

# Association of physical activity level and physical fitness with the cognitive function of patients in hemodialysis

*Asociación del nivel de actividad física y aptitud física con la función cognitiva de pacientes en hemodiálisis*

*Associação do nível de atividade física e aptidão física com a função cognitiva de pacientes em hemodiálise*

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## Abstract

This study aimed to correlate cognitive function with the physical activity level (PAL) and physical fitness over three years of patients undergoing hemodialysis and to compare the PAL and physical fitness over this period of patients with and without cognitive problems. Therefore, a cohort study was carried out, including patients evaluated between 2018 and 2020, through the Mini-Mental State Exam, functional physical record, Elbow Flexion test, Sit-to-stand test, Handgrip Strength test (HGS), and by the physical activity monitor. Data analysis was performed using the Pearson's Correlation test and the paired Student's t-test and its non-parametric equivalent, when necessary, with a significance level of 5%. The results showed that cognitive function assessed in the different years of the research was positively correlated with physical fitness and with PAL: in 2018, with HGS ( $r = 0.313$ ;  $p = 0.019$ ); in 2019, with cardiorespiratory fitness ( $r = 0.288$ ;  $p = 0.038$ ), with HGS ( $r = 0.235$ ;  $p = 0.033$ ) and with PAL on HD days ( $r = 0.359$ ;  $p = 0.010$ ) and on days without treatment ( $r = 0.314$ ;  $p = 0.026$ ); and in 2020, with the PAL up to date without HD ( $r = 0.387$ ;  $p = 0.014$ ). In addition, patients without probable cognitive deficit had higher PAL and physical fitness values in all years of analysis compared to those with the probable cognitive deficit: in 2018, this difference was significant in HGS and PAL on a day contrary to hemodialysis; in 2019, in cardiorespiratory fitness and PAL on a day contrary to treatment; and in 2020, in cardiorespiratory fitness, HGS and PAL on both days. It is concluded that patients with higher PAL and better physical fitness had a better cognitive function, suggesting the importance of physical activity practice as an effective alternative in improving physical fitness and, consequently, cognitive function in HD patients.

**Keywords:** Chronic Renal Failure; Musculoskeletal and Neural Physiological Phenomena; Physical Functional Performance; Motor Activity; Cognition.

## Resumen

Este estudio tuvo como objetivo correlacionar la función cognitiva con el nivel de actividad física (PAL) y la aptitud física durante tres años en pacientes sometidos a hemodiálisis, y comparar el PAL y la aptitud física en este período entre pacientes con y sin problemas cognitivos. Para ello, se llevó a cabo un estudio de cohorte que incluyó a pacientes evaluados entre 2018 y 2020, mediante el Mini-Examen del Estado Mental, registro físico funcional, prueba de flexión del codo, prueba de levantarse de la silla, prueba de fuerza de agarre manual (HGS) y mediante un monitor de actividad física. El análisis de datos se realizó utilizando la prueba de correlación de Pearson y la prueba t de Student emparejada y su equivalente no paramétrico, cuando fue necesario, con un nivel de significancia del 5%. Los resultados mostraron que la función cognitiva evaluada en los diferentes años de la investigación se correlacionó positivamente con la aptitud física y con el PAL: en 2018, con HGS ( $r = 0.313$ ;  $p = 0.019$ ); en 2019, con la aptitud cardiorrespiratoria ( $r = 0.288$ ;  $p = 0.038$ ), con HGS ( $r = 0.235$ ;  $p = 0.033$ ) y con el PAL en días de HD ( $r = 0.359$ ;  $p = 0.010$ ) y en días sin tratamiento ( $r = 0.314$ ;  $p = 0.026$ ); y en 2020, con el PAL actualizado sin HD ( $r = 0.387$ ;  $p = 0.014$ ). Además, los pacientes sin déficit cognitivo probable tuvieron valores más altos de PAL y aptitud física en todos los años de análisis en comparación con aquellos con el déficit cognitivo probable: en 2018, esta diferencia fue significativa en HGS y PAL en un día contrario a la hemodiálisis; en 2019, en la aptitud cardiorrespiratoria y el PAL en un día contrario al tratamiento; y en 2020, en la aptitud cardiorrespiratoria, HGS y PAL en ambos días. Se concluye que los pacientes con un PAL más alto y una mejor aptitud física tenían una mejor función cognitiva, lo que sugiere la importancia de la práctica de actividad física como una alternativa efectiva para mejorar la aptitud física y, en consecuencia, la función cognitiva en pacientes con HD.

