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Influence of Body Composition and Nutrition Parameters in Handgrip Strength: Are There Differences by Sex in Hemodialysis Patients?

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Abstract

Background: Hemodialysis (HD) patients are vulnerable to multiple metabolic and nutrition derangements, leading to changes in body composition. Handgrip strength (HGS) has been used as a nutrition marker. We aimed to evaluate the relationship between HGS and lean tissue mass (LTM) with several parameters in HD patients and develop HGS predictive equations. *Methods:* Cross-sectional study with 155 patients in HD treatment for ≥3 months. Body composition was assessed through bioimpedance spectroscopy. HGS was measured with a hydraulic hand dynamometer. Biochemical parameters were evaluated. Data were analyzed by sex. *Results:* Ninety-four were men, and mean age was 64.4 ± 14.7 years. We found positive correlation of HGS with LTM, lean tissue index, and body cell mass and negative correlation between HGS, age, and overhydration in both sexes. Serum albumin level presented a positive correlation and magnesium a negative correlation with HGS only in men. The LTM presented a positive correlation with protein intake, serum albumin level, and body cell mass and a negative correlation with age in both groups. A significant positive correlation with magnesium and a negative correlation with overhydration were observed in men. The predictability of the models was $R^2 = 0.618$ for men and $R^2 = 0.500$ for women. *Conclusion:* HGS is highly correlated with LTM, and both differ between sexes and are, therefore, differently correlated with the parameters studied. Body composition, overhydration, and some biochemical parameters explain changes in HGS. Predictive models including body composition and biochemical parameters may explain at least 50% of the variance of HGS. (*Nutr Clin Pract.* 2018;33:247–254)

Keywords

body composition; dialysis, handgrip strength; lean tissue mass

Several common causes of decreased muscle strength (MS) and muscle reserves have also been described in end-stage renal disease and hemodialysis (HD) patients, such as lower levels of physical activity, aging, and sex (being lower in women). In addition, high levels of urea and inadequate dialysis have also been associated with MS in this specific population.[1-3] The decrease of MS and muscle mass leads to worse quality of life and higher mortality rates, cachexia, and limited mobility.[1,2,4,5] Furthermore, HD patients with some degree of malnutrition show low handgrip strength (HGS).[6]

HGS is a measurement of the maximal voluntary force of the hand and arm, and this method is considered a useful tool to evaluate MS and muscle function as it is simple, noninvasive, and a reliable procedure.[3] The assessment of HGS has been used as a nutrition marker, as it may reflect changes in the lean tissue mass (LTM), is a good predictor of survival, and is a better predictor of outcomes than the LTM in HD patients.[7,8]

Schlüssel et al[9] defined cutoff points for HGS in healthy participants in the right and left hand according to sex; the cutoff points were 42.8 kg for the right hand and 40.9 kg for the left hand for men and 25.3 kg and 24 kg, respectively, for women. Massy-Westropp et al[10] indicated cutoff points for HGS in adults older than 20 years; HGS was between 32 and 47 kg in men and between 19 and 30 kg in women, depending of the hand measured. The Foundation for the National Institute of Health (FNIH) as part of the Sarcopenia Project identified cutoff points for distinguishing weakness in adults: HGS <26 kg in men and <16 kg in women.[11] In HD patients, a few studies have shown cutoff points. For example, García et al[12] verified the accuracy of the cutoff points of HGS for the diagnosis of malnutrition; the reference values used were <18 kg in

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women and <28.5 kg in men. On the other hand, Vogt et al[13] showed cutoff points to predict mortality in HD patients, and the values were 22.5 kg in men and 7 kg in women.

In HD patients, HGS can be up to 50% lower than in healthy participants.[14] It decreases with aging, and the loss of HGS is greater than the loss of LTM. Moreover, LTM can be maintained at the same time HGS decreases.[2] Besides this, HGS may be useful to monitor in malnourished patients while they are being treated with nutrition therapy.[5] Despite the utility and importance of the HGS measurement, it is not frequently used in routine assessment and not always available.

