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Short Communication

Total protein or leucine intakes are not associated with handgrip strength in hemodialysis patients: A pilot study

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SUMMARY

Background & aims: Inadequate protein intake is associated with lean body mass (LBM) loss. However, it is unclear whether high protein diet and leucine intake are associated with handgrip strength (HGS), a validated marker of muscle function. This study aims to: i) assess the prevalence of patients with low HGS; and ii) verify if HGS is correlated with high protein diet and leucine consumption in hemodialysis patients.

Methods: This cross-sectional study analysed patients at two center hemodialysis (HD) clinic and sixty-two patients aged ~39 years with length of time on HD ~60 months undergoing HD was carried out. Body weight (kg), LBM (kg) and body fat mass (%) assessments were performed by dual-energy X-ray absorptiometry and height (m) through portable stadiometer. Body mass index (BMI) (kg/m^2) was calculated using the body weight and height. HGS (kg) was measured using a hydraulic dynamometer. Fisher's exact test, Chi-square, Pearson's correlation, and logistic regression were done to test the hypothesis.

Results: Out of 62 patients, 47 (75.8%) presented low HGS. In addition, no correlation was found between protein intake (if in percentage or g/kg/d) and HGS ($r = 0.07$, $p = 0.58$; $r = -0.04$, $p = 0.70$, respectively). Although there is a low correlation among leucine intake (g/d) and HGS ($r = 0.39$, $p = 0.01$), low HGS was not associated with leucine intake in the crude model (OR: 0.86 95%CI(0.60–1.24) $p = 0.441$), nor after adjustment for age, sex and BMI (OR: 0.84 95%CI(0.56–1.26), $p = 0.422$).

Conclusions: Approximately 75% of patients undergoing hemodialysis presented low HGS. Additionally, neither a high protein diet nor leucine intake was associated with the HGS values.

1. Introduction

Handgrip strength (HGS) measures the voluntary force of the arm and hand, and is associated with muscle function loss in Brazilian patients on hemodialysis [1]. Using a cut-off of HGS for healthy individuals, previous studies [1,2] found a muscle function loss in approximately 56% of hemodialysis patients. During hemodialysis, patients commonly experience anorexia, increased HGS loss and mortality [3].

Although the main causes of malnutrition are reduced appetite and inadequate intake, an increased proteolysis with loss of 3.8–4.2 g of free amino acids during a hemodialysis session was observed in Brazilian patients undergoing hemodialysis [4]. In malnourished patients, a reduction in blood leucine, isoleucine, valine concentrations were found during hemodialysis [5]. Considering that blood branched-chain amino acid (BCAA) concentrations are positively associated with malnutrition and LBM in hemodialysis patients [5], it is probable that BCAA from diet is associated with protection LBM loss. Considering to chronic uremia leads to impaired muscle mTOR pathway signalling and that CKD rats receiving leucine via gavage are partially protect of the muscle wasting [6]. However, none of the previous studies evaluated leucine intake in humans. Additionally, the evaluation of food intake with focus on protein and leucine consumption in chronic

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kidney disease (CKD) patients undergoing hemodialysis is needed to predict muscle function in clinical practice.

Evidences suggests in healthy non-CKD African Americans and Chinese peritoneal dialysis patients have reported that protein consumption is associated with HGS [7,8]. However, is unknown whether protein intake and leucine affects the muscle function in Brazilian hemodialysis patients, once previous study demonstrated that HGS is linked to LBM [9].

Therefore, we hypothesized that normal HGS is good tool to evaluate muscle function, and is associated with a high protein diet and a leucine intake. The classification of HGS adopted was obtained using a reference specific for South American individuals, based on age and nutritional state using the BMI. The threshold adopted for women was ≤50 years (underweight: ≤25 kg, healthy weight and overweight: ≤27 kg and obese: ≤28 kg), for those with >50 years (underweight: ≤ 22 kg, healthy weight and overweight: ≤ 23 kg, obese ≤24 kg); for men ≤50 years (healthy weight: ≤41 kg, overweight: ≤45 kg and obese: ≤46 kg); and for those with >50 years (underweight: ≤33 kg, healthy weight: ≤ 36 kg, overweight: ≤ 40 kg and obese: ≤ 41 kg) [10].

Thus, we aimed to measure the prevalence of patients with low HGS and verify if HGS is associated with a high protein diet and a leucine consumption in CKD patients undergoing hemodialysis.

2. Methods

2.1. Study design and participants

The study design and sample composition has been described previously [11]. All adult patients were recruited at two different outpatient hemodialysis clinics. This study was approved by the Research Ethics Committee under protocol 1.919.324 and all patients signed the informed consent.

