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RESEARCH ARTICLE

Acute effects of hemodialysis on physical function from the 6-minute walk test: A randomized and crossover experiment

Jhenephan Macedo[1], Karina E. S. Silva[1], Denilson B. Porto[1], Erick H. P. Eches[1], Priscilla M. M. B. Maciel[1], Vinicius D. A. Delfino[2], Rodrigo A. C. Andraus[3], Alex S. Ribeiro[4], Crivaldo G. Cardoso Jr[1]

[1] Department of Physical Education, State University of Londrina. Londrina (PR), Brazil
[2] Department of Clinical Medicine, State University of Londrina. Londrina (PR), Brazil
[3] Program in Human Movement and Rehabilitation, Evangelical University of Goiás (UniEVANGELICA), Anápolis (GO), Brazil
[4] Faculty of Sports Sciences and Physical Education (FCDEF), University of Coimbra (CIPER), Coimbra, Portugal

Abstract

Background*:* Hemodialysis is a component of renal replacement therapy used for patients with end-stage chronic kidney disease. Nevertheless, its impact on physical function, as assessed by the 6-minute walk test, remains uncertain. **Objective**: This crossover and randomized study aimed to evaluate the acute effects of hemodialysis on 6-minute walk test performance. **Methods***:* Ten participants, half of whom were male, were enrolled. Participants were sourced from the hemodialysis unit of a renal institute, aged 18 or older, who had undergone hemodialysis for at least 1 month. Data on demographics and blood parameters were collected. The 6-minute walk test was conducted either before or after hemodialysis sessions, with walk distance and heart rate recorded. The cardiac efficiency index was calculated as the ratio of walking distance to heart rate. **Results**: Although no significant differences in heart rate were observed between pre- and post-hemodialysis sessions, a notable increase in walking distance was observed post-hemodialysis (19.4 ± 25.6 meters, $p < 0.05$). **Conclusions**: Our findings suggest that acute hemodialysis can effectively enhance walking distance and cardiac efficiency during the 6-minute walk test in patients with end-stage kidney disease.

Keywords: Kidney failure, chronic; cardiorespiratory fitness; renal dialysis; exercise test; physical functional performance.

Corresponding author: Alex Silva Ribeiro
Email: alex-silvaribeiro@hotmail.com

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BACKGROUND

Kidney replacement therapy is the last treatment choice for managing end-stage kidney disease (ESKD), aiming to alleviate symptoms and extend patient survival[1]. Haemodialysis (HD) is the commonest form of kidney replacement therapy, due to the availability of resources, presence in healthcare centers and hospitals, as well as physicians' and patients' familiarity with the procedure, and healthcare infrastructure[2]. Briefly, it emulates kidney function by facilitating the passage of blood through dialysis membranes, filtering waste, toxins, and excess fluids from the blood via diffusion and ultrafiltration. Its composition varies according to the patient's individual clinical circumstances and generally includes potassium, sodium, calcium, magnesium, chloride, acetate, bicarbonate, dextrose, and carbon dioxide[2].

Despite advances in the treatment, after HD, several symptoms are reported, with emphasis on fatigue, cramps, and dizziness, followed by headache, pruritus, and back pain[3]. Additionally, about 23% reported recovering from dialysis within minutes, 34% by the time they returned home, 16% by bedtime, 24% the next morning, and 3% just before the next dialysis session[3].

Therefore, it is presumptive to expect that physical function will worsen after HD. On the other hand, HD could enhance physical performance by facilitating the elimination of waste products, purifying substances, and regulating fluids, thereby creating a humoral and metabolic environment more favorable for muscular performance and physical activity.

The conjectures presented indicate that the effect of HD on physical performance remains uncertain, and unraveling this effect is relevant, since improving physical function is an integral aspect of the comprehensive management of ESKD patients, serving as an adjunctive therapy and playing a crucial role in mitigating the decline in key clinical outcomes and enhancing overall survival[4]. Additionally, it has been demonstrated to reduce morbidity and hospitalization rates while improving the quality of life in ESKD patients undergoing HD[5, 6].

