Table 1 Original articles used in the narrative review *(Continued)*

Study	Patients	Objectives	Principal results	Conclusions
		strength data for men and women aged 20 to 64 years	Significant differences between the right and left hands and across the age groups for both genders.	The results will help clinicians with decision making regarding grip strength.
Johansson et al., 1983 [19]	19 healthy volunteer male subjects	It was aimed to investigate the hypothesized correlation between volume of a verbal command and magnitude of a resulting voluntary isometric muscular contraction	With the volume increase, it was an increase of 8% in muscle contraction strength.	Through an awareness and use of the effects of voice volume on muscular contraction, the therapist may be able to improve the accuracy and consistency of examination methods and increase the efficacy and efficiency of therapeutic procedures.
Chang et al., 2011 [20]	128 clinically stable patients with CKD-ND	It was aimed to study whether PEW is associated with poor renal outcomes and whether the indicators of protein energy wasting can predict renal outcomes in patients with non-dialysis-dependent chronic kidney disease	Lower handgrip strength was associated to significantly poor renal outcomes.	Handgrip strength is an independent predictor of composite renal outcomes in CKD-ND patients and can be incorporated to clinical practice.
Vogt et al., 2016 [21]	256 patients on maintenance hemodialysis and peritoneal dialysis	It was aimed to verify if handgrip strength is associated with all-cause mortality in patients in maintenance hemodialysis and peritoneal dialysis	When adjusted for demographic, clinical and nutritional variables, handgrip strength remained a significant predictor of mortality, independent of dialysis modality	Handgrip strength was associated with mortality independent of dialysis modality.
Cigarrán et al., 2013 [22]	267 men with CKD stages 2–4	It was aimed to test if reduced endogenous testosterone associates with features of muscle wasting in men with CKD.	Testosterone significantly and independently contributed to explain the variances of handgrip strength and fat-free mass	The reduction in testosterone levels that accompanies CKD may further contribute to the procatabolic environment leading to muscle wasting.
Isoyama et al., 2014 [23]	330 incident dialysis patients	It was aimed to address phenotype and mortality associations of muscle strength and muscle mass dysfunction entities, alone or in combination	Old age, comorbidities, protein-energy wasting, physical inactivity, low albumin, and inflammation associated with low muscle strength, but not with low muscle mass. When combined, individuals with low muscle mass alone were not at increased risk of mortality.	Low muscle strength was more strongly associated with aging, protein-energy wasting, physical inactivity, inflammation, and mortality than low muscle mass.
Broers et al., 2017 [24]	44 CKD-5 non-dialysis patients, 29 dialysis patients, and 20 healthy controls	It was aimed to compare physical activity and performance between stage 5 chronic kidney disease and healthy individuals and to assess alterations during the transition from CKD-5 non-dialysis to dialysis.	Physical activity and handgrip strength were significantly lower in CKD-5 patients as compared to that in healthy controls. 6 months after starting dialysis, activity-related energy expenditure and walking speed significantly increased.	Transition phase from CKD-5 non-dialysis to dialysis is associated only with a modest improvement in activity-related energy expenditure.
Zhou et al., 2018 [26]	148 adult patients with an estimated GFR < 30 mL/min/1.72 m^2	It was aimed to investigate the relationships between muscle mass and measured glomerular filtration rate and between muscle mass and strength and balance in patients with CKD stages 3–5.	Lean mass, fat mass, appendicular skeletal muscle, and appendicular skeletal muscle index were associated with glomerular filtration rate. Handgrip strength was associated with arm lean mass. Men had more sarcopenia than women.	Two important markers of physical function, balance and strength, were significantly related to muscle mass.
Kalantar-Zadeh et al., 2001 [27]	83 outpatients on maintenance hemodialysis therapy for at least 3 months	It was aimed to develop and validate such an instrument to predict outcome in maintenance hemodialysis patients.	Malnutrition-Inflammation Score had stronger and pertinent correlation coefficients	This instrument appears to be a comprehensive scoring system with significant associations with prospective hospitalization and mortality, as well as measures of nutrition, inflammation, and anemia in maintenance hemodialysis patients.

Table 1 Original articles used in the narrative review *(Continued)*

Study	Patients	Objectives	Principal results	Conclusions
Pereira et al., 2015 [28]	287 non-dialysis-dependent CKD patients in stages 3–5	It was aimed to investigate the prevalence and mortality predictive power of sarcopenia, defined by three different methods, in non-dialysis-dependent CKD patients.	Frequency of sarcopenia was significantly higher among non-survivors. Sarcopenia diagnosed by bioelectrical impedance remained as a predictor of mortality after multivariate adjustment.	Prevalence of sarcopenia in CKD patients on conservative therapy varies according to the method applied. Sarcopenia defined as reduced handgrip strength and low skeletal muscle mass index estimated by BIA was an independent predictor of mortality in these patients.
Heimburguer et al., 2000 [30]	15 patients, aged younger than 70 years close to the start of dialysis therapy	It was aimed to assess the prevalence of malnutrition and study the relationship between various nutritional parameters in these patients	Malnourished patients differed in several aspects from well-nourished patients. Including handgrip strength measure.	High prevalence of malnutrition in predialysis patients with chronic renal failure and suggests that handgrip strength is a reliable, inexpensive, and easy-to-perform nutritional parameter in this population.

often found in patients undergoing dialysis therapy and reflect muscle mass depletion [9].