On the other hand, the LTM is frequently assessed in HD patients through different body composition methods, and it is an indicator of muscle mass. The LTM is a significant clinical marker as the low amount has been considered a predictor of unfavorable outcomes and has a complex relationship to all-cause mortality in HD patients.[2,15,16] Its assessment is also recommended in the guidelines and has been considered a strong nutrition status predictor.[17] Lower muscle mass has been associated with worse survival and is an adverse prognostic factor in these patients.[18]

The aim of this study was to evaluate the relationship between HGS and LTM with biochemical parameters and body composition in HD patients and to develop an HGS predictive equation for each sex.

Methods

Study Design

This was a cross-sectional study.

Study Population

A total of 155 HD patients from 1 HD unit in Portugal were included. Patients aged ≥18 years under HD treatment 3 times per week during 4 hours for ≥3 months (online hemodialfiltration technique) were included. All patients were dialyzed with high-flux (Helixone; Fresenius Medical Care, Bad Homburg, Germany) membranes and ultrapure water in accordance with the criteria of International Organization for Standardization regulation 13959:2009 (water for HD and related therapies).

Body Composition Analysis

In all patients, body composition was assessed with the Body Composition Monitor (BCM; Fresenius Medical Care). The BCM takes measurements at 50 frequencies from 5 to 1000 kHz. The measurement was performed approximately 30 minutes before the midweek HD sessions, with 4 conventional electrodes (Fresenius Medical Care) being placed on the patient, who was lying in a supine position: 2 on the hand and 2 on the foot contralateral to the vascular access. To ensure the quality of the measurements, all had to exceed 90% (quality indicator of the measures provided by the device).

The parameters obtained with the BCM were dry weight, body mass index (BMI), LTM, lean tissue index (LTI), fat mass (FM), fat tissue index (FTI), body cell mass, total body water (TBW), and relative overhydration (OH/extracellular water [ECW] predialysis).

HGS

HGS was measured using a North Coast Hydraulic Hand Dynamometer (Gilroy, CA). Dynamometry was performed on the opposite side to the vascular access according to previous studies that measured HGS.[19] The patient sat with the arm bent at an angle of 90° on a horizontal base and held the dynamometer with the fingers around it. Three measures were taken with 30 seconds of break between each measurement, and the average was considered for this study.

Biochemical and HD-Related Parameters Studied

We also analyzed HD vintage and biochemical parameters: serum albumin level, total protein, magnesium predialysis, and protein intake measured by normalized protein catabolic rate (nPCR).

Descriptive and Correlation Statistical Analysis

The Kolmogorov-Smirnov test was used to test for normality of the variables' distributions. Data were analyzed by sex. We used Student *t* tests to determine mean differences between groups in demographic, biochemical, and body composition parameters. Descriptive analyses are presented as mean ± standard deviation (SD), frequencies, and percentages. We determined the Pearson correlation coefficient between HGS and the variables of interest (body composition and biochemical parameters) and between LTM and the variables of interest.

Multivariate Regression Models

The predictors of HGS in men and women were explored, and 2 HGS predictive equations were determined. For the development of the multivariate regression models, a stepwise backward elimination (automatic procedure) was carried out. Therefore, to reach the best model, we started with all the candidate variables, tested the deletion of each one, deleted the variables to improve the model, and repeated this process until no further improvement was possible.

Statistical significance was accepted as $P < .05$, and all statistical tests were 2-tailed. The statistical analyses were performed using SPSS version 20 (SPSS, Inc, an IBM Company, Chicago, IL).

Table 1. Patients' Characteristics by Sex (N = 155).

