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Higher Handgrip Strength is Associated with Better Clinical Outcomes in Hemodialysis Patients

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ABSTRACT

Ribeiro H, Santos G, Soares G, Corrêa H, Maya A, Lauanna T, Neves R, Inda-Filho A, Viana J, Ferreira A, Rosa T. Higher Handgrip Strength Is Associated With Better Clinical Outcomes In Hemodialysis Patients. **JEPonline** 2019;22(1):118-127. The purpose of this study was to verify possible associations between relative handgrip strength (HGS) and clinical variables in patients with chronic kidney disease (CKD). A total of 39 patients with CKD from a private clinic in the city of Brasília participated in this study. The subjects' HGS was measured by a dynamometer. Body composition was estimated by bioimpedance. The biochemical analyses were performed by the private clinic. The sample was stratified into tertiles according to the relative HGS, forming two groups: G1 - lower and medium tertiles (n = 26) and G2 - superior tertile (n = 13). Pearson correlation test was used and, for the comparative analysis between groups, the Student's *t*-test for independent samples (P<0.05). The G2 group presented better results in the variables body mass index, fat mass, body fat, C-reactive protein (CRP), and creatine phosphokinase (CPK) compared to the G1 group. Relative HGS was associated with CRP, CPK, lean body mass, and body fat. Higher values of relative HGS presented better results for the variables that predict cardiovascular diseases and mortality.

Key Words: Body Composition; End-Stage Renal Disease; Muscle Strength; Obesity Paradox

INTRODUCTION

The number of people affected by chronic kidney disease (CKD) corresponds to 10% of the worldwide population. In Brazil, the total estimated number of patients dependent on hemodialysis (HD) is greater than 120,000. The Brazilian Society of Nephrology estimates that 90% of patients with CKD are undergoing renal replacement therapy (1). However, although 70% of Brazilians present some degree of renal dysfunction, only 10% are aware of the diagnosis since the symptoms appear seemingly harmless in advanced stages of the disease (2). In addition, the Brazilian Unified Health System points out that for 2017 ~R$ 4 billion were allocated to hospitalizations, transplants, and medicines. Chronic kidney disease resulted in the disbursement of the greatest resource by the Ministry of Health (3).

Although CKD has a varied etiology, the two most common causes are diabetes and high blood pressure (4). End-stage patients who undergo HD may experience cramps, headaches, hypotension, and dizziness. All are events that are made worse by physical inactivity, thus becoming a vicious circle. Fortunately, there is evidence that indicates CKD patients with a body mass index (BMI) above 30 $kg \cdot m^{-2}$ tend to have a longer life expectancy even with a high percentage of body fat and a higher production of proinflammatory cytokines (i.e., what is called the obesity paradox) (5-7).

Although the use of BMI is part of the practical practice, using only anthropometric measures in the clinical routine may not be the best strategy to predict the health status of the patient. For that matter, studies have shown that cardiorespiratory fitness can significantly alter the relationship between adiposity and clinical prognosis in patients with cardiovascular diseases (8-12). On the other hand, such studies did not address neuromuscular parameters related to the obesity paradox, especially in regards to CKD.

It is clear that mass and muscle strength are directly correlated with clinical outcomes, especially endocrine-metabolic changes, systemic inflammation, osteomioarticular injuries, as well as the increased chance of hypertension and diabetes, which may decrease life expectancy (13). Consequently, the use of simple, cheap, and feasible functional tests, such as the handgrip strength (HGS) test, is widely adopted in the literature as a clinical practice for the prediction of cardiovascular, renal, and mortality outcomes (14). Even though the HGS test was previously described as an independent predictor of mortality and renal outcomes in CKD patients (15,16), the association of different levels of HGS on metabolic, clinical, and biochemical parameters in the HD population it is not fully understood.

Thus, the purpose of this study was to determine the influence of relative HGS on anthropometric and immunometabolic variables of patients with CKD. We hypothesized that relative HGS would show good discriminatory power for clinical health compared to body fatness in patients with CKD undergoing HD.

METHODS

Subjects

This is a cross-sectional study approved by the Research Ethics Committee of the Catholic University of Brasilia (nº 2.497.191). The volunteers who agreed to participate this study signed the informed consent form (ICF) after being informed of the risks and benefits. The sample consisted of 39 patients (20 men and 19 women) with CKD from the HD treatment program of a private clinic in the city of Brasília, Brazil.

The volunteers who participated in this study included: (a) patients on HD who signed the ICF; (b) those who had more than 3 months of HD; and (c) those who were approved by the physician. The exclusion factors included the following considerations: (a) decompensated arterial hypertension; (b) ischemic heart disease; (c) missing the last dialysis session before the physical tests began; (d) recent acute myocardial infarction or by-pass surgery 3 months; (e) cognitive changes that affect participation; and (f) disability of performing physical tests.