A recent systematic review of 18 studies in populations submitted to hemodialysis and peritoneal dialysis has described associations of reduced HS with dialysis and clinical and nutritional parameters. Associations with reduced levels of serum hemoglobin, presence of diabetes mellitus, decreased renal function, inflammation, carnitine deficiency, and varying degrees of PEW were found. Higher survival in these populations was related to values of HS above the average obtained [6].

Vogt et al. established cutoffs of HS to identify all-cause mortality risk in dialysis patients, most of them on hemodialysis, in different genders. The authors showed that PEW has been independently associated with poor outcomes, such as longer hospitalization and mortality. Moreover, HS cutoffs that predicted mortality were higher for men (22.5 kg) than for women (7.0 kg) [22].

Levels of testosterone in uremia are additional factors that contribute to decline of muscle mass and strength in men with CKD [23]. Low muscle strength is associated with aging, PEW, and physical inactivity, according to Isoyama et al. [24]. End stages of renal disease individuals have, commonly, high levels of physical inactivity that contribute to decrease functional capacity and decreased HS values [25].

The data analyzed suggests that a dynamometer can be considered a useful tool in evaluation of muscle function related to the nutritional status of dialysis patients [6]. There are, to date, few studies that discuss associations of HS measurement and clinical outcomes in patients with non-dialytic ESRD.

Five observational, transverse, and longitudinal studies were found in the literature, which described associations between dynamometry and the occurrence, prevalence, and predictive power of sarcopenia mortality, and a literature review that addressed aspects of combating severe mass loss and muscle strength in uremic non-dialytic ESRD individuals [6, 10, 21, 26, 27].

Of the most relevant nephro-protective clinical strategies in ESRD, we highlight the nutritional and body compartment evaluation. Depleted nutritional status and decrease in muscle mass contribute to an accelerated loss of renal function and an increased risk of early death in pre-dialytic ESRD patients [21].

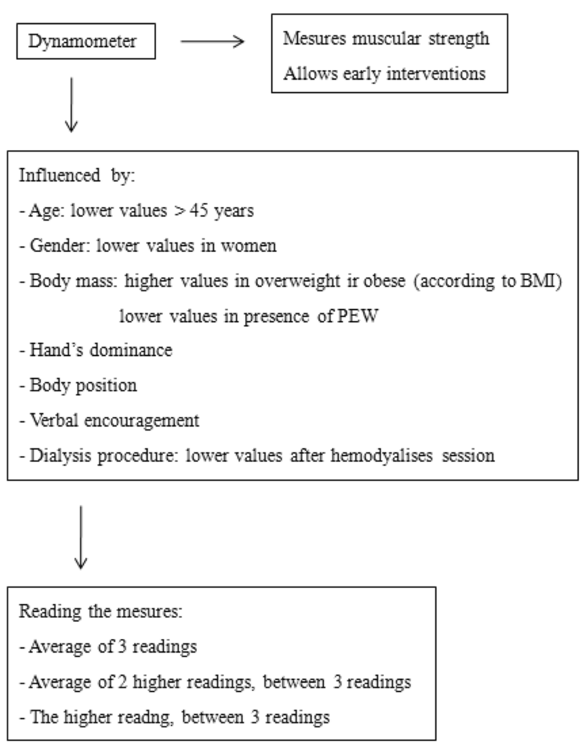

Fig. 1 The dynamometer measures characteristics

A study performed by Amparo et al. observed associations of HS measurement in CKD stages 2 to 5 patients with some parameters: lower HS were older, lower renal function and lower serum albumin, and worse evaluation by the Malnutrition-Inflammation Score [3]. Malnutrition-Inflammation Score (MIS) is a nutritional assessment tool capable to predict negative clinical outcomes, proposed by Kalantar-Zadeh et al. in 2001 [28].

Hiraki et al. investigated physical functionality of non-dialytic patients according to CKD stage. Some parameters of physical evaluation were used, among them, the dynamometer. All parameters showed worse results with disease progression, being more significant in period before dialysis therapy initiation [10].

Zhou et al. showed that two important markers of physical functionality, balance, and strength tests were significantly related to muscle mass and glomerular filtration rate decline, demonstrating the development risk of sarcopenia during CKD evolution [26].