Characteristic	Men (n = 94), Mean ± SD	Women (n = 61), Mean ± SD	*P* Value
Age, y	64.7 ± 14.96	64.02 ± 14.4	.778
HD vintage, mo	67 ± 54.24	89.36 ± 79.32	.057
Serum albumin level, g/dL	4.03 ± 0.29	3.97 ± 0.32	.285
Total proteins, g/dL	6.91 ± 0.49	6.74 ± 0.44	.034[a]
Potassium, mEq/L	5.23 ± 0.73	5.18 ± 0.71	.693
Magnesium, mg/dL	2.34 ± 0.38	2.31 ± 0.24	.459
Serum phosphorous, mg/dL	4.71 ± 1.52	4.52 ± 1.13	.39
Serum calcium, mg/dL	8.97 ± 0.68	8.92 ± 0.8	.674
nPCR, g/kg/d	1.11 ± 0.25	1.1 ± 0.18	.63
Dry weight, kg	70.8 ± 12.15	66.77 ± 14.07	.09
BMI, kg/m^2	25.12 ± 3.84	27.76 ± 5.44	.001[a]
TBW, L	37.93 ± 5.65	30.59 ± 4.78	<.001[a]
OH/ECW predialysis, %	12.1 ± 6.58	11.18 ± 7.61	.388
Urea volume, L	34.79 ± 5.32	27.8 ± 4.41	<.001[a]
LTM, kg	40.37 ± 9.34	28.54 ± 7.43	<.001[a]
LTI, kg/m^2	13.79 ± 3.03	11.43 ± 2.75	<.001[a]
Fat Mass, kg	22.13 ± 9.82	28.05 ± 11.63	.001[a]
FTI, kg/m^2	10.27 ± 4.42	15.4 ± 6.53	<.001[a]
Body cell mass, kg	22.28 ± 6.57	15.05 ± 5.1	<.001[a]
HGS, kg	25.74 ± 8.83	14.24 ± 7.09	<.001[a]

BMI, body mass index; FTI, fat tissue index; HD, hemodialysis; HGS, handgrip strength; LTI, lean tissue index; LTM, lean tissue mass; nPCR, normalized protein catabolic rate; OH/ECW, overhydration/extracellular water; TBW, total body water.
[a]Significant *P* values ($P < .05$).

Statement of Ethics

This study was approved by the president of the ethics committee, and an informed written consent was previously signed by the patients.

Results

Patients' Characteristics

We analyzed data of 155 patients, and the mean and SD for the parameters studied are shown in Table 1. Among men, 30.9% (n = 29) had diabetes, whereas in the group of women, this value was 24.6% (n = 15). We found statistical differences between men and women with respect to total proteins, BMI, TBW, urea volume, LTM, LTI, FM, FTI, body cell mass, and HGS.

HGS and LTM

The correlation between the HGS and the variables of interest was analyzed. All correlations were determined by sex (Table 2). The highest correlations for both groups were with LTM (Figures 1 and 2) (men: $r = 0.668$, $P < .001$; women: $r = 0.475$, $P < .001$).

The correlations between HGS and LTM, LTI, and body cell mass were statistically significant. Age and OH/ECW were negatively correlated with HGS in both groups. Regarding serum albumin level, magnesium, and BMI, we found a positive and statistically significant correlation only in men. The correlation between nPCR, total protein, and HD vintage with HGS was not statistically significant correlated in any of the 2 groups.

The correlation between LTM and the variables of interest is described in Table 3. All the correlations were also divided in women and men.

The LTM presented positive and statistically significant correlations with serum albumin level, total protein, and body cell mass in both sexes. Protein intake and magnesium were also positively correlated but only statistically significant in men. In contrast, the correlation with OH/ECW was negative and statistically significant also in men. Finally, a negative correlation was observed regarding age in both groups.

The coefficient of variation (CV) in women was 49.7% for the HGS values and 26% for the LTM values. In men, the CV was 34.3% for the HGS values and 23.1% for the LTM values.