**Palabras clave:** Insuficiencia Renal Crónica; Fenómenos Fisiológicos Musculoesqueléticos y Neurales; Rendimiento Funcional Físico; Actividad Motora; Cognición

## Resumo

Este estudo teve como objetivo correlacionar a função cognitiva com o nível de atividade física (NAF) e com a aptidão física ao longo do período de três anos de pacientes submetidos à Hemodiálise e comparar o NAF e a aptidão física ao longo desse tempo dos pacientes com e sem problemas cognitivos. Para tanto, foi realizado um estudo de coorte, incluindo os pacientes avaliados entre 2018 e 2020, por meio do Mini Exame de Estado Mental, prontuário físico funcional, teste de flexão de antebraço, teste de sentar e levantar, teste de força de preensão manual (FPM) e pelo monitor de atividade física. A análise dos dados foi realizada pelo teste de Correlação de Pearson e pelo teste T de Student pareado e seu equivalente não paramétrico quando necessário, com nível de significância de 5%. Os resultados mostraram que a função cognitiva avaliada nos diferentes anos da pesquisa correlacionou-se positivamente com a aptidão física e com o NAF: em 2018, com a FPM ( $r = 0,313$ ;  $p = 0,019$ ); em 2019, com a aptidão cardiorrespiratória ( $r = 0,288$ ;  $p = 0,038$ ), com a FPM ( $r = 0,235$ ;  $p = 0,033$ ) e com o NAF em dia de HD ( $r = 0,359$ ;  $p = 0,010$ ) e em dia sem tratamento ( $r = 0,314$ ;  $p = 0,026$ ); e em 2020, com o NAF em dia sem HD ( $r = 0,387$ ;  $p = 0,014$ ). Além disso, pacientes sem provável déficit cognitivo obtiveram maiores valores no NAF e na aptidão física em todos os anos de análise em relação àqueles com provável déficit cognitivo: em 2018, essa diferença foi significativa na FPM e no NAF em dia contrário à hemodiálise; em 2019, na aptidão cardiorrespiratória e no NAF em dia contrário ao tratamento; e em 2020, na aptidão cardiorrespiratória, FPM e NAF em ambos os dias. Conclui-se que pacientes com maior NAF e melhor aptidão física apresentaram melhor função cognitiva, sugerindo a importância da prática de atividade física como alternativa eficaz na melhora da aptidão física e consequentemente da função cognitiva de pacientes em HD.

**Palavras-chave:** Insuficiência renal crônica; fenômenos fisiológicos musculoesqueléticos e neurais; desempenho físico funcional; atividade motora; cognição.

## Introduction

Chronic kidney disease (CKD) is globally considered a common disorder and is characterized as a public health problem (Hu & Coresh, 2017). It is currently defined by abnormalities of renal structure or function, assessed, and categorized by glomerular filtration rate (GFR), albuminuria, and duration of kidney injury (Glassock, Warnock & Delanaye, 2017).

Its global prevalence is estimated between 5% and 10%, which reveals the dimension of this pathology. The increase is driven mainly by Diabetes Mellitus prevalence, systemic arterial hypertension, obesity, and the aging process (Lv & Zhang, 2019), which are the main risk factors. In the most advanced stage of CKD, known as chronic renal failure (CRF) –in which the GFR is  $< 15 \text{ mL/min/1.73 m}^2$ – hemodialysis (HD) is the predominant method of renal clearance, adopted for 92% of patients on renal replacement therapy (Neves et al., 2020).

Although efficient to maintain the balance of the body, HD treatment involves a monotonous routine with several restrictions, causing psychological impairments, physical and functional deficiencies, and social limitations (Bernardo et al., 2019). In addition, the CKD phenotype is associated with several harmful outcomes to the health

of patients, such as depression (Khan et al., 2019), frailty (Perez et al., 2019), poor quality of life (Marinho, et al., 2017), and higher mortality (Teixeira et al., 2015).