Procedures

The subjects completed the International Physical Activity Questionnaire (IPAQ) short version and a sociodemographic questionnaire during the HD sessions. In the following sessions, the subjects were evaluated after the HD sessions into 2 moments: (a) anthropometric evaluation were carried out using tetrapolar bioimpedance (Biodynamics, ®310e, São Paulo, Brazil) in which the subjects' lean mass, fat mass, fat percentage, basal metabolic rate (BMR), BMI; stature and body mass via scales and stadiometer (FilizolaTM, Beyond Technology, PL - 200, São Paulo, Brazil); and (b) evaluation of HGS (Jamar, J00105, Illinois, USA).

The HGS was measured in the non-fistulated or dominant arm for those with catheter access while the subjects were seated with the shoulder in a neutral position. The elbow was flexed at 90º and the wrist was in the neutral position. Three attempts were performed with an interval of 30 sec. The highest value was recorded. The results of the biochemical tests were obtained through blood tests carried out in an automated way within the clinic.

Statistical Analyses

Initially, the normality of the data was analyzed through the Shapiro Wilk test. Descriptive statistics were used by mean and standard deviation values. The HGS values were adjusted to relative strength by the formula (kgf/body mass) and then divided into 2 groups: G1 - lower and medium tertiles (n = 26) and G2 - upper tertile (n = 13). The independent Student *t*-test was used to compare the quantitative variables according to the G1 and G2 groups. In addition, the Pearson correlation test was used to verify the associations between the quantitative variables. The value of $P<0.05$ was used to point out the statistically significant differences. The program Statistical Package for the Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA) was used.

RESULTS

Figure 1 shows the correlation analysis between the relative HGS and the CRP ($r = 0.51$) and lean mass ($r = 0.35$), which were positively associated, as well as body fat and CPK, which were negatively associated, with $r = -0.44$ and $r = -0.49$, respectively ($P<0.05$).

