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RESEARCH

The relationship between grip strength with health-related quality of life and mortality in hemodialysis patients

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Abstract

Purpose Hemodialysis (HD) is a therapeutic modality that enables the highest survival for individuals with chronic kidney disease (CKD). In contrast, HD contributes to the pro-inflammatory state and may negatively affect the muscle strength and quality of life (QoL) of these individuals. To date, few studies have evaluated the association between decrease in strength and QoL in HD patients. Thus, our objective was to assess whether diminished muscle strength is associated with worse health related QoL and mortality.

Methods We included patients aged $\geq$ 18 years on HD. Clinical and demographic data were collected from patients' medical records. Clinical data, nutritional status (laboratory, anthropometry, bioimpedance analysis) and health-related QoL (World Health Organization's quality of life questionnaire, WHOQOL-Bref) were analyzed at baseline. Mortality was recorded for 32 months.

Results Among the 105 patients evaluated, the median age was 52 (43–64) years, and males were predominant (n = 73; 70%). The general median of QoL was 66.8 ± 11.9. Approximately 30% of patients were considered to have a worse QoL and 12,4% to have low muscle strength. This was not associated with QoL and mortality. HD vintage greater then to 5 years was associated with higher dissatisfaction in the perception of the environmental domain and overall QoL.

Conclusion Our data suggest that low muscle strength was not associated with health-related QoL using the WHOQOL-Bref instrument and mortality.

Keywords Quality of life · Mortality · Grip strength · Muscle strength · Chronic kidney disease · Hemodialysis

Background

Chronic kidney disease (CKD) is considered a public health problem due to its global prevalence, between 10 and 13% [1]. Among renal replacement therapies, hemodialysis (HD) is the most used [2–4]. Although necessary, the 5-year survival of HD patients is 40 to 50% [5]. HD patients commonly present exacerbated catabolism, food restrictions, endocrine, and pro-inflammatory alterations [6]. These changes inherent to CKD can lead to impact muscle function that is associated with impaired of quality of life (QoL) and shorter survival [7, 8]. The health-related QoL (HRQoL) is 10% [9] lower in these patients than in the general population [10].

HRQoL is the subjective self-perception of well-being and health status, which includes physical, psychological, social, and environmental domains that reflect a total score to deal with the mental and emotional aspects of life [11]. Some characteristics in the treatment have negative impacts on the aspects of life and further affect the emotional well-being of patients [12]. HD patients may have an increased perception of stress associated with the disease and a decreased perception of HRQoL symptoms [13].

Several questionnaires have been used for patients with CKD, including the Kidney Disease Quality of Life (KDQOL) [14], the Medical Outcomes Study Short Form Questionnaire (SF-12) [12], the 36-Item Short Form Survey

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(SF-36) [15], EuroQol 5 Dimensions (EQ-5D) [13], and the short version of Quality Questionnaire of the World Health Organization (WHOQOL-Bref) [11]. Although there is a specific instrument for patients with kidney diseases [14], several studies use other alternatives to assess HRQoL in this population [11, 16]. This happens because the KDQOL presents difficulties and limitations in the application, such as the size of the questionnaire, which includes 80 items and takes approximately 16 min to complete, which can increase the respondent's burden [17]. In addition, it contains questions related to the psychological state that can cause discomfort to be answered [17].

Low grip strength is a powerful predictor of poor outcomes such as longer hospital stays, increased functional limitations, poor HRQoL, and mortality [18]. Previous studies show that loss of muscle strength is more strongly associated with aging, wasting of protein energy (PEW), physical inactivity, inflammation, and mortality than low muscle mass. Thereby, decreased strength may have a greater impact on clinical conditions than low muscle mass [19]. Observational study that included 277 patients on HD and used the KDQOL to assess QoL identified that individuals with low strength had lower medians of the physical component of the HRQoL (77; IQR: 50–90 vs 85; IQR: 65–95; $p < 0.001$) [20]. However, few studies have evaluated the association between decrease in strength and QoL in HD patients. Thus, our objective was to assess whether diminished muscle strength is associated with poor HRQoL and mortality.

