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Association between handgrip strength and mortality in individuals undergoing hemodialysis: A retrospective cohort study

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SUMMARY

Background and objectives: Handgrip strength offers a valuable method to detect changes and reduced muscle strength and frailty and can help improve prognosis by early diagnosis. Therefore, the aim of the study was to evaluate the association between reduced muscle strength and mortality in individuals undergoing hemodialysis.
Methods: Retrospective cohort study with 994 individuals. Sociodemographic, clinical, and lifestyle variables were obtained from a 2019 study. Mortality data were sourced from death certificates recorded from 2019 to 2022 in the Mortality Information System. Muscle strength was classified based on the following cut-off values: <27 kg for men and <16 kg for women. Survival curves were constructed using the Kaplan–Meier method and Cox Regression was used to evaluate the effect of handgrip strength and age on the time.
Results: More than 65 % of individuals in the sample show depleted strength, most of which were older adults (43.25 %, $p < 0.001$) and men (41.32 %, $p = 0.008$). Older adults with depleted strength showed a significantly higher number of observed deaths than expected ones ($p < 0.001$). After adjustment, HGS remained a significant predictor, associated with a 49 % increased risk of death (95 % CI: 1.16–1.91, $p = 0.002$). Having more than 11 years of formal education demonstrated a protective effect, reducing the risk of death by 1.6 times (95 % CI: 0.41–0.88, $p = 0.009$). Diabetes was found to be associated with almost a twofold increase in the risk of mortality (95 % CI: 1.54–2.49, $p < 0.001$).
Conclusions: The decrease in handgrip strength predicts mortality in individuals undergoing hemodialysis with the risk being higher among older adults, those with diabetes and individuals with fewer than 11 years of education.

1. Introduction

Chronic kidney disease (CKD) has significantly increased in recent years. Millions of individuals worldwide suffer from this disease, which shows an average prevalence of 9.5 % [1,2]. This

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growing burden has substantially increased the number of patients undergoing hemodialysis. About 155,000 individuals receive dialysis in Brazil every year [3]. Estimates expect the further rise of the incidence of CKD in the next years due to the exponential increase in its primary underlying causes (which include diabetes and hypertension) [3–5]. Moreover, CKD greatly contributes to mortality rates, which increased more than 40 % in recent decades [1].

In patients with CKD, reduced muscle strength is closely linked to nutritional status and contributes to disease progression, accelerating the onset of end-stage renal disease [6–8]. Individuals undergoing hemodialysis tend to have lower muscle strength, and this impairment is associated with negative outcomes, poorer prognoses, and an increased risk of mortality [8–12]. Additionally, reduced muscle strength is linked to a higher risk of physical disability and hospitalizations due to cardiovascular events, regardless of muscle mass reserves in this population [6,13,14].

In this context, it is important to emphasize that reduced muscle strength is one of the main diagnostic criteria for sarcopenia, as established by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2). According to this consensus, handgrip strength is considered a key measure for identifying probable sarcopenia, since loss of strength precedes loss of muscle mass and is directly associated with worse clinical outcomes [15].

Handgrip strength offers a valuable method to detect changes in muscle strength and reduced muscle strength and frailty [15]. As mortality rates are highest during the first year of hemodialysis, HGS can help improve prognosis by early diagnosis as declines in strength often precede changes in muscle mass and are amenable to modification and recovery [16,17]. Therefore, the present study aims to evaluate the association between reduced muscle strength, assessed by handgrip strength, and mortality in individuals undergoing hemodialysis.

2. Methods

This retrospective cohort study used data that were derived from a linkage process. Sociodemographic, clinical, and lifestyle variables were obtained from a 2019 study that included individuals undergoing hemodialysis at clinics in the metropolitan region of Espírito Santo, Brazil [18]. The inclusion criteria were: age ≥18 years, confirmed diagnosis of chronic kidney disease (CKD) - by ICD codes: ICD 10: N18 (chronic renal failure), ICD 10: N180 (end-stage renal disease), ICD 10: N188 (other chronic renal failure), ICD 10: N189 (unspecified chronic renal failure) and ICD 10: N19 (unspecified renal failure); being on hemodialysis for at least 6 months and being ambulatory. Individuals with contact precautions, acute conditions that limited participation in the study, and speech and hearing impairments were excluded from the study. Mortality data were sourced from death certificates recorded from 2019 to 2022 in the Mortality Information System, provided by the Espírito Santo State Health Department, with the underlying cause of death classified according to the International Classification of Diseases, 10th revision. All participants with muscle strength data were included in this study. Participants were followed-up up to December 2022.