Another variable influenced by pathology and treatment is cognitive function. Studies show that the reported prevalence of cognitive impairment in this population ranged from 6.6% to 51% (San et al., 2017). Patients at all stages of CKD are at higher risk of developing cognitive impairment, especially those with eGFR < 30 mL/min/1.73 m<sup>2</sup> (Murray et al., 2016), regardless of age-related changes, and tend to worsen with the beginning of dialysis (Tamura et al., 2017).

The mechanisms involved in this picture are not yet established, but some factors such as neuronal damage induced by uremic toxins, ischemic cerebrovascular lesions, oxidative stress, chronic inflammation, anemia, hyperhomocysteinemia, and endothelial dysfunction may be the most significant aggravating factors (Matta et al., 2014).

Considering the effects of hemodialysis treatment and the high rates of cognitive impairment, supervised physical exercise is an essential tool in maintaining the patients' health on HD, influencing several variables (Lacerda et al., 2018). It can improve Kt/V (a method that assesses hemodialysis adequacy/quality), exercise capacity, depression, and life quality, as well as reducing blood pressure without increasing the incidence of adverse events (Pu et al., 2019).

A systematic review that sought to identify factors correlated with cognitive impairment in patients with CKD on HD pointed out that the risk of cognitive impairment can be significantly higher in elderly, women, with stroke, with difficulties in activities of daily living, with minor hemoglobin concentrations, with higher levels of pain, with sleeping difficulties, and with depression (Oh, Mo & Seo, 2019).

The cross-sectional study by Fukushima et al. (2019) compared physically active and inactive patients and revealed that the mean total score on the cognitive test was lower than recommended and that those on HD physically active obtained a significant score in the domain of verbal fluency. These results suggest that a higher physical activity level can contribute to a higher cognitive function score, being a potential therapeutic alternative.

On the other hand, cohort epidemiological studies in this population are still scarce, and few have sought to analyze the cognitive function and its associations. In this sense, the present study aimed to correlate cognitive function with the physical activity level (PAL) and physical fitness of patients undergoing HD over three years and to compare the PAL and physical fitness of individuals on HD with and no cognitive problems over the same period.

## Methods

This quantitative cohort study was carried out at the nephrology clinic of the Hospital São Vicente de Paulo, a reference center in the northwest region of Rio Grande do Sul, located in Cruz Alta, between 2018 and 2020. The population was constituted of 91 patients with CRF on HD from the Renal Clinic of that hospital who met the inclusion criterion, which was to be on hemodialysis for more than three months in 2018.

To calculate the baseline sample size (2018), the formula for calculating prevalence through a simple casual sample was used, plus 20% predicted losses and 15% for association studies (parameters: size of renal clinic population= 91 patients; 95% confidence level; and sampling error= 1 to 5 percentage points), resulting in a sample size of 73 people.

Therefore, all patients were invited to participate in the study. Of these, 30 refused, totaling 61 patients. The refusals were mainly because people reported tiredness in all collection attempts and/or that the surveys are very long and exhaustive.

All received guidance about the study and signed the Free and Informed Consent Form (FICF) before being included in the research. The patients underwent cognitive function assessment using the Mini-Mental State Exam (MMSE). In Brazil, this questionnaire was translated and validated by Bertolucci et al. (1994) and consists of 30 questions about temporal and spatial orientation, fixation memory, evocation, attention, calculation, and language. Illiterate individuals with a score below 20 points and those with formal education with less than 24 points were considered with a probable cognitive deficit (Almeida, 1998).

The functional physical record was also used to collect age information (years) and HD duration (months). To assess the strength and endurance of upper limbs, the forearm flexion test was used: the participants sit on a chair with the back straight and feet on the floor, hold the dumbbell (men, 4 kg; and women, 2 kg) with the preferred hand and perform as many push-up reps as they can for 30 seconds; the total is counted by the evaluator and is classified according to the person's gender and age (Rikli & Jones, 2008).

In the case of the lower limbs, the sit-to-stand test was chosen: the patient remains seated in a chair 45 cm high with the back straight, feet flat on the floor and shoulder-width apart; gets up and sits down for 30 seconds, and the maximum number of repetitions is recorded, classified according to gender, and age (Rikli & Jones, 2008).