Materials and methods

Study design

This study used the database of a prospective observational study of HD patients who underwent 3 HD sessions per week at the two clinics in Brazil. Patients were eligible for enrollment if they were 18 years or older of both sexes. The exclusion criteria were being amputees; whether they use pacemakers; whether they had chronic liver disease, sepsis, intestinal malabsorption, cancer, or acquired immunodeficiency syndrome; and whether they were recently hospitalized (which occurred in the last 3 months).

Baseline data were collected in July 2018, and clinical and sociodemographic data, such as age, sex, etiology of CKD, level of education, smoking, HD vintage, and interdialytic weight gain were collected from patients' medical records. Thirty-two months after the initial collection, the medical records of the patients were consulted again to collect only mortality. No other data were checked during the second consultation with medical records. The protocol was approved by the Ethics Committee of our institution. Written informed consent was obtained from all patients before their inclusion in the study (register number: 82445417.5.0000.5083).

Health-related quality of life

HRQoL was evaluated using the WHOQOL-Bref instrument [11]. The WHOQOL-Bref is composed of 26 questions divided into four domains: physical (pain and discomfort, energy and fatigue, sleep and rest, mobility, activities of daily living, dependence on medication or treatments, and work capacity), psychological (positive feelings, thoughts, learning, memory, and concentration; self-esteem, body image, and appearance; negative feelings; and spirituality/religion/personal beliefs), social (personal relationships and social support), and environmental (physical security and protection, home environment, financial resources, health and social care, opportunities to acquire new information and skills, participation and leisure opportunities, physical environment-pollution/noise/traffic/climate and transport). The final result of each domain was transformed into a scale from 0 to 100, with higher scores indicating better QoL [11]. To classify QoL as good, a cutoff point of bigger then 60 was adopted for the total score [21].

Muscle strength

Handgrip strength (HGS) was assessed in the hand of the limb without the arteriovenous fistula, using a Saehan® model SH5001 hydraulic dynamometer (Saehan Corporation, Korea). Patients were instructed to apply maximum force after voice command. The measurement was performed three times with an interval of 1 min. For the analysis, the highest value obtained was considered [22, 23]. The cutoff points used for low muscle strength were HGS < 16 kg for women and < 27 kg for men [8].

Assessment of anthropometry and body composition

Body mass was obtained on an electronic scale [24]. Height was measured using a mobile rod stadiometer with a bilateral millimeter scale (1-mm resolution). To calculate the body mass index (BMI), the ratio between body weight and height squared was performed. Waist circumference (WC) was measured in duplicate with an inelastic measuring tape with a 1.0-mm interval; the mean between the two measurements was calculated. WC was measured at normal expiration at the midpoint between the lower edge of the last rib and the iliac crest [25].

To assess body composition, a multifrequency, octapolar electrical bioimpedance test was used (Seca®, mBCA 525), with a frequency of 50 kHz, at a current of 100 μA. Resistance and reactance were used to estimate phase angle (PhA), appendicular muscle mass, and fat mass (FM). The appendicular skeletal mass index (ASMI) was calculated by dividing the appendicular muscle mass (kg) by the squared height (m^2) [26]. Fat mass index (FMI) was calculated by dividing the fat mass (kg) by the squared height (m^2) [27]. The Edema index was subsequently calculated using the ratio of extracellular water to total body water (ECW/TBW)[28].

Laboratory data

The method used to assess post-urea was enzymatic activity. The ion-selective electrode method was used to assess serum potassium levels. The calorimetric method was used to assess the serum phosphorus, calcium, and albumin levels. To high-sensitivity C-reactive protein (hsCRP) assessment, blood samples were obtained before the HD session (except for urea) during the middle session of the week whereas hsCRP concentrations were evaluated using the Roche® Diagnostic Kit by the immunoturbidimetry method ("COBAS c 701" equipment).