Equations for Estimating HGS by Sex

We also analyzed the variables in regression models by sex (Table 4). A stepwise backward elimination procedure led to the selection of body composition parameters and biochemical values for the development of the best models for predicting HGS in both groups. The predictability of the

Table 2. Pearson's Correlation of Handgrip Strength by Sex.

	Handgrip Strength, kg			
	Men (n = 94)		Women (n = 61)	
Variable	*r*	*P*	*r*	*P*
Age, y	−.526	<.001[a]	−.396	.002[a]
HD vintage, mo	−.027	.793	−.214	.097
BMI, kg/m^2	.232	.024[a]	.113	.384
Serum albumin level, g/dL	.295	.004[a]	.225	.081
Total protein, g/dL	.139	.182	.237	.065
nPCR, g/kg/d	.028	.797	.115	.390
Magnesium, mg/dL	.275	.008[a]	−.054	.681
LTM, kg	.668	<.001[a]	.475	<.001[a]
LTI, kg/m^2	.592	<.001[a]	.331	.009[a]
Body cell mass, kg	.652	<.001[a]	.432	.001[a]
OH/ECW predialysis, %	−.427	<.001[a]	−.336	.008[a]

BMI, body mass index; HD, hemodialysis; LTI, lean tissue index; LTM, lean tissue mass; nPCR, normalized protein catabolic rate; OH/ECW, overhydration/extracellular water.
[a]Significant *P* values ($P < .05$).

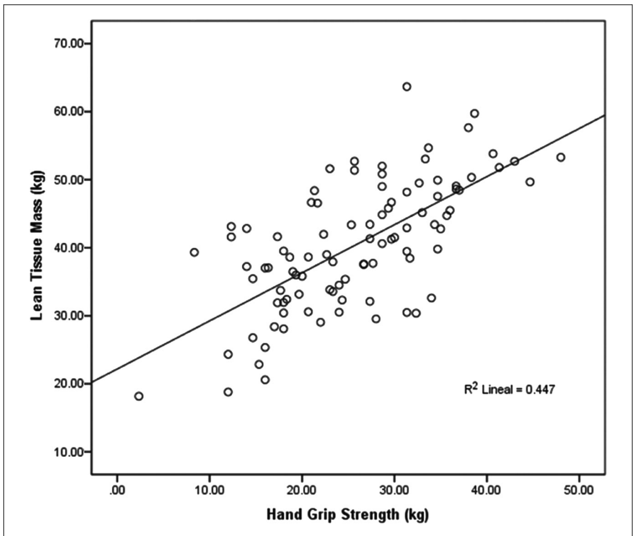

Figure 1. Correlation between handgrip strength and lean tissue mass in men.

developed models was $R^2 = 0.618$ and $R^2 = 0.500$ for men and women, respectively.

$$\text{HGS (males)} = 22.2 + 1.9(\text{BCM}) - 3.2(\text{LTI}) - 0.1(\text{age})$$
$$-9.1(\text{protein intake})$$
$$+4.9(\text{serum albumin level})$$
$$+3.5(\text{Mg}) - 0.5(\text{OH/ECW})$$

$R^2 = 0.618$, $F = 20.41$, standard error of the estimate (SEE) = 5.52, with HGS (kg), BCM (kg; $P < .001$), LTI (kg/m^2; $P = .001$), age (years; $P = .013$), protein intake (g/kg/d; $P = 0.001$), serum albumin level (g/dL; $P = .024$), magnesium (Mg; mg/dL; $P = .041$), and OH/ECW predialysis (%; $P < .001$).