2.2. Anthropometric assessment

All anthropometric assessments were performed after the intermediate hemodialysis session, to prevent LBM variation due to muscle mass hydration, as previously described [11]. Body weight (kg) was obtained after the hemodialysis session using Dual energy X-ray absorptiometry (DXA) (Hologic, Waltham, USA) and height (m) through portable stadiometer (SECA®, Hamburg, Germany). Body mass index (BMI) (kg/m^2) was calculated using the body weight and height. Body fat percentage and LBM were acquired using the DXA (Hologic, Waltham, USA). HGS (kg) was measured using a hydraulic dynamometer (Takei®, Japan) on the non-fistula side. Normal or low HGS measurements was classified according to previous epidemiologic study [10] using a reference specific for South American individuals, based on nutritional state using the BMI and age. The threshold adopted for women was ≤50 years (underweight: ≤25 kg, healthy weight and overweight: ≤27 kg and obese: ≤28 kg), for those with >50 years (underweight: ≤ 22 kg, healthy weight and overweight: ≤ 23 kg, obese ≤24 kg); for men ≤50 years (healthy weight: ≤41 kg, overweight: ≤45 kg and obese: ≤46 kg); and for those with >50 years (underweight: ≤33 kg, healthy weight: ≤ 36 kg, overweight: ≤ 40 kg and obese: ≤ 41 kg) [10]. All anthropometric assessments were performed by trained nutritionists.

2.3. Food intake consumption assessment

Energy, macronutrients and leucine consumption were obtained from the three 24 h food recalls that was performed on non-consecutive days, two on weekdays and one on the weekend. Food composition analysis was performed using the Dietpro® software, version 5.8, Viçosa, Brazil, using the United States Department of Agriculture (USDA) Food Database [12] or nutritional facts labels.

2.4. Statistical analyses

Sample size required whether an expected correlation coefficient between leucine intake vs. HGS differs from zero, we adopted an alpha 0.05 and beta 0.20; thus, a total sample size is 47 patients.

Data normality was confirmed using the *Shapiro–Wilk* test. Data was expressed as mean and standard deviation. Fisher's exact test was applied to assess how many of the patients were male and how many were female based on the results. The Chi-square test was done to evaluate the cause of disease. Student t test was applied to assessed to verify the difference in age, length of time the patient has undergone hemodialysis and how long ago the diagnosis of the CKD was first given, anthropometric and food intake assessments. Pearson's correlation was assessed between the daily protein (% and g/kg) and leucine (g) intake with the HGS. Logistic regression was performed to assess: the association of normal or low HGS with the total protein (% and g/kg of body weight) and leucine consumption. Two models were performed, crude model (unadjusted) and model 1 (adjusted by age, sex and BMI). All statistical tests were performed using the MedCalc® Seoul, Korea, software, and the $p < 0.05$ was assumed as significant.

3. Results

The prevalence of patients with low HGS is 75.8%. The characteristics of patients are described in Table 1. Although the patients that had undergone hemodialysis for approximately sixty months, they showed no difference in HGS values. In addition, the main cause of CKD is hypertension (Table 1). No difference for sociodemographic, anthropometric and food intake variables was verified among the groups. In addition, the characteristic of diet is normocaloric, hyperlipidic and normoproteic (Table 1). A subgroup analysis among underweight and overweight was performed in the low HGS group, but no difference in energy, carbohydrate, fat, nor protein consumption was found (Supplementary Table 1).

Pearson's correlation analysis showed no difference between protein intake (if in percentage or g/kg/d) and HGS ($r = 0.07$, $p = 0.58$; $r = -0.04$, $p = 0.70$, respectively). Although there is a low correlation among leucine intake (g/d) and HGS ($r = 0.39$, $p = 0.01$) (Supplementary Fig. 1), logistic regression analysis did not find associations in the Crude Model between the normal or low HGS and % protein, g/kg/d protein and leucine intake, nor after adjusting for age, sex and BMI (Model 1) (Table 2).

4. Discussion

The present study shows that 75.8% of patients have low HGS. In addition, we found a weak correlation between daily leucine intake and HGS or LBM quality, as well as no association between HGS (normal or low) and protein or leucine consumption. Additionally, no association was found between those who consumed high (≥1.2 g/kg/d) or low amounts of protein (≤0.8 g/kg/d) and HGS values in CKD patients on hemodialysis.

In contrary, Leal et al., 2011 [1] found low HGS in 56% of patients on hemodialysis. The probable explanation is that Leal et al., 2011 [1] used a cut-off established by Schlussel et al., 2008 [2], was determinated using HGS reference values in a study that included only Brazilian patients. Although, Garcia et al., 2013 [9], identified the cut-off values of HGS for adult and elderly hemodialyzed patients, it was sex specific. In addition, they did not identify the prevalence of patients with low HGS. Based on these discrepancies

Table 1
Characteristics of patients undergoing hemodialysis.