2.1. Clinical and sociodemographic characteristics

Sociodemographic variables obtained were reported by participants. They included race/ethnicity (White, Brown, Black, Indigenous, and Asian), years of schooling (<8, 8–11, >11), marital status (living with a partner or not living with a partner), income in minimum wages (<1, 1–2, 2–5, >5), and occupation (paid work, unpaid work, or retired) Participants were dichotomously classified based on their physical activity levels, alcohol consumption, and smoking status. Data on clinical variables were collected on the type of vascular access for hemodialysis (catheter or fistula), dialysis vintage in years (<1, 1–5, >5), Kt/V according to the cut off point ≥1.2 (adequate and inadequate) [19] and the presence of comorbidities (diabetes and hypertension).

2.2. Handgrip strength

Handgrip strength was measured after a hemodialysis session in both arms. However, as most individuals had a fistula in their non-dominant arm, data from the dominant arm were used for analysis. Measurements were performed by a Saehan® SH1001 dynamometer. Following the protocol of the American Society of Hand Therapists, participants were instructed to sit in a chair without armrests, with their elbow flexed at a 90° angle without resting it on the abdomen, and placing their feet flat on the floor [19]. In total, three measurements were taken, with an average interval of 20 s between trials, and the maximum strength (in kilograms) was used for analysis. Muscle strength was classified as preserved or reduced based on the following cut-off values: <27 kg for men and <16 kg for women [15].

2.3. Statical analysis

The data were first analyzed and corrected. Mortality data were obtained through a link between the NefroSaudES database and the Mortality Information System using deterministic linkage. Deterministic linkage enables the identification of pairs of concordant records based on common identifiers [20]. The R software was used for all analyses, through the installation and reading of the “lubridate” package. In the present study, the variables full name, date of birth, and municipality code were used, and from the cross-referencing of data, pairs referring to the same individual were detected. After the formation of the new database, the other variables of interest were included. Records with missing data on HGS were excluded from the analyses, as it would not be possible to adequately estimate the outcome without this measurement. All deaths were identified in the Mortality Information System. To minimize the main limitations related to systematic errors, the records were checked visually and carefully. Study variables were described by absolute and relative frequencies. Pearson's chi-squared (χ^2) test assessed differences in proportions between the independent variables and handgrip strength. To evaluate the effect of handgrip strength and age on the time (in months) up to death from any cause, survival curves were constructed using the Kaplan–Meier method, followed by the non-parametric log-rank test to compare the curves [21]. For the Cox Regression analysis, only variables that met the assumptions of proportional hazards, absence of multicollinearity, and no influential observations were included [22,23]. All analyses were performed on R (version 4.4.1) at a significance level of $p < 0.05$.

3. Results

In this study, 363 of the 994 included participants died. More than 65 % of individuals in the sample show depleted strength, most of which were older adults (43.25 %, $p < 0.001$) and men (41.32 %, $p = 0.008$). Additionally, over 44 % had less than eight years of schooling ($p < 0.001$). Regarding occupational activity, nearly two-thirds of participants were retired (59.44 %, $p = 0.017$) and more than 42 % had reduced muscle strength. More than half of the sample had diabetes (53.45 %, $p < 0.001$), of whom 73.7 % showed strength depletion (Table 1).

When analyzing the Kaplan–Meier curves, it is possible to observe that individuals with depleted strength show a lower

Table 1
Descriptive table of sociodemographic and clinical variables of individuals undergoing hemodialysis for Handgrip Strength (HGS).