The increasing focus on assessing physical performance in patients with ESKD highlights the importance of evaluating cardiorespiratory fitness. Recent evidence has reinforced that physical function is markedly impaired in patients with CKD and is a strong predictor of adverse outcomes, including mortality and hospitalization[7]. In this sense, the 6-minute walk test (6MWT) assesses the combined responses of several physiological systems during exercise, with a focus on the respiratory, cardiovascular, and neuromuscular systems. Furthermore, it measures functional capacity at submaximal levels, aligning with most of these patients' daily activities and indicating a lower risk of complications.

Recent studies have demonstrated that the 6MWT is strongly correlated with peak oxygen uptake in patients undergoing HD, reinforcing its clinical utility[8]. A meta-analysis[4] found that patients who covered longer distances during the 6MWT had a reduced risk of all-cause mortality compared to those who covered shorter distances. However, the evidence for those outcomes was not stronger than for other indicators of physical performance, such as upper limb strength and gait speed[4]. It is possible that part of the weakness in determining the clinical relevance of these physical performance tests as predictors of patient outcomes is related to the timing of the test, specifically whether it is administered before or after hemodialysis.

Therefore, investigating the acute effects of hemodialysis on 6MWT performance is important, as it can provide insights into the impact of HD and, most importantly, improve the monitoring of physical functionality in patients with ESKD. The purpose of this randomized crossover study was to evaluate the acute effects of HD on the 6MWT in patients with ESKD.

METHODS

Design and participants

This study was designed to examine the acute effect of HD on physical function, as assessed by the 6MWT, in patients with ESKD. The sample comprised ESKD patients from the HD Unit of the Kidney Institute of Londrina, Brazil, who participated in this crossover study. Given that ESKD affects individuals of both genders, various age groups, and those with multiple comorbidities requiring drug therapies, we aimed to enroll a comprehensive sample to initially explore the acute effects of HD on walking distance and heart rate responses.

After screening and approval by a nephrologist, ESKD patients aged 18 years or older, of both sexes, who had been undergoing HD via a brachial arteriovenous fistula for at least 1 month prior to the study, were invited to participate. Exclusion criteria included clinical decompensation, inability to perform functional tests, or any health condition preventing exercise. The study adhered to ethical standards and obtained approval from the local Ethics Committee (Approval Number: 1.863.432 - CAAE 61824916.0.0000.5231). All participants provided informed written consent.

After initial measurements, eligible participants were enrolled in two experimental sessions: a 6MWT before HD (PRE-HD) or after HD (POST-HD). An external researcher used the website https://www.randomizer.org/ to generate random numbers for a simple draw of the time (PRE or POST HD) of the first 6MWT. After a 48-hour interval, the test was replicated using the opposite option condition from the first session.

Preliminary evaluation

Data on participants' age, height, and dry weight were obtained from their medical records. During the functional test reference period, a venous blood sample was collected to measure blood glucose, hematocrit, hemoglobin, iron, creatinine, calcium, pyruvate transaminase, parathyroid hormone, phosphorus, and potassium. The calcium and phosphorus products were calculated from monthly blood tests performed by a private laboratory.

6-minute walk test

The 6MWT was conducted either 30 minutes before or after HD. Participants were instructed to walk along a 20-meter corridor marked with tape at 2-meter intervals, and the maximum distance covered within 6 minutes was recorded. Resting and peak heart rates were measured by palpating the fistula within 15 seconds of the procedure. The cardiac efficiency index was calculated as the quotient of the total distance walked and the peak heart rate. The 6MWT was chosen due to its safety, low cost, and strong association with functional capacity and prognosis in CKD populations, as supported by recent literature[7].

Hemodialysis

Patients underwent HD using Fresenius Medical Care model 4008S or 4008B machines, with Nipro Elisio-21M polypropylene hollow fiber synthetic dialyzers and pure water in the dialysate. The HD efficiency was quantified using the urea reduction percentage and Kt/V index. HD occurred three times per week, lasting 210 to 240 minutes each time. Other parameters, including dialysis efficiency, treatment system, water quality and distribution, disinfection, and capillary reuse, were in accordance with the guidelines outlined in Resolution of the Collegiate Board of Directors (RDC) No. 11, March 2014.

Statistical analysis

A priori sample size calculation was performed to determine the minimum number of participants required. With an alpha error probability of 0.05 and a statistical power of 80%, a minimum sample size of 10 participants was required. Data normality was assessed prior to inferential analysis using the Shapiro-Wilk test. The Student’s paired-sample t-tests were performed to compare the effects of HD on physical function. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 28.0; IBM Corp., Armonk, NY, USA). Statistical significance was predefined and set at $p < 0.05$ for all analyses.