To measure cardiorespiratory capacity, the six-minute walk test was used, which assesses the maximum distance walked during this time, allowing the participant to dictate the pace of steps and stop walking in case of limiting symptoms (Rikli

& Jones, 2008). Patients were classified according to gender and age, as suggested by the authors.

The handgrip test (dynamometry) was applied to measure handgrip strength. Three attempts were made –with a recovery period of one minute between them– and the longest one was used (Bohannon, 2008).

To measure the physical activity level through the number of daily steps, the OMRON activity monitor model HJA-310<sup>o</sup> (pedometer) was used. To be considered active, the patients had to perform 4600 steps or more daily (Tudor-Locke et al., 2011). The equipment was delivered to them on the day of treatment before it started and asked to return it in the following HD session, before the start of the session, accounting for two days of use. Thus, people were evaluated on two moments: on a treatment day (first 24 hours) and a non-treatment day (last 24 hours); they were instructed to wear the device in their pocket attached to their clothes and record the complications in a form.

Data collection took place in June 2018 and 2019, and in December 2020, due to the health protocols for coping with COVID-19. First, data normality was tested using the Kolmogorov–Smirnov test, mean and median analysis, and histogram. For characterizing the study sample and the outcome prevalence, descriptive statistics were performed, using absolute and relative frequencies (for qualitative variables) and measures of central tendency and dispersion (for quantitative variables), with the respective confidence intervals of 95% (95% CI).

The correlation of the outcome with the PAL and physical fitness variables was tested individually in each year, based on Spearman's correlation; on the other hand, the comparison of PAL and physical fitness over three years of HD patients with and without cognitive problems was tested using the student's t-test for independent samples or the Mann-Whitney U test, adopting a significance level of 5%.

The study was approved under the consolidated opinion of the Research Ethics Committee No. 4.171.948, CAAE No. 33286120.1.0000.5350. It followed the recommendations of Resolution 466/2012 of the National Health Council, which indicates the procedures for researching with human beings (Ministério da Saúde, 2012).

## Results

Table 1 shows that the mean age of the patients surveyed was  $57.65 \pm 5.22$  years, and the treatment time,  $58.72 \pm 15.63$  months. It can also be seen that the mean cognitive function was  $21.62 \pm 5.02$  (in 2018),  $23.15 \pm 4.92$  (2019), and  $24.65 \pm 5.13$  (2020).

**Table 1.** Sociodemographic and health characteristics of patients with CRF on HD. Cruz Alta, Rio Grande do Sul, Brazil, 2018, 2019, and 2020.

Variables	Mean	Standard Deviation
Age in years (n = 61)	57.65	± 5.22
Hemodialysis time in months (n = 61)	58.72	± 15.63
Cognitive function in 2018 (n = 61)	21.62	± 5.02
Cognitive function in 2019 (n = 58)	23.15	± 4.92
Cognitive function in 2020 (n = 40)	24.65	± 5.13

The correlations between cognitive function with PAL and physical fitness can be seen in Table 2. According to these results, it is possible to identify that cognitive function in HD patients was positively and significantly correlated with HGS ( $r=0.313$ ,  $p=0.019$ ) in the 2018 analysis; with cardiorespiratory fitness ( $r=0.288$ ,  $p=0.038$ ), handgrip strength ( $r=0.235$ ,  $p=0.033$ ), physical activity level assessed by the number of steps on hemodialysis day ( $r=0.359$ ,  $p=0.010$ ), and level of physical activity assessed by the number of steps on the day contrary to hemodialysis ( $r=0.314$ ,  $p=0.026$ ) in 2019; and with the physical activity level assessed by the number of steps on the day contrary to that of hemodialysis ( $r=0.387$ ,  $p=0.014$ ) in 2020. These correlations occurred with weak and moderate strength (moderate greater than 0.3) (Leotti et al., 2020).

**Table 2.** Correlation between cognitive function with the level of physical activity and physical fitness of patients with CRF on HD over three years. Cruz Alta, Rio Grande do Sul, Brazil, 2018, 2019, and 2020 (n = 61).