VARIABLES	Handgrip Strength		p-value	Total n (%)
	Reduced n (%)	Preserved n (%)		
Sex			0.008	
Female	88 (24.24)	65 (17.91)		153 (42.15)
Male	150 (41.32)	60 (16.53)		210 (57.85)
Age			**<0.001**	
Adult	81 (22.31)	80 (22.04)		161 (44.35)
Older adult	157 (43.25)	45 (12.40)		202 (55.65)
Race/color[a] (n = 362)			0.967	
White	68 (18.78)	35 (9.67)		103 (28.45)
Brown	107 (29.56)	60 (16.57)		167 (46.13)
Black	59 (16.30)	29 (8.01)		88 (24.31)
Indigenous	1 (0.28)	0 (0.00)		1 (0.28)
Asian	2 (0.55)	1 (0.28)		3 (0.83)
Schooling (years) (n = 359)			**<0.001**	
<8	159 (44.29)	53 (14.76)		212 (59.05)
8–11	52 (14.48)	54 (15.04)		106 (29.52)
>11	23 (6.41)	18 (5.02)		41 (11.43)
Income (MW) (n = 344)[a]			0.310	
<1	30 (8.96)	10 (2.90)		40 (11.86)
1–2	91 (26.45)	56 (16.28)		147 (42.73)
2–5	75 (21.80)	33 (9.13)		108 (30.93)
>5	30 (8.96)	19 (5.52)		49 (14.48)
Marital status			0.280	
Living with a partner	135 (37.20)	79 (21.76)		214 (58.96)
Not living with a partner	103 (28.37)	46 (12.67)		149 (41.04)
Access (n = 361)			0.344	
Catheter	53 (14.68)	22 (6.10)		75 (20.78)
Fistula	183 (50.69)	103 (28.53)		286 (79.22)
Smoking status			0.471	
Yes	11 (3.03)	8 (2.20)		19 (5.23)
No	129 (35.54)	73 (20.11)		202 (55.65)
Past smoking history	98 (27.00)	44 (12.12)		142 (39.12)
Alcohol use (n = 362)			0.179	
Yes	11 (3.04)	11 (3.04)		22 (6.08)
No	226 (62.43)	114 (31.49)		340 (93.92)
Occupational situation (n = 360)			**0.017**	
Paid work	59 (16.40)	40 (11.11)		99 (27.51)
Leave from paid work	25 (6.94)	22 (6.11)		47 (13.05)
Retired	153 (42.50)	61 (16.94)		214 (59.44)
Physical activity (n = 356)			0.219	
Yes	39 (10.96)	93 (7.59)		136 (18.55)
No	197 (55.33)	93 (26.12)		290 (81.45)
Hypertension			0.765	
Yes	206 (56.75)	106 (29.20)		312 (85.95)
No	32 (8.82)	19 (5.23)		51 (14.05)
Diabetes			**<0.001**	
Yes	143 (39.40)	51 (14.05)		194 (53.45)
No	95 (26.17)	74 (20.38)		169 (46.55)

MW: Minimum wage. The minimum wage is the lowest wage companies can pay employees based on the number of worked hours. It is instituted by law and is reassessed annually based on the cost of living of the population. Its creation was based on the minimum amount persons spend to ensure their survival. In 2019, the minimum wage was R$998.
Chi-squared test ($p < 0.05$).
[a] Fisher's exact test.

probability of survival (Fig. 1). Older adults with depleted strength showed a significantly higher number of observed deaths was that of expected ones, suggesting that reduced strength may be associated with a lower probability of survival (Table 2). In contrast, adults with preserved muscle strength had a higher number of expected deaths than observed deaths, which may indicate better survival associated with preserved muscle strength. The survival curves between HGS categories showed a statistically significant difference (Table 2). These findings suggest that the probability of survival differs between individuals with preserved strength and those with strength depletion.

Individuals with reduced muscle strength had a 1.9-fold higher risk of mortality compared to those with preserved strength ($p < 0.001$) (Table 3). After adjustment, HGS remained a significant predictor, associated with a 49 % increased risk of death (95 % CI: 1.16–1.91, $p = 0.002$). Furthermore, older adults exhibited a 43 % higher risk of mortality compared to younger adults (95 % CI: 1.12–1.82, $p = 0.004$). Conversely, having more than 11 years of formal education demonstrated a protective effect, reducing the risk of death by 1.6 times (95 % CI: 0.41–0.88, $p = 0.009$). Diabetes was found to be associated with almost a twofold increase in the risk of mortality (95 % CI: 1.54–2.49, $p < 0.001$) (Table 4).