Statistical analysis

The Shapiro-Wilk test was used to examine the normality of the data. Data were expressed as mean ± standard deviation, median (including the interquartile range), or percentage. For data processing and analysis, categorical variables were analyzed by chi-square or Fisher's exact test, and the continuous variables were analyzed by the Student's t-test or Mann-Whitney *U*-test. To compare clinical and demographic variables with HRQoL, the chi-square test and analysis of variance (ANOVA) or the corresponding test for variables with non-parametric distribution was performed. To calculate the sample size of the study, the previous objective, referring to the matrix project, was considered. We estimated the sample size using GPower 3.1. with a test power of 80%, a significance level of 5% and an effect size of 0.73.

Results

Among the 105 HD patients evaluated, the median age was 52 (43–64) years, and the participants were predominantly men ($n = 73$; 69.5%). The median duration of HD was 48.5 (17.0–56.0) months. In the population studied, 12.4% of the patients were considered to have low muscle strength. The median BMI was 24.8 (22.0–28.2) kg/m [2]. The general media of QoL was 66.8 ± 11.9, being 59.6 ± 16.5 for the physical domain, 69.8 ± 13.9 for the psychological domain, 75.0 (62.5–87.5) for the social domain, and 64.5 ± 13.0 in the environment domain (Table 1).

Approximately 30% of patients were considered to have a poor QoL (< 60) and were associated with have stopped smoking. At the follow-up, 91 baseline subjects were evaluated. The mortality rate was 30.8% and was not associated with low strength (Table 1) and HRQoL (Table 2). Smaller PhA and ASMI were significantly associated with low strength. No statistically significant differences were observed among the other analyzed variables (Table 2).

The sociodemographic and clinical characteristics according to each QoL domain are described in Table 3. Individuals > 60 actually had higher environmental satisfaction compared to those aged 35–60. Women showed greater dissatisfaction with the psychological domain. An HD vintage greater than 5 years was associated with higher dissatisfaction in the perception of the environmental domain and overall QoL.

Discussion

According to the results of the present study, low muscle strength was not associated with health-related QoL using the WHOQOL-Bref instrument and risk of death. It is important to highlight that the WHOQOL-Bref tool is subjective and does not assess QoL itself, but rather the individuals' perception of their condition [29]. Thus, aspects inherent in their understanding, resilience towards the disease, and willingness to answer the questionnaire sincerely may influence the results obtained [30]. We also highlight the low prevalence of dynapenia in the population of the present study, which differs from patients undergoing renal replacement therapy [31].

Excess circulating urea, chronic inflammatory state, and endocrine disorders inherent to CKD make this population more exposed to impaired muscle function [32]. Uremic toxins increase oxidative stress and can affect mitochondrial metabolism and energy supply to muscle [33]. Furthermore, malnutrition and presence of comorbidities such as cardiovascular disease and diabetes also contribute to functional impairment in patients with CKD [34, 35]. The state of oxidative stress, inflammation, and overlap complications may contribute to reduced strength and other components of functionality. Reduced muscle strength is known to affect the ability to perform activities of daily living and, therefore, potentially, the overall HRQoL [36]. Low strength also increases the feeling of weakness and fatigue, common complications in HD patients [37]. Therefore, low strength

Table 1 Clinical, body composition, and hydration data of hemodialysis patients according to skeletal muscle strength