Variables	CF 2018 M±SD	R / p	CF 2019 M±SD	R / p	CF 2020 M±SD	R / p
CRFit	368.2±166.6	0.240 0.166	367.1±196.9	0.288 0.038*	390.4±219.9	0.290 0.069
MRLl	12.5±6.6	0.139 0.315	13.5±7.8	0.177 0.201	11.9±4.8	0.212 0.189
ULMRS	16.1±5.7	0.186 0.186	16.7±6.4	0.254 0.069	15.9±6.3	0.226 0.160
HGS	27.8±9.7	0.313 0.019*	27.3±10.0	0.235 0.033*	26.9±10.4	0.276 0.084
PAL HD	2875.4±2996.3	0.070 0.620	2644.1±2571.3	0.359 0.010*	2509.7±3092.7	0.216 0.181
PAL NHD	3417.8±3770.9	0.165 0.242	2763.4±2439.7	0.314 0.026*	1800.4±2094.1	0.387 0.014*

**Notes:** CF = cognitive function (Mini-Mental State Exam score); CRFIT = cardiorespiratory fitness (distance in meters); MRLl = muscle resistance located in the lower limbs (number of repetitions in 30 seconds); ULMRS = upper limb muscle resistance strength (number of repetitions in 30 seconds); HGS = handgrip strength (KgF); PAL HD = physical activity level assessed by the number of steps on hemodialysis day; PAL NHD = physical activity level assessed by the number of steps on the day contrary to hemodialysis; M = mean; SD = standard deviation;  $p \leq 0.05$  for Spearman correlation.

Based on the data presented in tables 3, 4, and 5, it is noted that HD patients without a probable significant deficit had higher PAL and physical fitness values in all years of analysis compared to those with a probable cognitive deficit. In 2018, this difference was significant in the HGS and NAF HD variables; in 2019, this occurred in ACR and PAL NHD, and in 2020, in CRFit, HGS, PAL HD, and PAL NHD.

**Table 3.** Physical activity level and physical fitness of HD patients with and without cognitive problems. Cruz Alta, Rio Grande do Sul, Brazil, 2018 (n = 61).

Variables	Cognitive function		p
	No probable cognitive deficit (n = 22)	With probable cognitive deficit (n = 18)	
	M±SD	M±SD	
CRFIT	397.09±180.62	340.90±154.53	0.233
mrll	12.91±7.51	12.23±6.11	0.713
ulmrs	16.78±5.42	15.62±6.09	0.477
hgs	32.43±8.80	24.76±9.19	0.003*
pal hd	3245.2±3025.4	2625.2±3029.4	0.465**
pal nhd	4521.4±5003.3	2432.4±1732.0	0.039**

**Notes:** CRFIT = cardiorespiratory fitness (distance in meters); MRLL= muscle resistance located in the lower limbs (number of repetitions in 30 seconds); ULMRS = upper limb muscle resistance strength (number of repetitions in 30 seconds); HGS = handgrip strength (KgF); PAL HD = physical activity level assessed by the number of steps on hemodialysis day; PAL NHD = physical activity level assessed by the number of steps on the day contrary to hemodialysis; M = mean; SD = standard deviation;  $p \leq 0.05$  for Spearman correlation; \*  $p \leq 0.05$  for Student's t-test for independent samples; \*\* Mann-Whitney U Test was applied.

**Table 4.** Physical activity level and physical fitness of HD patients with and without cognitive problems. Cruz Alta, Rio Grande do Sul, Brazil, 2019 (n = 58).

Variables	Cognitive function		p
	No probable cognitive deficit (n = 23)	With probable cognitive deficit (n = 17)	
	M±SD (n = 23)	M±SD (n = 17)	
CRFIT	426.52±202.94	315.80±182.37	0.048*
mrll	14.92±8.20	11.92±6.51	0.150
ulmrs	17.38±7.48	16.24±5.38	0.535
hgs	30.04±11.03	25.21±8.93	0.082
pal hd	3065.40±1763.56	2307.78±3285.47	0.319**
pal nhd	3633.44±2869.83	1875.30±1596.21	0.013**

**Notes:** CRFIT = cardiorespiratory fitness (distance in meters); MRLL= muscle resistance located in the lower limbs (number of repetitions in 30 seconds); ULMRS = upper limb muscle resistance strength (number of repetitions in 30 seconds); HGS = handgrip strength (KgF); PAL HD = physical activity level assessed by the number of steps on hemodialysis day; PAL NHD = physical activity level assessed by the number of steps on the day contrary to hemodialysis; M = mean; SD = standard deviation;  $p \leq 0.05$  for Spearman correlation; \*  $p \leq 0.05$  for Student's t-test for independent samples; \*\* Mann-Whitney U Test was applied.