4. Discussion

Our findings suggest that older adults with reduced handgrip strength have a higher risk of mortality than those with preserved handgrip strength. Additionally, a higher level of education seems to configure a protective factor that reduces the risk of death.

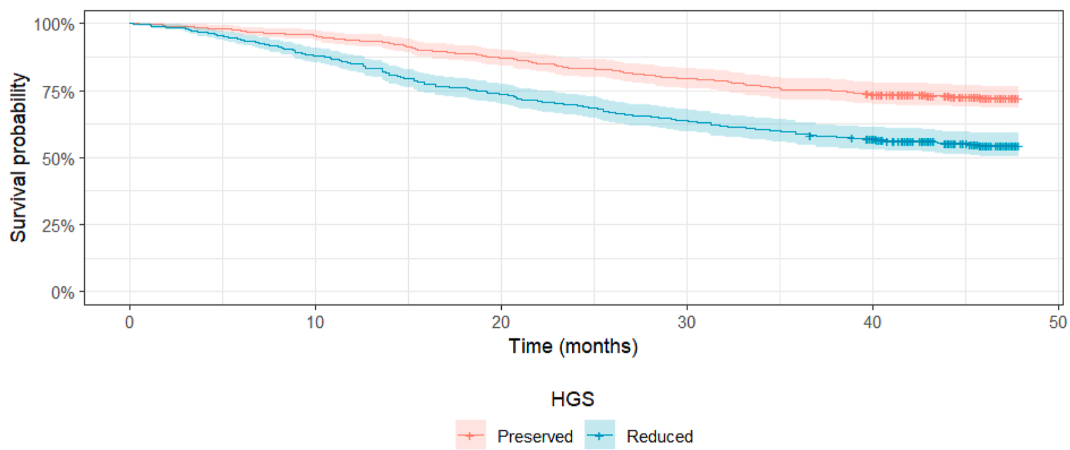

Fig. 1. Kaplan–Meier survival curves of the population (follow-up time) categorized by handgrip strength (preserved and reduced).

Table 2
Expected and observed number of deaths according to Handgrip Strength and Age Group.

HGS – Age Group	N	Observed deaths (O)	Expected deaths (E)	(O-E)2/E	(O-E)2/V
Reduced, adult	237	81	85.9	0.279	0.366
Reduced, older adult	296	157	95.2	40.089	54.543
Preserved, adult	333	80	133.8	21.601	34.296
Preserved, older adult	128	45	48.1	0.205	0.236

HGS: Handgrip Strength. Chi-squared: 62.4, p < 0.001.

Handgrip strength is recognized as a simple, accessible, and effective method for assessing muscle function [24]. Moreover, as a low-cost measure, it has been widely used in individuals with chronic kidney disease (CKD) to evaluate nutritional and functional status [25].

There is still no consensus in the literature on the ideal time to measure handgrip strength. Hwang et al. (2019) reviewed and classified the available studies according to the timing and method of measuring HGS. Among the studies analyzed, four performed the measurement before the dialysis session, two after the session, one during the session, and two did not specify the timing of the assessment. These findings reaffirm the heterogeneity and absence of an established protocol [9,26].

According to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, it is recommended that anthropometric measurements and calculations be made using the individual's dry weight (post-dialysis) [27]. In their most recent update, the guidelines mention the determination of body composition, suggesting that measurements be taken 30 min after the hemodialysis session—the time necessary and sufficient for fluid redistribution [28].

The clinical manifestations of fluid retention combined with azotemia – commonly observed prior to the hemodialysis session – can compromise the accuracy of anthropometric measurements [29]. In addition, after hemodialysis, individuals are expected to have lower hydration and, consequently, a reduction in hydroelectrolytic imbalance [30].

Table 3
Brute cox regression results.

Variables	HR[1]	95%CI[2]	p-value
HGS			
Preserved	–	–	
Reduced	1.92	1.54–2.38	<0.001

HR = Hazard Ratio, CI = confidence interval, Concordance = 0.581 (se = 0.015); Likelihood ratio test = 36.37 on 1 df, p=<0.001; Wald test = 34.55 on 1 df, p < 0.001; Score (log-rank) test = 35.78 on 1 df, p < 0.001.