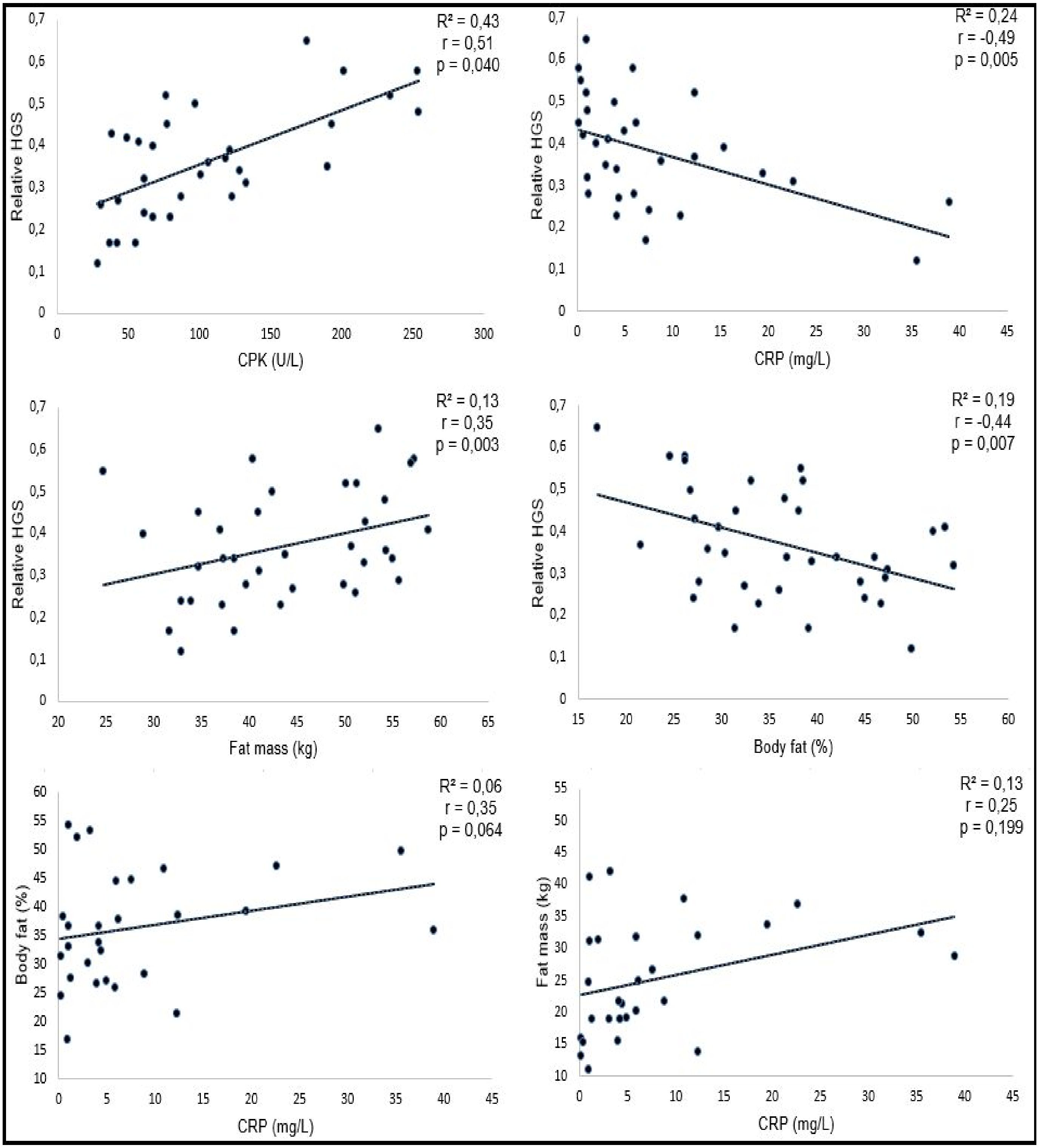

Figure 1. Correlation of Relative HGS, CPK, CRP, Lean Mass, Fat Mass, and Body Fat Variables.

Patient characteristics were stratified according to relative HGS in two groups, G1 - lower and middle tertiles (n = 26) and upper G2 - tertile (n = 13). Both groups are presented in Table 1. The variables age, BMI, fat mass, and body fat presented significant differences between the groups. As for the values of the biochemical variables, there was a significant difference for G1 in the variable CRP and for G2 in CPK.

Table 1. Comparison between Groups by Anthropometric, Functional, and Biochemical Variables (n = 39)**.**

Variables	**Group 1** (n=26)	**Group 2** (n=13)	P
HD vintage (months)	19.6 ± 16.8	19.9 ± 15.3	0.943
Age (yrs)	61.8 ± 13.1	47.3 ± 17.6	0.010*
Weight (kg)	70.5 ± 13.6	65.6 ± 14.2	0.305
Height (m)	1.62 ± 0.08	1.65 ± 0.09	0.381
Abdominal circumference (cm)	99.7 ± 10.4	94.1 ± 16.2	0.216
Waist circumference (cm)	94.7 ± 11.4	89.3 ± 16.1	0.246
BMI ($kg{\cdot}cm^{-2}$)	31.8 ± 6.3	27.9 ± 3.6	0.049*
Lean mass (kg)	42.6 ± 8.8	46.5 ± 9.9	0.234
Fat mass (kg)	28.2 ± 9.9	20.3 ± 6.8	0.019*
Body fat (%)	39.2 ± 9.4	30.3 ± 6.8	0.006*
BMR (kcal)	1315.0 ± 275.9	1414.4 ± 303.6	0.332
METs	254.4 ± 370.7	874.6 ± 1879.6	0.701
Glucose ($mg{\cdot}dL^{-1}$)	131.7 ± 53.7	92.8 ± 14.2	0.079
Triglycerides ($mg{\cdot}dL^{-1}$)	194.2 ± 126.7	167.0 ± 76.2	0.984
HDL ($mg{\cdot}dL^{-1}$)	42.8 ± 9.21	43.0 ± 13.5	0.959
LDL ($mg{\cdot}dL^{-1}$)	91.5 ± 27.5	103.9 ± 13.9	0.400
CRP ($mg{\cdot}L^{-1}$)	10.9 ± 11.1	3.1 ± 3.7	0.005*
Urea post HD ($mg{\cdot}dL^{-1}$)	63.5 ± 25.2	61.3 ± 24.3	0.803
Creatinine ($mg{\cdot}dL^{-1}$)	8.4 ± 3.3	10.0 ± 3.1	0.172
Albumine ($g{\cdot}dL^{-1}$)	3.9 ± 0.2	4.3 ± 0.9	0.129
CPK (U/L)	82.6 ± 41.9	179.7 ± 154.2	0.037*

BMI = Body Mass Index; **BMR** = Basal Metabolic Rate; **HD** = Hemodialysis; **METs** = Metabolic Equivalent of Task; **HDL** = High Density Lipoprotein; **LDL** = Low Density Lipoprotein; **CRP** = C-Reactive Protein; **CPK** = Creatine Phosphokinase; *Significant difference (P<0.05)

DISCUSSION

Our results indicate that the group with higher relative HGS presented better results in the biochemical, anthropometric, and inflammatory variables. Moreover, the relative HGS was also moderately associated with variables related to CVD mortality and risk. Thus, we confirmed our initial hypothesis that the relative HGS presented good discriminatory power for variables related to cardiovascular health in patients undergoing HD.