**Table 5.** Physical activity level and physical fitness of HD patients with and without cognitive problems. Cruz Alta, Rio Grande do Sul, Brazil, 2020 (n = 40).

Variables	Cognitive function		p
	No probable cognitive deficit (n = 27)	With probable cognitive deficit (n = 13)	
	M±SD	M±SD	
CRFIT	455.30±203.71	255.85±195.31	0.006*
mrll	12.78±4.78	10.08±4.46	0.096
ulmrs	17.15±5.44	13.23±7.21	0.063
hgs	29.00±11.17	22.54±7.24	0.035*
pal hd	2896.22±3223.91	1707.08±2744.40	0.026**
pal nhd	2398.74±2314.24	557.77±412.81	0.007*

**Notes:** CRFIT = cardiorespiratory fitness (distance in meters); MRLL= muscle resistance located in the lower limbs (number of repetitions in 30 seconds); ULMRS = upper limb muscle resistance strength (number of repetitions in 30 seconds); HGS = handgrip strength (KgF); PAL HD = physical activity level assessed by the number of steps on hemodialysis day; PAL NHD = physical activity level assessed by the number of steps on the day contrary to hemodialysis; M = mean; SD = standard deviation;  $p \leq 0.05$  for Spearman correlation; \*  $p \leq 0.05$  for Student's t-test for independent samples; \*\* Mann-Whitney U Test was applied.

## Discussion

One of the aims of this study was to correlate cognitive function with PAL and physical fitness of HD patients over three years. The other was to compare the PAL and physical fitness of HD patients with and without cognitive problems in the same period. In this sense, the results showed that those with the best cognitive function were those with higher PAL and better physical fitness and that HD patients without a probable significant deficit had higher PAL and physical fitness values in all years of analysis. In 2018, this difference was significant in the variables handgrip strength (HGS) and physical activity level assessed by the number of steps a day contrary to hemodialysis (PAL NHD); in 2019, in the variables cardiorespiratory fitness and physical activity level assessed by the number of steps on the day contrary to hemodialysis (PAL NHD); and in 2020, in the variables cardiorespiratory fitness, HGS, PAL HD, and PAL NHD.

Similar findings have already been found in other international studies (Fukushima et al., 2019; Manfredin et al., 2017; Stringuetta-belik et al., 2019; Stringuetta-belik et al., 2012; Martins et al., 2011). However, none analyzed data longitudinally in a panel format, highlighting their importance in this article.

It is known that the prevalence of cognitive impairment is high in this population (Chaiben et al., 2019) and that hemodialysis treatment contributes to the worsening of this clinical condition (Erken et al., 2019). Studies indicate that cognitive deficit is

related to age, years of education, and time on hemodialysis (Gesualdo et al., 2017) and that patients with such impairment are at increased risk of poor health outcomes (Kaltsatou et al., 2015).

As it is a systemic disease, that is, one that affects multiple systems, the correlations found between PAL, physical fitness, and cognitive function can be attributed to several physiological mechanisms arising from physical exercise that interfere with cognitive function. Some pathways are related to immune improvement and inflammation (Müller-Ortiz et al., 2019); activation of NRF2, which acts in neuroprotection against oxidative stressors and mitochondrial toxins (Abreu et al., 2017); improvement in endothelial function, vascular mechanism that affects both the brain and the kidneys (Silva et al., 2019); significant improvement in Kt/V, serum creatinine, serum urea, serum potassium, and phosphorus (Paluchamy & Vaidyanathan, 2018), biochemical markers that influence the clinical picture of the pathology.

It has been pointed out that systematic physical training seems to improve cognitive function in patients with CRF, inducing positive changes in brain metabolism and favoring better scores in their cognitive function (Kaltsatou et al., 2015). Avoiding cognitive impairment through physical training protocols in the routine clinical treatment of HD patients can be a cost-effective alternative, reducing non-adherence to medication, increasing quality of life, and even survival (Schneider et al., 2015)

In this sense, physical activity is potentially related to the physical fitness of hemodialysis patients. It was verified in the present research an improvement in the variables cardiorespiratory fitness, muscle resistance located in the lower limbs, HGS, which is also correlated with the improvement in cognitive function.