RESULTS

The primary etiologic factors for CKD in the sample included arterial hypertension (n = 4, 30.8%), polycystic kidney disease (n = 2, 15.4%), focal segmental glomerulosclerosis, glomerulonephritis, bilateral hydronephrosis, systemic lupus erythematosus, diabetic nephropathy, primary membranous nephropathy, and nephrotic syndrome (n = 1, 7.7%). Additional clinical information, including anthropometric and metabolic data, is presented in Table 1.

Table 1. Clinical, anthropometric, and metabolic data of the sample

Variables	Values
n, male/woman	10, 5/5
Age (y)	57.4 (11.6)
Heigth (m)	1.68 ± 0.10
Dry Weight	67.7 ± 12.1
Dry body mass index (kg/m²)	23.8 ± 4.1
Glycemia (mg/dL)	112 ± 18
Hematocrit (%)	38.2 ± 5,3
Hemoglobin (g/dL)	12.5 ± 1.6
Iron (mg/dL)	55.0 ± 12.3
Calcium (mg/dL)	8.4 ± 1.3
Phosphate (mg/dL)	5.9 ± 2.2
Calcium Phosphate Product	49.4 ± 21.4
Piruvic Glutaminic Transaminase	9.8 ± 3.4
Parathyroid hormone (pg/dL)	648 ± 785
Creatinine (mg/dL)	11.4 ± 2.3

Note: Data are presented as mean and standard deviation

The average duration of hemodialysis prior to the study was 7.4 ± 3.8 years. Each hemodialysis session lasted 3.5 ± 0.3 hours and resulted in a weight loss of -2.8 ± 0.5 kg. The urea concentration before and after hemodialysis, along with the percentage of urea clearance, were 158 ± 34, 51 ± 13, and 67.5 ± 4.7%, respectively. The KT/V index was 1.34 ± 0.18.

Table 2 presents the effects of HD on body mass, heart rate, and functional performance at PRE-HD and POST-HD. Following the HD session, body mass decreased significantly ($p < 0.05$), reflecting effective fluid removal during the procedure. Regarding functional performance, a significant increase in distance covered during the 6MWT was observed ($p < 0.05$). Initial heart rate did not differ significantly between the PRE-HD and POST-HD conditions ($p > 0.05$). However, the final heart rate showed a non-significant tendency to be lower after HD. In addition, significant improvements ($p < 0.05$) were observed in functional efficiency indices, as evidenced by increases in the distance-to-heart rate ratio (6MWT/HR) and the distance-to-body mass ratio (6MWT/BM). Taken together, these findings indicate that acute HD not only promotes body mass reduction through ultrafiltration but also improves functional performance and cardiorespiratory efficiency during submaximal exercise.

Table 2. Changes in body mass, heart rate, and functional performance before and after hemodialysis

Variables	Pre-Hemodialysis	Post-hemodialysis	Δ	Δ%
Body mass (kg)	69.9 ± 12.7	67.2 ± 12.7*	-2.7 ± 0.6 (-3.2; -2.3)	-4.0 ± 1.1 (-4.9; -3.2)
6MWT (m)	413.2 ± 93.6	432.6 ± 86.6*	19.4 ± 25.6 (1.1; 37.7)	5.5 ± 7.8 (-0.1; 11.1)
Initial HR (bpm)	80.8 ± 17.9	79.6 ± 14.9	-1.2 ± 12.8 (-10.4; 7.9)	0.1 ± 14.9 (-10.5; 10.8)
Final HR (bpm)	111.6 ± 31.8	96.8 ±15.2	-14.8 ± 26.3 (-33.6; 4.0)	-9.5 ± 18.9 (-23.0; 4.0)
6MWT relative to HR (m/bpm)	3.80 ± 0.7	4.56 ± 1.1*	0.8 ± 0.9 (0.1; 1.4)	20.9 ± 24.0 (3.8; 38.1)
6MWT relative to body mass (m/kg)	6.14 ± 1.38	6.66 ± 1.35*	0.5 ± 0.3 (0.3; 0.8)	9.7 ± 8.3 (3.3; 16.0)

Note: HR = heart rate. 6MWT = 6-minute walk test. * $p < 0.05$ vs. pre-hemodialysis.