Furthermore, previous studies indicate that HGS does not appear to be influenced by hydration status [25,31,32]. In this sense, despite being considered a measure of functional capacity, it was decided to standardize data collection and measure strength and other anthropometric parameters after the hemodialysis session.

Individuals undergoing hemodialysis may experience muscle fiber atrophy, which seems to constitute a primary cause of weakness and may be followed by muscle replacement with fatty and fibrous infiltration, further exacerbating muscle strength impairment [33,34]. However, nutritional alterations can also contribute to fatigue and changes in muscle contraction patterns [35].

Among the methods to assess strength, HGS is considered as a reliable indicator of nutritional status and muscle function [36], thus being able to infer that complications from compromised nutritional status, such as malnutrition, along with the presence of comorbidities, may contribute to the increased risk of mortality associated with strength depletion. Previous studies support this by showing its association with nutritional status and a higher prevalence of comorbidities [37–39].

In line with our findings, a previous meta-analysis demonstrated an inverse relationship between handgrip strength and mortality [40]. Regarding the determination of a more appropriate cutoff point for individuals undergoing hemodialysis, evidence is conflicting in the literature [6]. In studies conducted in Asian populations, based on the Asian Working Group for Sarcopenia (AWGS), differences have been reported in the predictive capacity of strength in relation to mortality [13,41].

There is still no consensus on the best way to address this variable. Chen et al. (2024), in a dose–response meta-analysis, reported that HGS may be associated with mortality risk in a U-shaped pattern, suggesting that both low and high values may be related to increased risk of death [42]. Conversely, in a North

Table 4
Cox Regression for all-cause mortality according to handgrip strength adjusted for sex, age group, marital status, scholling, income, dialysis vintage, Kt/V, diabetes and hypertension.

Variables	HR[1]	95%CI[2]	p-value
HGS			
Preserved	–	–	
Reduced	1.49	1.16–1.91	0.002
Sex			
Female	–	–	
Male	0.93	0.74–1.17	0.5
Age group			
Adult	–	–	
Elderly	1.43	1.12–1.82	0.004
Marital status			
Not living with a partner	–	–	
Living with a partner	1.12	0.88–1.42	0.4
Schooling (years)			
<8	–	–	
8–11	0.82	0.63–1.06	0.13
>11	0.60	0.41–0.88	0.009
Income (MW)			
<1	–	–	
1–2	0.94	0.64–1.37	0.7
2–5	0.96	0.64–1.44	0.9
>5	1.02	0.62–1.66	>0.9
Dialysis vintage (years)			
<1	–	–	
1–5	0.96	0.63–1.46	0.8
>5	0.92	0.59–1.46	0.7
Kt/V			
Adequate	–	–	
Inadequate	1.16	0.57–2.37	0.7
Diabetes			
No	–	–	
Yes	1.95	1.54–2.49	<0.001
Hypertension			
No	–	–	
Yes	0.88	0.64–1.22	0.4

HGS = Handgrip Strength, MW = Minimum Wage, HR = Hazard Ratio, CI = Confidence Interval. Concordance = 0.65 (se = 0.016); Likelihood ratio test = 92.89 on 14 df, p=<0,001; Wald test = 90.95 on 14 df, p < 0,001; Score (logrank) test = 96.02 on 14 df, p < 0,001.

American cohort study, modeling strength as a continuous variable showed a significant association with mortality, indicating that dichotomization may be a limiting factor, given the linear relationship between the two [32].

The mechanisms underlying the association between muscle strength and mortality in the hemodialysis population remain unclear. Dialysis treatment itself is believed to contribute to muscle atrophy, resulting in a consequent reduction in strength [43]. Individuals with CKD tend to experience marked catabolism, along with reduced contractile protein synthesis and impaired muscle regeneration, all of which contribute to loss of strength [44,45]. Furthermore, individuals undergoing hemodialysis are known to be more physically inactive [46]. The relationship between muscle strength and physical activity is characterized by a negative feedback loop, whereby reduced strength leads to lower physical activity, which in turn further aggravates muscle weakness [40,46].