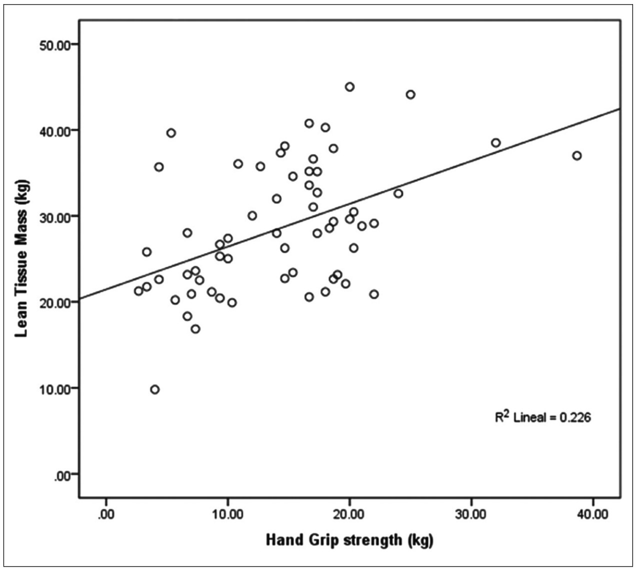

Figure 2. Correlation between handgrip strength and lean tissue mass in women.

$$\text{HGS (females)} = 51.9 + 3.4(\text{BCM}) - 5.5(\text{LTI})$$
$$-7(\text{Mg}) - 0.3(\text{OH/ECW})$$

$R^2 = 0.500$, $F = 14.21$, SEE = 5.07, with HGS (kg), BCM (kg; $P < .001$), LTI (kg/m^2; $P < .001$), OH/ECW predialysis (%; $P = .001$), and Mg (mg/dL; $P = .017$).

Different models were also tested. In men, the model without magnesium decreased the predictability by 1.6% ($R^2 = 0.618$ changed to $R^2 = 0.602$). The model without OH/ECW decreased the predictability by 9.2% ($R^2 = 0.618$ changed to $R^2 = 0.526$).

In women, the model without magnesium decreased the predictability by 4.7% ($R^2 = 0.500$ changed to $R^2 = 0.453$), and the model without OH/ECW decreased the predictability by 13.4% ($R^2 = 0.500$ changed to $R^2 = 0.366$).

Discussion

In the present study, men showed higher levels of HGS, TBW, urea volume, LTM, LTI, and body cell mass and lower levels of FM, FTI, and BMI than women.

Using the cutoff points of FNIH in our study, 51.1% of men and 54.1% of women had low MS.[20] According to the cutoff point proposed by Vogt et al[13] to predict mortality in maintenance dialysis, 18.3% of women and 23.2% of men satisfied the criteria in our study. We also observed that

Table 3. Pearson's Correlation of Lean Tissue Mass by Sex.

	Lean Tissue Mass, kg			
	Men (n = 94)		Women (n = 61)	
Variable	*r*	*P*	*r*	*P*
Age, y	−.598	<.001[a]	−.463	<.001[a]
HD vintage, mo	−.056	.594	−.180	.165
BMI, kg/m^2	.151	.147	−.151	.147
Serum albumin level, g/dL	.259	.012[a]	.310	.015[a]
Total protein, g/dL	.247	.016[a]	.421	.001[a]
nPCR, g/kg/d	.301	.005[a]	.100	.453
Magnesium, mg/dL	.256	.013[a]	.202	.119
Body cell mass, kg	.996	<.001[a]	.993	<.001[a]
OH/ECW predialysis, %	−.297	.004[a]	−.162	.211

BMI, body mass index; HD, hemodialysis; nPCR, normalized protein catabolic rate; OH/ECW, overhydration/extracellular water.
[a]Significant *P* values ($P < .05$).

our sample had lower values of HGS than the references described for the healthy population.

In HD patients, the sex of the patient influences MS, which is usually higher in men than in women, as in the general population. Several studies developed in HD patients showed similar results to our study, with women having lower HGS than men.[3,4,21,22] In our study, the MS assessed with HGS showed statistically significant differences with sex.