Variables	Normal HGS	Low HGS	*P value*
	n = 15 (24.2%)	n = 47 (75.8%)	
Age (years)†	39.06 ± 11.13	39.80 ± 11.57	.825
Sex#			
Male (%)	10 (16.2)	32 (51.6)	.829
Female (%)	5 (8.0)	15 (24.2)	
Age of diagnostic of CKD (years)†	31.93 ± 12.25	32.51 ± 13.59	.884
Length of time on hemodialysis (months)†	59.13 ± 50.71	60.95 ± 55.77	.911
Cause of illness‡			
Hypertension	3	21	.217
Diabetes	1	4	
Glomerulonephritis	1	5	
Other	10	17	
Anthropometric assessments			
Body weight (kg)†	71.29 ± 14.91	62.29 ± 16.79	.059
Body mass index (kg/m^2)†	25.84 ± 5.66	23.14 ± 5.13	.114
Body fat (%)†	31.48 ± 12.01	28.23 ± 12.77	.377
Lean body mass (kg)†	46.70 ± 10.55	41.86 ± 9.26	.126
Handgrip strength (kg)†	42.36 ± 10.16	30.22 ± 8.10	.0004*
Food intake assessments			
Energy (kcal)†	1761.18 ± 614.84	1566.35 ± 694.18	.310
Energy (kcal/kg of body weight)†	25.66 ± 10.82	26.41 ± 12.69	.826
Total carbohydrate (%)†	48.21 ± 8.29	46.37 ± 6.70	.444
Total fat (%)†	34.70 ± 6.44	36.20 ± 4.76	.416
Total protein (%)†	17.25 ± 3.65	17.27 ± 3.95	.984
Total protein (g/kg of body weight)†	1.09 ± 0.56	1.07 ± 0.56	.921
Leucine (g)†	2.95 ± 1.78	2.59 ± 1.47	.491

CKD: Chronic kidney disease; HGS: handgrip strength; LBM: lean body mass; SD: standard deviation; † Student t test; # Fisher's exact test. ‡Chi-square of Pearson. Data are expressed as mean and standard deviation.
* $p < 0.05$ when compared to Normal HGS group.

Table 2
Associations of handgrip strength (normal or low) with protein or leucine intake in patients undergoing hemodialysis.

Continuous variables	Odds Ratio (95% IC)			
	Crude	*P value*	Model 1	*P value*
HGS (normal or low) x protein				
Total protein (%)	1.00 (0.85–1.16)	.985	1.01 (0.85–1.19)	.881
Total protein (g/kg of body weight)	0.94 (0.33–2.65)	.919	0.68 (0.23–2.01)	.493
Leucine (g)	0.86 (0.60–1.24)	.441	0.84 (0.56–1.26)	.422

Model 1: adjusted by age, sex and body mass index.
HGS: handgrip strength.

in reference values among studies, we chose an HGS cut-off acquired in evaluated healthy patients from different South American countries (Argentina, Brazil, Colombia, and Chile) which took into account sex, BMI, and ethnicity [10]. It is important to note that the Brazilian population is made up of many ethnicities. Therefore, independently of the cut-off selected, the prevalence of patients on hemodialysis with low HGS reinforces the importance of muscle function evaluation by HGS assessment, especially considering its ease and economically-viable nature.

Our data differs from that of Dong et al., 2011 [8], which observed that the daily protein intake of ≥0.94 g/kg/d is associated with higher HGS compared to patients undergoing peritoneal dialysis consuming ≤0.73 g/kg/d. Dialysis patients that are taking in protein at >1.2 g/kg/d are associated with lower risks for malnutrition, which we evaluated by serum albumin or BMI, compared to those who ate <0.8 g protein/kg/d [13]. However, our study does not support the fact that the protein intake of 1.1 g/kg/d offers a protection against muscle function loss.

Although during hemodialysis, the anorexia, HGS loss, and mortality may occur [3], we did not find an association between HGS loss and reduced daily protein intake. In contrast, we speculate that patients with low leucine consumption (~2.7 g/day), are prone to increased muscle catabolism [5]. Additionally, low physical activity level may explain the reduced HGS.

4.1. Strength and limitations

This is the first study to evaluate leucine consumption in CKD patients undergoing hemodialysis and its relation with HGS. Previous studies only investigated the plasma amino acid profile, but not the leucine content of the meals. However, the cross-sectional design did not allow us to establish the cause to effect relationship between the HGS and leucine intake. Moreover, limited number of patients included did not allow to generalize these data for all CKD patients.

In summary, 75% of patients undergoing hemodialysis for CKD presented low HGS. Additionally, neither a high protein diet nor daily leucine intake was associated with the HGS.

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Statement of authorship

ACBM and RDM participated of collection of data. ATV, AL, CP, and GDP participated of interpretation of data and revision of the manuscript. ACBM and GDP carried out the conception and design of the study, interpretation and analysis of data, and wrote the manuscript. All authors approved the final version manuscript.

Conflict of interest statement

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2019.05.017.

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