A recent review discusses strategic hypotheses of mass loss attenuation and decreased muscular function related to age and uremic state. Authors affirm that after establishing strategies to increase muscle mass, such as adequate nutritional support, metabolic acidosis correction, and resistance exercises, other strategies can be considered, such as testosterone and growth hormone replacement, stimulation of mitochondrial biogenesis, and stem cells [8].

Sarcopenia and frailty in CKD

The term "sarcopenia" has recently been redefined as a syndrome of progressive decline in age-related mass and muscle function and associated with an increased risk of frailty, physical disability, and mortality risk [4, 29].

Sarcopenia is associated to functional impairment and worsening quality of life, especially in ESRD, influenced by aging, sedentary lifestyle, low vitamin D levels, high circulating potassium levels, arterial hypertension, insulin resistance, deficient macronutrients, and low socioeconomic level, as demonstrated by the NHANES III study [30].

Definition of sarcopenia in this population depends on the method applied. When defined by reduced values of HS and skeletal muscle mass, evaluated by electric bioimpedance test, Pereira et al. found a higher predictive power of mortality in this population [29].

Frailty is defined as a physiological state of greatest vulnerability to stress present in the elderly, characterized by a significant deterioration in cognitive, functional, and health status. It was initially described in geriatric population, but currently, there is a high prevalence in young and old CKD individuals, reaching from 26 to 68% in ESRD [31].

Sarcopenia and frailty have been associated to increased risk of hospitalizations, falls, and mortality in CKD [11, 31]. Diagnostic methods and interventions can improve quality of life, minimize functional disabilities, and reduce unfavorable clinical outcomes [31].

Although it is not considered a unique method of diagnosis of sarcopenia by International Society of Renal Nutrition and Metabolism, researchers have used the HS in patients submitted to dialysis therapy to aid in their diagnosis and treatment [6].

A recent study estimated the prevalence of 6 to 10% of sarcopenic stages 3 and 5 CKD patients aged 18 to 80 years old. Diagnostic criteria used in this study were HS measurements by the dynamometer (< 30th percentile of a population-based reference) and other anthropometric assessments [29].

In a systematic review, Leal et al. showed that HS is widely used as a method of diagnostic criteria of sarcopenia, and its results are similar to general population: HS values are associated with age and gender, capable to predict clinical complications. However, the authors highlighted that it is necessary to standardize the techniques used for HS, the position of measurement, and reference values for this population [6].

Reference values

Although dynamometry is currently used in several clinical situations and is capable of assisting clinical interventions, one of the major obstacles to its use is the lack of cutoff points, both in healthy population and in populations with comorbidities, including ESRD [6].

The proposal to define cutoff points or reference values of HS in different populations is important for real and reliable comparisons between obtained and normative values [3, 7]. Calibration protocols must be followed to maintain the measurement consistency.

Few studies have developed cutoff points for HS, but they have portrayed its importance in classifying muscle mass and function loss degrees, predicting unfavorable outcomes and designing interventions that may improve muscle function [3, 7, 9, 21].

Pereira et al., in 2015, evaluated sarcopenia prevalence in 287 individuals with stages 3 to 5 CKD, according to HS measurements and others parameters of muscle mass reduction. In this study, in absence of reference values for non-dialytic ESRD population, reference values of a population study were considered [7, 29].

The establishment of measurement protocols that ensure the definition of cutoff points for ESRD individuals is necessary to better evaluate muscle function and reduce unfavorable clinical event occurrence.

Conclusions

Handgrip strength is one of the most widely used muscle functional evaluation methods currently available and has been considered a practical and reliable measure of skeletal muscle function in the general population and also in ESRD patients.

The early nutritional and muscle function diagnosis, obtained by the nutritional and muscle strength assessment, is important to avoid unfavorable consequences such as reduced quality of life, PEW, and early death.

In this review, we presented studies that dealt with occurrence, prevalence, and predictive power of poor clinical outcomes, mortality, and aspects to combat the marked loss of muscle mass and strength in uremic individuals. These topics are important and may base greater studies.

The measure of HS are influenced by age, gender, body mass, presence of sarcopenia and uremia, the stage of CKD, hand's dominance, body position, verbal encouragement, and dialysis procedure. It can be considered to clinical and research practice the average of three HS readings, or the average of two higher readings, between three readings, or the higher reading, between readings.

Further studies are needed to standardize the techniques used for HS, establishment protocols, and reference values to assist preventive measures of unfavorable outcomes in ESRD population.

Abbreviations
BMI: Body mass index; CKD: Chronic kidney disease; ESRD: End stage of renal disease; HS: Handgrip strength; MIS: Malnutrition-Inflammation Score; PEW: Protein energy wasting

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
MCO contributed to the conception and design of the study, acquisition and interpretation of data, and drafting the article. MNBB and ALB contributed to the conception and design of the study, in drafting the article, revising it critically for important intellectual content, and final approval of the version. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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