The results of our study showed a negative correlation between HGS and age in both sexes, and this trend has already been described in the literature.[8,23,24] However, this correlation was much stronger in men ($r = -0.526$ in men and $r = -0.396$ in women). Other authors found that HGS also declines throughout life in males and females in the healthy population.[25]

On other hand, HGS has been pointed out as a sensitive measurement of short-term response to nutrition therapy and deprivation, and its values may be dependent on the nature and duration of nutrition deprivation.[5] Moreover, intervention studies with oral nutrition supplementation have shown to improve HGS, and also a better malnutrition inflammation score classification has been related to a higher HGS.[26,27] Therefore, we consider that the assessment of HGS in HD patients is important to evaluate changes in short periods.

The nPCR is a parameter frequently used to evaluate dietary protein intake in HD patients. Surprisingly, protein intake did not show a statistically significant correlation with HGS, but it contributed to explain changes in HGS in men. Similar to our results, Bataille et al[28] associated HGS and nPCR in a multivariate analysis including several clinical parameters and did not find any significant association. Nonetheless, one of the most important factors to preserve muscle mass is protein intake.[29] Other authors have observed that protein intake is positively related to HGS,[30] both in middle-aged and elderly people, with a higher protein intake being associated with higher values of HGS and arm muscle circumference.[31] As stated here, various results have been described, but most of the studies showed a relationship between protein intake and HGS.[32,33]

It has already been described that whole body protein, body cell mass, and muscle mass affect MS.[26] Body cell mass is the metabolically active part of the muscle mass without bone mineral mass and ECW. Some authors consider it an adequate nutrition status predictor for HD patients because body cell mass does not include ECW.[16] As far as we know, this is the first study including and analyzing the relationship between body cell mass and HGS, showing a statistically significant correlation in both sexes. Apart from this and according to the multivariate analysis, body cell mass and LTI showed a high variance inflation factor (VIF) that indicated the strong collinearity between both parameters with HGS.

In previous studies, apart from age, sex, nPCR, and LTM, other parameters have been associated with HGS such as serum albumin level, transthyretin, predialysis creatinine, and predialysis urea.[28] In summary, MS is not only about muscle size; other entities may be associated, such as age, sex, biochemical parameters, and OH.[2] Comparing our predictive models with the literature, we observed that the previous authors just included body composition parameters and demographic characteristics. Angst et al,[34] in a multivariate regression, explained 76.6% of the variance in grip strength in healthy participants, including in the model sex, age, body height and weight, and occupational demand of the hand. Lopes et al,[35] in a model developed in young and middle-age adults to explain HGS by sex, showed that forearm circumference and hand length influence HGS. Vaz et al[36] included parameters to predict HGS such as sex, age, and forearm circumference in Indian male and female participants. There is a lack of studies that have developed models to predict HGS in HD patients. Comparing them with the equations for healthy populations, we can observe that our model is the only one that includes biochemical and other body composition parameters.

It has been pointed out that the hydration status may be influenced by malnutrition.[37] In our study, patients with higher levels of OH presented lower HGS, which may be associated with a poor nutrition status also found among these patients.

Regarding HGS and biochemical parameters, we found a positive and statistically significant correlation with serum albumin level only in men. In patients undergoing peritoneal dialysis, this correlation has also been described.[24] Most studies that suggest that serum albumin level is associated with HGS did not differentiate data between sexes as we have done in our study.[2,4,14,28] Beberashvili et al[38] found a positive and statistically significant correlation between

Table 4. Multivariate Linear Regression Analysis of Handgrip Strength.

	Men (R^2 = 0.618)			Women (R^2 = 0.500)		
Variable	B	*P* Value	VIF	B	*P* Value	VIF
Body cell mass, kg	1.95	<.001[a]	20.91	3.66	<.001[a]	28.97
Lean tissue index, kg	−3.15	.001[a]	20.51	−5.48	<.001[a]	27.55
Age	−0.133	.001[a]	1.76	−0.090	.088	1.38
nPCR, g/kg/d	−9.05	.001[a]	1.23	0.04	.683	
Serum albumin level, g/dL	4.85	.024[a]	1.12	0.094	.926	1.38
Magnesium, mg/dL	3.45	.041[a]	1.2	−6.95	.018[a]	1.25
OH/ECW predialysis, %	−0.45	<.001[a]	1.27	−0.31	.001[a]	1.11