HGS can be considered a protective factor against cognitive decline (Fritz, Mccarthy & Adamo, 2019). A cohort study showed that each 1 lb reduction in HGS was associated with a 1.4% increase in the risk of developing neurocognitive pathologies over time (Buchman et al., 2007). A stronger handgrip strength may reflect the integrity of the neuromuscular system, resistance to oxidative stress, and inflammation (Weaver et al., 2002). Another work justified this association due to the shared pathology related to hormonal levels (testosterone) and inflammatory biomarkers (IL-6) (Fritz et al., 2019), factors that influence the preservation of cognitive function.

There are explicit links between the motor and cognitive systems (Mcgrath et al., 2019; Bohannon, 2019). The learning of motor skills and motor performance depends on the activity of the frontal and parietal regions of the brain, and the interconnection between these regions is related to motor performance. Thus, improving muscle strength and endurance, that is, physical fitness, reduces the likelihood of developing a cognitive deficit.

The systematic review by Sexton et al. (2016), which sought to elucidate the relationship between physical fitness and cognitive function in the elderly, demonstrated that higher levels of physical fitness have beneficial effects on this function. According to the authors, higher levels of physical fitness were associated with larger volumes of gray matter in the brain (GM) and reduced amount or severity of GM lesions or improved measures of GM microstructure.

In the research by Pentikäinen et al. (2019), the relationship between cognitive function was evaluated through an extensive battery of neuropsychological tests and cardiorespiratory fitness of 421 individuals with a mean age of 69 years, using peak oxygen consumption (VO<sub>2</sub>peak, L/min) for 24 months. Over two years of follow-up, this function decreased from 0.15 to 0.14 points on average, and cardiorespiratory fitness was associated with executive functions and processing speed, and also with general cognitive function (Pentikäinen et al., 2019).

Erickson, Leckie, and Weinstein (2014) showed a correlation between physical activity, physical fitness, and cognitive function in adults, elderly, long-lived, and elderly people with different pathologies. Higher levels of physical activity and cardiorespiratory fitness are routinely associated with a larger volume of gray matter in the prefrontal cortex and hippocampus and less consistently in other regions; this suggests that the prefrontal cortex and hippocampus remain flexible at the end of life and that moderate-intensity exercises for six months to a year are sufficient to change the size of these areas (Erickson et al., 2014).

However, it is noteworthy that patients on hemodialysis tend to be less physically active due to the phenotype of the disease. A study using accelerometers identified that people on HD are more sedentary (47.4%) when compared to healthy individuals (10.5%), especially on dialysis days (reduction of 2645 steps on average, Gomes et al., 2015).

The daily life of patients on HD requires changes in eating habits, water restrictions, restrictions on travel, work, and activities of daily living, due to the weakness imposed by the treatment (ARAÚJO et al., 2016). Thus, professionals involved in the health care of chronic renal patients should always be encouraging the regular practice of physical activities.

This research has some limitations, such as the size of the population evaluated, which did not reach the sample size calculation, and sample losses to follow-up. On the other hand, the fact that there is no study in the literature that monitors and assesses the natural history of a condition, such as the correlation and comparison of cognitive function, PAL, and physical fitness over the period of three years of patients undergoing HD, as proposed here.

## Conclusion

It is concluded that the cognitive function of the participants in this study was correlated with the activity level and physical fitness. Patients on HD without probable cognitive deficit had higher values in PAL and physical fitness (HGS, localized muscle resistance of the lower limbs, and cardiorespiratory fitness) in all years of analysis compared to those with probable cognitive deficit. The results indicate physical activity as an effective alternative in improving the physical fitness and cognitive function of these people.

Although this study provides important evidence to health professionals, especially in encouraging patients to participate in training protocols with intradialytic physical exercise, it is suggested that further investigations be carried out using accelerometers or that assess the direct effect of physical exercise practice (such as intervention studies) to reinforce the findings of this work. It is important to highlight that physical activities in environments outside renal therapy units, such as commuting, leisure, and work, and the reduction of sedentary behavior are measures that should be encouraged.

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