Variables	Total $n=105$	Muscle strength		*p value*
		Low $n=13$	Appropriate $n=92$	
Age (in years)	52.0 (43.0–64.0)	58.0 (47.5–63.5)	51.0 (40.2–64.8)	0.240
Male gender, *n* (%)	73 (69.5%)	12 (92.3%)	62 (67.4%)	0.065
HD vintage (months)	48.5 (17.0–56.0)	59.0 (21.0–170.5)	50.0 (18.0–74.8)	0.197
Anthropometric data				
Weight (kg)	70.1 ± 14.9	64.9 ± 8.3	70.8 ± 15.5	0.178
BMI (kg/m^2)	24.8 (22.0–28.2)	23.3 (21.4–24.8)	25.1 (22.3–28.9)	0.08
IWG (%)	3.6 (2.2–4.6)	4.2 (3.4–5.0)	3.5 (2.0–4.5)	0.07
WC (cm)	92.4 ± 13.4	89.6 ± 9.7	92.8 ± 13.8	0.427
Bioimpedance data				
FMI (kg/m^2)	7.9 (5.6–10.6)	6.4 (4.4–8.4)	7.9 (5.8–11.0)	0.122
ASMI (kg/m^2)	8.0 (6.7–8.8)	7.2 (6.3–8.0)	8.1 (6.7–8.8)	**0.03**
Phase angle (°)	6.0 ± 1.2	5.1 ± 1.1	6.2 ± 1.1	**< 0.001**
ECW/TBW	0.43 ± 0.03	0.44 ± 0.03	0.43 ± 0.03	0.319
Quality of life				
Overall QoL	66.8 ± 11.9	67.6 ± 10.9	66.6 ± 12.1	0.796
Physical domain	59.6 ± 16.5	58.5 ± 10.2	59.8 ± 17.2	0.792
Psychological domain	69.8 ± 13.9	73.1 ± 15.9	69.3 ± 13.7	0.369
Social domain	75.0 (62.5–87.5)	75.0 (75.0–75.0)	75.0 (62.5–87.5)	0.788
Environment domain	64.5 ± 13.0	62.7 ± 12.4	64.7 ± 13.1	0.604
Mortality, *n* (%)	28 (30.8%)	4 (33.3%)	24 (30.4%)	0.836

HD, hemodialysis; *BMI*, body mass index; *IWG*, interdialytic weight gain; *WC*, waist circumference; *FMI*, fat mass index; *ASMI*, appendicular skeletal mass index; *ECW/TBW*, ratio of extracellular water to total body water; *QoL*, quality of life. Data were expressed as mean ± standard deviation, median (including the lowest and highest quartile), or percentage. Student's *t*, *Mann–Whitney, chi-squared, or Fisher's tests were performed. Values lower than 0.05 were considered statistically significant

impacts how a physical and psychological symptom affects social relationships and the environment [36].

We believe that there was no association between muscle strength and QoL, because in our population the prevalence of low strength was very low. The prevalence of low strength in studies on HD patients ranges from 29 [20] to 52% [38], whereas in the present study it was only 12.4%. Furthermore, in general, the patients had good QoL, which also differs from the literature, in which general health scores of 25 (IQR 15–35) are observed in HD patients with sarcopenia [20].

Prospective cohort study with a follow-up of 72 months and 635 HD patients evaluated all-cause mortality predictors. Decreased HGS was one of the predictors of mortality (HR: 3.61; 95% CI: 1.70–7.68, $p < 0.001$) [39]. On the other hand, HD patients also tend to have a worse perception of QoL, given the chronic treatment three times a week, which ends up compromising functional capacity, social relationships, and the environment [9].

The lack of association between HRQoL and mortality can be understood by the characteristics of the population studied. The subjects were predominantly male, "young adults" with good nutritional status and on HD for a relatively short time, factors that contribute to a better survival. Furthermore, individuals may have had different reasons for death, including infection with the COVID-19 virus. In addition, impaired quality of life reflects a compromised physical, social, environmental, and emotional state. Such aspects are more associated with the worsening of health status and not necessarily as a direct cause of mortality [40].

In agreement with the researchers' study, QoL using the WHOQOL-Bref questionnaire in elderly patients with peripheral ischemia showed no worsening conditions in the QoL scores during follow-up and that the QoL was also not associated with mortality [41]. A Brazilian prospective observational study with an 8-year follow-up and consisting of 1162 patients (884 on HD and 278 on peritoneal dialysis) found that there is an association between mortality and the physical component of the SF-36 questionnaire (HR: 0.993; 95% CI, 0.989 to 0.997) [42]. Among the ten (10) domains evaluated in the questionnaire, six (6) domains were below

Table 2 Sociodemographic and clinical characteristics of hemodialysis patients according to quality of life