B, constant; nPCR, normalized protein catabolic rate; OH/ECW, overhydration/extracellular water; VIF, variance inflation factor.
[a]Significant *P* values ($P < .05$).

serum albumin level and HGS in both sexes in HD elderly patients. Heimbürger et al[39] did not find any association between HGS and serum albumin level in dialysis patients. Gama-Axelsson et al[40] analyzed the result of prevalent and incident dialysis patients who were not inflamed and found that, within the incident group, the LBM and HGS were lower in patients with poor nutrition status but did not find the same result with serum albumin level. They concluded that serum albumin level correlates poorly with several markers of nutrition status.

Serum magnesium levels have been associated with muscle mass and MS. Magnesium intake may play a role in the prevention of age-related low strength and muscle mass, as magnesium depletion causes structural damage to muscle cells.[41,42] In our data, we observed a positive and statistically significant correlation with HGS and magnesium in men. However, magnesium contributes to explain HSG changes in men and women. Dominguez et al[42] investigated the relationship between serum magnesium concentrations and muscle performance in older participants and showed a strong correlation between grip strength and serum magnesium, concluding that magnesium supplementation improves muscle function.

Contrary to our results, Welch et al[43] examined associations between intake of magnesium, body composition, and MS in women and did not find an association between magnesium and HGS in this sex.

The strongest correlation with HGS was the LTM in both groups. However, generally men tend to have more muscle mass than women, even HD patients.[8,23] Schlüssel et al[9] also reported a high and statistically significant correlation in healthy men. Muscle mass is one of the determinants of MS. MS loss is due to the loss of muscle mass, as demonstrated by high correlations in cross-sectional studies.[22] Leal et al[4] found a significant and positive correlation between HGS and lean body mass in HD patients.

The LTM was significantly correlated with more parameters than HGS. We found a negative correlation with age and a positive correlation with serum albumin level and body cell mass in both sexes. Apart from that, we also observed a positive and significant correlation with total protein (men and women) and with protein intake but only in men. According to the literature, LTM decreases with aging, and serum albumin level has been associated with muscle mass, as we found in our study.[1,2,15,22,44]

Considering the predictive models that we have developed, body composition, OH, biochemical parameters, and age are variables that contribute to explain HGS variability in women and men. In men, the biochemical parameters are those with more weight in the model, whereas in women, the body composition parameters are the strongest. The parameters that are more important when predicting this outcome variable are protein intake, serum albumin level, and magnesium in men (higher constant [B] values) and LTI as well as body cell mass in women.

Practical Application

The equations intend to predict the HGS, and monitoring HGS could facilitate early detection in patients with HGS loss as it can lead to worse quality of life and higher mortality rates, cachexia, and limited mobility in HD patients. In addition, HGS may be useful to monitor malnourished patients while being treated with nutrition therapy but is not always available.

We also consider that the assessment of HGS in HD patients is important to evaluate changes in short periods. As we measure body composition monthly, with these equations, we could be able to frequently monitor patients' predicted HGS.

In conclusion, we observed that HGS is significantly correlated with LTM; both are different by sex and are, therefore, differently correlated with the parameters studied. Body composition, OH, and some biochemical parameters explain changes in HGS.

Despite the considerable number of patients included, this was a single-center study. A possible limitation of this study is that data regarding OH could be unavailable in some clinical centers. As a result, the proposed model could not be used in some dialysis settings. We recognize that the prediction equation will require validation.

On the other hand, a strength of this study is that, to our knowledge, this is the first study that has analyzed the influence of body cell mass and OH in HGS.

Statement of Authorship

C. Garagarza, A. L. Flores, and A. Valente contributed to the conception/design of the research; contributed to the acquisition, analysis, or interpretation of the data; drafted the manuscript; critically revised the manuscript; agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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