Figure 1 illustrates the individual responses to HD for the 6MWT distance (Panel A) and the cardiac efficiency index (Panel B). Most participants demonstrated improvements in walking distance after the HD session, while a smaller number showed minimal change or slight reductions. The mean change indicated a positive overall effect of HD on functional performance, with the 95% confidence intervals confirming a consistent trend towards improvement at the group level. A similar pattern was observed for the cardiac efficiency index, with individual responses ranging from modest decreases to marked improvements, but with a clear increase in the group mean after HD. These findings highlight the predominantly favorable acute effect of HD on functional capacity and cardiovascular efficiency during submaximal exercise.

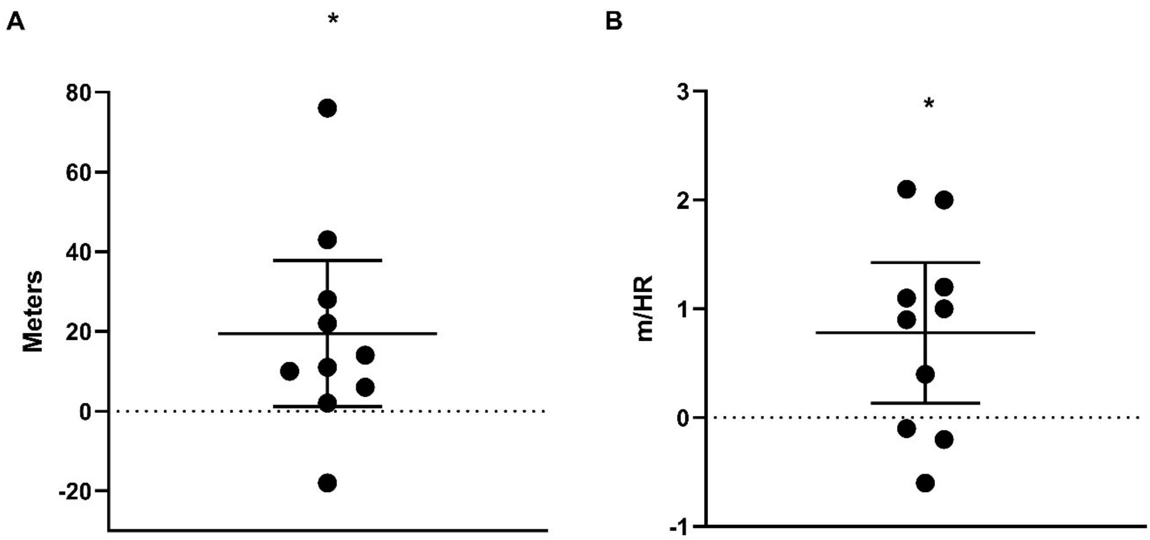

Figure 1. Mean and individual changes in 6-minute walk test performance (Panel A) and cardiac efficiency index (Panel B) after hemodialysis. Each point represents a participant's score. Bars indicate the mean values, and error bars represent the 95% confidence intervals (95% CI). * $p < 0.05$ between Pre-and post-hemodialysis.

DISCUSSION

The main purpose of this randomized crossover study was to evaluate the acute effects of HD on the 6MWT in patients with ESKD. The primary findings of this study reveal that HD increases walking distance and enhances cardiac performance during the 6MWT in patients with ESKD.

The 6MWT is commonly utilized to evaluate functional capacity in both healthy individuals and those with chronic illnesses[9, 10]. Additionally, the 6MWT has demonstrated prognostic value in predicting mortality and morbidity among adults with chronic diseases[11, 12]. Notably, the strong correlation observed between 6MWT parameters and VO2max in patients with chronic kidney disease underscores the reliability and safety of this test as a submaximal cardiopulmonary evaluation tool for assessing functional capacity in patients with ESKD[13]. Numerous studies have consistently shown that individuals with ESKD undergoing HD have diminished functional capacity, which may contribute to increased sedentary behavior and hinder their ability to engage in basic activities, leisure pursuits, work-related tasks, and social interactions, consequently impacting their overall quality of life[14]. The prevalence of atrial fibrillation among patients with ESKD surpasses that of the general population and is linked to heightened mortality rates. As highlighted by Franczyk et al.[15], the HD procedure may serve as a trigger for atrial fibrillation.