Moreover, the symptoms and complications associated with end-stage chronic kidney disease (CKD), such as acidosis, anemia, accumulation of uremic toxins, and the inherent catabolic effects of dialysis treatment, contribute to reduced muscle strength and increased frailty [47,48]. A previous meta-analysis, which included studies employing different cut-off points and assessment protocols, identified an inverse relationship between handgrip strength (HGS) and mortality [9]. In the present study, age emerged as a factor associated with mortality, both in relation to depleted HGS and when analyzed independently. The number of deaths observed among elderly individuals with reduced strength was considerably higher than expected.

Furthermore, the aging process shows a decline in muscle strength and mass and an increased risk of mortality [49,50]. In individuals with chronic kidney disease, this process may occur at an accelerated pace, a phenomenon referred to as premature aging syndrome, which may be further exacerbated by the uremic phenotype associated with renal failure [51]. The divergence between chronological and biological age due to CKD may also affect other systems, such as muscles and blood vessels, exacerbating frailty [52,53].

Regarding education level, higher education constituted a protective factor against mortality risk. This association may be explained by the fact that individuals with higher education tend to delay the initiation of dialysis and take preventive measures against complications, which contributes to their longer survival [54]. Consistent with our findings, previous studies have found lower education levels as a factor associated with an increased risk of mortality. Among individuals with CKD, those with no formal education had twice the risk of death of those with higher education [55,56].

The association between CKD and diabetes can be considered bidirectional, as glycemic decompensation may accelerate the decline in kidney function, while reduced kidney function can, in turn, worsen diabetes [57]. In a study evaluating more than one million individuals with diabetes, Birkland et al. (2021) reported that kidney disease is among the earliest and most frequent complications and is associated with a twofold increase in mortality risk [58]. The results of the present study further highlight diabetes mellitus (DM) as a risk factor in hemodialysis patients, nearly doubling the risk of death. Similarly, a study conducted in individuals with end-stage CKD showed that those with diabetes had lower survival rates and a higher risk of mortality [59].

This study has limitations inherent to its retrospective design, including the possibility of selection and information biases, since the data analyzed were previously collected for other purposes. In addition, HGS was assessed only at baseline, without considering changes during follow-up, which makes it impossible to assess the evolution of this measure and its temporal relationship with the outcomes. Potential unmeasured confounding factors—biochemical, inflammatory, and nutritional status markers—may have influenced the results and reduced the ability to fully control for these effects in the analysis. The sample consisted of individuals residing in the Southeast region of Brazil, which may limit the generalization of the findings to other regions of the country, given the sociodemographic, cultural, and healthcare differences.

Although the retrospective longitudinal design allows the identification of temporal associations, it does not permit establishing causal relationships. Nevertheless, the incorporation of HGS assessment into clinical protocols can contribute to the monitoring and care of this population and should be encouraged in conjunction with strategies for training professionals and planning preventive actions. Additionally, the lack of standardization in the HGS protocol in the literature and the absence of a consensus on the appropriate cut-off point for the hemodialysis population also offer limitations. Further studies are needed to address these issues.

5. Conclusions

Our findings indicate that the decrease in handgrip strength predicts mortality in individuals undergoing hemodialysis and that risk increases in older adults and those with less than 11 years of education. Furthermore, early diagnoses leads to better prognoses. Thus, including the HGS assessment as a clinical protocol is crucial to monitor individuals with chronic kidney disease, focusing on accurate diagnosis. This approach can be implemented by enhanced professional training, the planning of preventive measures, and the promotion of health and protection for this vulnerable population, particularly older adults and those with low levels of education.

Author contribuition

Conception and design: L.P.S.K, C.A.M; data sorting and cleaning: L.P.S.K, C.A.M, K.S.B, L.V.B.L; data analysis: L.P.S.K, C.A.M; data interpretation: L.P.S.K; manuscript interpretation and critical review: M.C, A.C.C, A.C.O.S, C.B.P, J.R.S.F, F.Z.P, J.A.S, F.K.H, E.V.H.F, E.T. S.N, L.B.S; manuscript supervision and final approval: L.B.S.

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Conflict of interest

The authors declare no conflict of interest.

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