Variables	Quality of life			*p* value
	Total *n* = 105	Poor *n* = 31	Good *n* = 74	
Education				
Illiterate	23 (21.9%)	7 (22.6%)	16 (21.6%)	0.768
Primary	45 (42.9%)	11 (35.5%)	34 (46.0%)	0.768
Secondary	31 (29.5%)	11 (35.5%)	20 (27.0%)	0.768
University	6 (5.7%)	2 (6.5%)	4 (5.4%)	0.768
Smoking status				
Current, *n* (%)	12 (11.4%)	4 (12.9%)	8 (10.8%)	0.09
Former, *n* (%)	32 (30.5%)	9 (29.0%)	23 (31.1%)	**0.04**
Never, *n* (%)	93 (88.6%)	27 (87.1%)	66 (89.2%)	0.09
Laboratory data				
Urea (mg/dL)	27.0 (17.5–36.0)	27.0 (16.0–35.0)	27.0 (17.5–37.5)	0.727
Potassium (mmol/L)	5.3 (4.8–5.8)	5.3 (5.0–5.9)	5.1 (4.7–5.8)	0.328
Phosphorus (mg/dL)	4.9 (4.0–5.8)	4.9 (3.8–5.8)	5.0 (4.2–6.1)	0.716
Calcium (mg/dL)	9.3 ± 0.7	9.4 ± 0.1	9.3 ± 0.1	0.553
Albumin (g/dL)	4.1 ± 0.3	4.0 ± 0.05	4.1 ± 0.03	0.438
hsCRP (mg/dL)	0.4 (0.2–1.1)	0.5 (0.2–1.1)	0.3 (0.1–1.4)	0.421
HGS (kg)	32.0 (26.0–38.0)	32.5 (26.0–39.0)	32.0 (26.0–38.0)	0.585
Low muscle strength, *n* (%)	12 (11.4%)	2 (6.5%)	10 (13.5%)	0.300
Mortality, *n* (%)	28 (30.8%)	10 (34.5%)	18 (29.0%)	0.600

HGS, handgrip strength; *hsCRP*, high-sensitivity C-reactive protein. Data were expressed as mean ± standard deviation, median (including the lowest and highest quartile), or percentage. Student's *t*, Mann–Whitney, chi-squared, or Fisher's tests were performed. Values lower than 0.05 were considered statistically significant

60 [42]. In the present study, only the physical domain had an average of less than 60.

One of the factors that could justify the satisfactory perception of the QoL in this study was the short duration of HD. A cross-sectional study of 150 HD patients used the WHOQOL-Bref questionnaire to assess the QoL and found that longer HD vintage together with low-income status was the only independent negative predictor of QoL ($p < 0.05$) [29]. The long-term treatment of HD is related to immunosenescence, defined as a decline in the immune system's ability to generate effective cell and antibody responses, resulting in a state of "inflammaging" [43].

This study had some limitations. The instrument used was not specific to CKD patients. However, the WHOQOL-Bref was developed in a collaborative project of 15 centers to obtain an applicable and valid instrument for use in different cultures [11] and was validated for the Portuguese language of Brazil, which was carried out according to the methodology recommended by the WHOQOL-Bref Center [11]. Moreover, the WHOQOL-Bref presents less invasive questions than the other instruments. As all data collection was carried out by dietitians without the support of psychologists, this instrument was chosen to avoid any kind of embarrassment to the respondent. This is a sub-analysis, where the original research had another main objective. Another limitation is that 32 months of follow-up is a short time, considering advances in dialysis treatment.

As a strength of the study, we highlighted muscle strength in the assessment of nutritional status, as it is a practical, non-invasive, inexpensive method, and is associated with outcomes such as cardiovascular events and mortality. We also highlight the evaluation of the perception of QoL in a more detailed way and the follow-up time of patients. Such evaluation is relevant to understanding the association of HRQoL and its domains with impacting aspects in the course of CKD, such as inflammation, HD vintage, and survival. In addition, we believe that the data collected contribute to relevant knowledge regarding the better understanding of the perception of the QoL and the importance of including it in the nutritional assessment of HD patients.