Therefore, implementing preventive measures for atrial fibrillation is crucial in dialysis patients. In this study, no complications arose during the 6MWT, indicating its reliability and tolerability in both experimental settings (pre- and post-hemodialysis). This underscores its potential as a cost-effective tool for monitoring functional exercise capacity in individuals with ESKD.

Functional capacity relies on the intricate interplay between the respiratory and cardiovascular systems and peripheral muscles. Individuals with ESKD often experience reduced exercise tolerance due to a multitude of factors, including anemia, metabolic acidosis, electrolyte imbalances, bone disorders, malnutrition, physical inactivity, uremic muscle dysfunction, and worsening comorbidities associated with chronic kidney disease[16, 17]. Consequently, hematocrit plays a pivotal role in the active transport of oxygen and carbon dioxide in peripheral muscles and may impact walking distance. The Canadian Erythropoietin Study Group observed that exogenous erythropoietin increases hemoglobin and hematocrit levels without impacting 6MWT performance[18]. Thus, it appears that hemoglobin and hematocrit levels may not reliably predict 6MWT walking distance in non-anemic ESKD patients.

Matsuo et al.[19] observed a high prevalence of cardiac structural and functional abnormalities, such as calcified aortic sclerosis, in ESKD patients undergoing chronic hemodialysis HD. They highlighted that older age and parathyroid hormone levels were associated with aortic valve stenosis in these patients. After HD, there is a decrease in the left ventricular diastolic diameter and an augmentation in wall thickness.

Conversely, before HD, left ventricular dilation with eccentric hypertrophy is common, which transitions to concentric hypertrophy after the HD session[20]. This acute cardiac response induced by HD, attributed to volume depletion from ultrafiltration, results in improved cardiac contractile function. Nixon et al.[21] demonstrated, using ventricular function curves, that ultrafiltration induces a pure Frank-Starling effect, whereas hemodialysis, with or without volume depletion, shifts the curves, thereby enhancing left ventricular contractility. Thus, the alterations in left ventricular function induced by regular HD stem from a decrease in end-diastolic volume and an augmentation in left ventricular contractile state. In our study, we observed an improvement in the cardiac efficiency index after HD, indicating reduced chronotropic demand at the same distance traveled.

Although limited data are available regarding the effects of interventions on changes in 6MWT distance in patients with chronic kidney disease, the present study identified the smallest detectable change of 19.4 ± 25.6 meters. This finding provides an important benchmark for interpreting clinically meaningful changes in functional performance in this population. From a clinical perspective, an improvement of approximately 20 meters in the 6MWT may be considered a relevant functional gain, reflecting a measurable enhancement in mobility and submaximal exercise tolerance. Importantly, even modest increases in walking distance may translate into better performance of daily living activities, enhanced independence, and potentially improved health-related quality of life in patients with chronic kidney disease[22]. These findings also support the use of the 6MWT as a sensitive outcome measure for future interventional studies, particularly those investigating the effects of exercise training, rehabilitation programs, or optimized dialysis strategies, and highlight the need for larger studies to further refine minimal clinically important differences in this population.

The present study has some limitations that should be recognized. The relatively small sample size may restrict the generalizability of our results. Additionally, the absence of more advanced physiological techniques limited a deeper investigation into the mechanisms behind HD's immediate effects on walking performance.

Future research should focus on including comprehensive hemodynamic, metabolic, and imaging assessments to better understand these mechanisms. Furthermore, symptom burden appeared to vary by sex, age, dialysis session length, ethnicity, and dialysis center practices.

Recovery time after dialysis ranged from minutes to hours and was generally shorter in men and patients with longer dialysis vintage, but longer in those undergoing extended treatment sessions and reporting a higher intradialytic symptom burden. Nonetheless, additional studies with larger sample sizes and more detailed physiological evaluations are necessary to clarify the mechanisms driving these acute effects and to assess their long-term clinical significance.

CONCLUSION

In summary, our study demonstrates that a single HD session acutely increases walking distance and improves cardiac efficiency during the 6MWT in patients with ESKD. These findings suggest that, beyond its essential metabolic and fluid-regulating functions, hemodialysis may transiently enhance functional exercise capacity and cardiovascular efficiency in this population. These results have relevant clinical implications, particularly for the timing of functional assessments and exercise prescription in patients undergoing maintenance HD. The findings support using the post-dialysis period as a potentially favorable window for functional testing and rehabilitation.

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