It is known that excess body adiposity is responsible for the overproduction of pro-inflammatory molecules (e.g., CRP). However, a good level of physical fitness appears to protect against these immune-metabolic changes. Anthropometric variables that differ between groups (BMI, fat mass, and body fat) have an important relationship with the development of CVD, and it has been verified in several studies (17-20) that body composition has been shown to be a predictor of mortality in patients with DRC. Caetano and colleagues (2) reported that BMI has an important role in predicting 1-yr mortality in HD patients. This finding suggested that malnutrition may be a risk factor for mortality, with 2.98 times more chances than those with BMI ≤18.5 $kg \cdot m^{-2}$. Curiously, patients on HD treatment who present high BMI (overweight and obesity) have a higher survival rate, and this phenomenon is known as the obesity paradox (5)..

Kalantar-Zadeh et al. (13) analyzed the phenomenon of the obesity paradox in more than 120,000 hemodialytic patients for 5 yrs and identified that high BMI alone does not guarantee a higher survival rate. However, when analyzed along with muscle mass, it was observed that the overweight and obese patient with elevated serum creatinine levels obtained a higher survival rate compared to those with a decrease in serum creatinine. Evaluating muscle mass as an indicator of metabolic and functional health seems to be more important than body weight per se. Additionally, associating physical fitness in this type of analysis seems to be of great importance, since in other special populations, overweight individuals with good physical fitness present a lower risk of mortality and development of CVD when compared to eutrophic individuals with low physical fitness (8,22).

Likewise, the maintenance and improvement of HGS, a variable of physical fitness, has been evidenced as a protective factor for CVD and increased survival (23), which reinforces our findings, since in the present study the relative HGS was positively associated with lean mass (r = 0.34) and negatively with body fat (r = -0.44). In addition, increased body fat induces an inflammatory condition (24), and this low-grade inflammation may impair the production of muscle strength via increased oxidative stress (25). Nonetheless, physical fitness is essential in the regulation of inflammatory cytokines, since IL-6 derived from muscle contraction reduces the production of TNF-α and promotes an increase in the production of other cytokines, such as IL-10 and irisin that produce an anti-inflammatory effect (26). This suggests that patients with CKD who present greater muscle strength may have higher levels of myokine capable of balancing the inflammatory balance, even with high body fat and BMI.

The inflammatory state of patients with CKD directly impacts survival and physical capacity, which is evident in this population given the systemic state of inflammation. Of the inflammatory markers, CRP has been shown to be the most commonly used for the evaluation of the inflammatory state (27). In our study, the group with the highest values of relative HGS had a lower value for CRP when compared to the weaker group. In addition, there was a negative association between relative HGS and plasma CRP (r = -0.49). This finding suggests that patients with greater HGS values manifest better blood inflammatory status. In this sense, Moraes et al. (23) evaluated the effects of resistance training, a therapeutic exercise that promotes an increase in muscle strength during 6 months of intervention in 37 HD patients. They reported a reduction in CRP levels of 2.3 ± 0.9 to 1.6 ± 0.6 of which they explained was due to the increase in strength levels and muscle mass.

When the isolated association between body fat and CRP was analyzed, a significant correlation was not observed (Figure 1). This finding seems to indicate that muscle strength may be a variable with better discriminatory power for the inflammatory state when compared to body fat. These results are supported by other studies which have pointed out that higher levels of muscle mass and strength seem to protect the renal tissue from inflammation and fibrosis (29,30). Thus, a lower inflammation observed in our patients with higher HGS seems to reflect also in renal tissue. Such information should be taken with caution since it was not evaluated in the kidney.

Another important finding from the present study was that the CPK levels differed between the groups. The higher values were observed in the stronger group while a positive correlation was observed with relative HGS (r = 0.51). Meeting these findings, Flahault et al. (7) followed up CPK values for 12 yrs in 1,801 pre-dialytic conservative CKD patients, where at the end of the study individuals in the lower tertile of CPK had a 40% higher chance of mortality. The authors pointed out that the CPK levels indicated a relationship with nutritional status, especially with lean mass that was possibly related to the level of physical activity and, consequently, muscle-metabolic health.

Limitations in this Study

This study presents some limitations, one of which is the absence of the analysis of other inflammatory variables such as IL-6, IL-10, and TNFα, which could have allowed for more robust correlations with muscular strength and physical fitness. However, the high cost to evaluate these variables allowed for the evaluation for only CRP, a usual marker in the clinical routine, low cost, and good applicability. Also, the need to establish a better correlation between CPK and physical activity could have been better clarified with the use of other tools, which were not available.

CONCLUSIONS

Patients who obtained better values of relative HGS presented better results for anthropometric and inflammatory variables, particularly in some related to the development of CVD and mortality. Additionally, the relative HGS was also associated with variables related to mortality and risk of CVD. Thus, relative HGS seems to be a functional variable with better discriminatory power in patients undergoing HD when compared to body composition, which leads us to believe that factors related to physical fitness are better predictors than those related to body composition.

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