Table 3 Comparison of WHOQOL-Bref domain mean scores with clinical data

Variable	WHOQOL-Bref domain				
	Physical	Psychological	Social	Environmental	Overall QoL
Age (years)					
21–34	64.5 ± 16.7	72.86 ± 12.5	65.2 ± 27.8[a]	71.0 ± 11.0[a]	68.4 ± 13.2
35–60	59.1 ± 16.4	67.4 ± 15.1	70.1 ± 19.5[a]	61.3 ± 12.1[b]	64.5 ± 11.9
≥ 60	58.6 ± 16.6	72.4 ± 12.0	81.1 ± 13.3[b]	67.0 ± 14.0[a,b]	69.8 ± 11.1
p value	0.314*	0.169	**0.010***	**0.014**	0.103
Gender					
Male	61.4 ± 16.4	71.7 ± 13.4	73.8 ± 17.8	65.4 ± 12.9	68.1 ± 11.4
Female	55.6 ± 16.0	65.5 ± 14.3	71.5 ± 23.8	62.5 ± 13.2	63.8 ± 12.7
p value	0.094	**0.034**	0.582	0.301	0.088
Etiology of CKD					
Hypertensive nephrosclerosis	59.3 ± 16.2	67.4 ± 13.3	69.7 ± 21.3	62.6 ± 14.1	64.8 ± 12.2
Diabetic nephropathy	55.3 ± 15.6	70.0 ± 16.6	78.0 ± 16.2	64.4 ± 13.8	66.9 ± 13.0
Glomerulonephritis	64.3 ± 18.7	70.0 ± 19.7	68.0 ± 33.1	70.5 ± 11.1	68.2 ± 18.1
Others	61.4 ± 16.7	72.2 ± 11.3	75.0 ± 15.3	65.0 ± 11.8	68.2 ± 9.3
p value	0.459	0.523	0.601*	0.442	0.605
HD vintage					
3 months–1 year	71.1 ± 15.5	79.0 ± 9.1	77.5 ± 12.9	75.3 ± 9.4[a]	75.7 ± 9.0[a]
1–5 years	58.0 ± 17.5	68.9 ± 14.1	72.0 ± 23.1	63.8 ± 14.3[b]	65.7 ± 13.0[b]
≥ 5 years	59.1 ± 14.4	68.8 ± 14.1	73.4 ± 16.0	62.7 ± 10.6[b]	66.0 ± 10.2[a,b]
p value	0.065	0.089	0.809*	**0.019**	**0.043**
Mortality					
Yes	61.1 ± 9.2	67.7 ± 17.0	73.7 ± 20.2	62.5 ± 15.4	66.2 ± 11.3
No	59.0 ± 15.3	69.9 ± 12.6	71.4 ± 20.3	64.6 ± 11.8	66.2 ± 14.2
p value	0.582	0.486	0.645	0.519	0.995

QoL, quality of life, total score; *CKD*, chronic kidney disease; *HD*, hemodialysis. Values presented as mean ± standard deviation, with a significant difference for $p \leq 0.05$, one-way ANOVA test or *Kruskal–Wallis test. Superscript letters (a, b) represent the statistical analysis: different letters mean significant differences

Conclusion

Our data suggest that low muscle strength was not associated with HRQoL and mortality. The absence of association can be justified by low prevalence of low muscle strength and good HRQoL in patients.

Abbreviations CKD: Chronic kidney disease; HD: Hemodialysis; QoL: Quality of life; HRQoL: Health-related quality of life; KDQOL: Kidney Disease Quality of Life; SF-12: Medical Outcomes Study Short Form Questionnaire; EQ-5D: EuroQol 5 Dimensions; WHOQOL-Bref: World Health Organization; HGS: Handgrip strength; BMI: Body mass index; WC: Waist circumference; PhA: Phase angle; FM: Fat mass; ASMI: Appendicular skeletal mass index; FMI: Fat mass index; ECW/TBW: Edema index; hsCRP: C-reactive protein; IQR: Interquartile range

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Data availability Not applicable.

Declarations

Ethical approval and consent to participate The present study was approved by the Research Ethics Committee of the Universidade Federal de Goiás and all participants signed an informed consent form.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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