Patient perception of vitality and measured physical activity in patients receiving haemodialysis

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Abstract

Aim: Fatigue in haemodialysis (HD) patients can be captured in quality of life questionnaires and by the dialysis recovery time (DRT) question. The associations between fatigue and measured physical activity has not been explored until the present. We tested our hypothesis that the patient perception of chronic and post-dialysis fatigue would be associated with lower physical activity.

Methods: This study was a cross sectional evaluation of baseline data from HD patients recruited in the HDFIT trial. Vitality scores from the Kidney Disease Quality of Life (KDQOL-36) and the dialysis recovery time (DRT) question were used as indicators of chronic and post dialysis fatigue, respectively. Granular physical activity was measured by accelerometers as part of the study protocol.

Results: Among 176 patients, Vitality score was 63 ± 21 and the DRT was ≤30 minutes in 57% of patients. The mean number of steps was 5288 ± 3540 in 24 hours after HD and 953 ± 617 in the 2-hour post-HD period. The multivariable analysis confirmed Vitality scores were associated with physical activity in the 24-hour post-HD period. In contrast, DRT was not associated with physical activity captured by the accelerometer in the period immediately (2 hours) after the HD session.

Conclusion: Chronic fatigue was negatively associated with step counts, while patient perception of post-dialysis fatigue was not associated with physical activity. These patterns indicate limitations in interpretation of DRT. Since physical activity is an important component of a healthy life, our results may partially explain the associations between fatigue and poor outcomes in HD patients.

Keywords
accelerometery, dialysis recovery time, end stage kidney disease, fatigue, HDFit, health related quality of life, patient reported outcomes, physical activity
Haemodialysis (HD) broadly impairs quality of life in patients with chronic kidney disease (CKD); however, from all components of quality of life, fatigue has been identified as one of the most important symptoms from a HD patient’s perspective. Fatigue is a complex, multidimensional and multifactorial phenomenon defined as a persistent state of tiredness, weakness and physical and/or mental exhaustion. In previous studies, multiple patient demographic characteristics, comorbidities and HD-related factors have been associated with fatigue.

Fatigue is common in HD individuals and can be captured in quality of life assessment tools in kidney disease (functional capacity and vitality scores), such as the validated KDQOL questionnaire. In addition, the dialysis recovery time (DRT) question can be used to assess post-HD fatigue. Low vitality scores and longer DRT are common, highly prioritized by patients as issues to be addressed, and are associated with poor outcomes in HD.

Physical activity can be objectively measured using pedometers and accelerometers that assess activity patterns during daily living activities. Physically active lifestyle is an important component of a healthy life, including in individuals on HD. Active patients with CKD seem to experience better outcomes compared to sedentary ones even after the adjustment for confounders. Similarly, self-reported sedentarism is associated with an increased risk of mortality in HD.

It is plausible that both post-dialysis and chronic fatigue may negatively impact physical activity patterns in HD patients. The associations between fatigue, including vitality domains for KDQOL-36 and the DRT, and objectively measured physical activity have not been described until the present. We hypothesized the patient perception of more fatigue associates with lower physical activity, specifically activity following HD treatments. The aim of this study was to describe associations between patient reported chronic and post-dialysis fatigue and the patterns of physical activity in daily living.

1 | METHODS

The data used in our study were derived from baseline assessments in the HDFIT study conducted in Brazil (Impact of Hemodiafiltration on Physical Activity and Self-reported Outcomes: a Randomized Controlled Trial; ClinicalTrials.gov Identifier: NCT02787161). The trial objectively measured granular physical activity levels and other clinical and self-reported outcomes in end-stage kidney disease (ESKD) individuals randomized to be treated with hemodiafiltration (HDF) or continue high-flux HD; the HDFIT protocol has been detailed in a previous publication.

Adult patients on HD for at least 3 months and no more than 24 months were recruited from clinics in the south and southeast of Brazil. Individuals who provided their consent to participate in the study underwent a baseline run-in period of 4 weeks on high-flux HD, during which demographic, social and clinical data were evaluated, and physical activity levels were measured. At the time of randomization, laboratory tests were collected and baseline parameters of quality of life were obtained by questionnaires.

SUMMARY AT A GLANCE

This cross-sectional study evaluates the association between patient perception of chronic and post-dialysis fatigue and physical activity. Vitality was found to be associated with physical activity, while dialysis recovery time was not shown to be associated with physical activity within the two hours after a haemodialysis session.

The trial was performed in accordance to the Declaration of Helsinki and the study documents were approved by local ethics review board (central application # 54926916.7.1001.0020; approval number 1.538.784).

We used data collected from the first consultation (baseline) during which the patients responded to the Short-Form 36 (SF-36). Individuals were also asked to respond to the DRT survey that asked the question: “How long does it take for you to recover from a haemodialysis session?”, and responses were answered in minutes. In addition, laboratory test results were collected and analysed.

Physical activity levels were measured using a validated tri-axial accelerometer (ActiGraph TM wGT3X-BT model) and the date and time were updated upon routine HD visits. Individuals were instructed to remove the physical activity monitor when sleeping and bathing. Accelerometer data were captured and recorded during a 7-day period. For this study, physical activity data were computed from the time of the end of each HD treatment to the period 24 hours after on HD days. During the immediate post-HD period, physical activity data were recorded in 30 minutes intervals up to 2 hours, resulting in four segments of data.

1.1 | Statistical analysis

For the present study, we analysed the total step counts per 24 hours after HD, as well as the step counts in the immediate 2-hour period after HD. We hypothesized shorter DRTs would be associated with the most with steps taken in the 2 hours post-HD period. Only individuals with available physical activity data at baseline were included in this study. DRT was categorized according to the following cut-off points: zero, less than 60 minutes and more than 60 minutes for descriptive analysis. Comparisons for continuous data were performed by t-tests or Wilcoxon tests for two groups, when appropriate. Comparisons for more than two groups of continuous variables, according to DRT categories, were done by the ANOVA or Kruskal-Wallis test, following the assumptions of data distribution. Categorical data were tested by the Chi-square test. Pearson’s correlation coefficients were estimated between step counts and self-reported outcome variables.

In order to assess the association between measured physical activity and components of fatigue (ie, KDQOL Vitality scale and DRT), independently from other predefined correlated physical health
related quality of life (HRQOL) subdomains, a multivariate regression model was used with steps as the outcome. We included as covariates the Physical Functioning and Physical Role of KDQOL-36, as they are correlated subdomains of physical HRQOL and would presumably be associated both to fatigue domains and step counts. We performed separate analyses for the 24-hour post-HD period and for the 2-hour post-HD period in order to check for any potential effect modification of the period in reference to HD for associations between steps and DRT or Vitality. The assumptions of normality and homoscedasticity for residual data were evaluated for each model. The results were summarized in forest plots. All analyses were performed in R version 3.5.1.

2 | RESULTS

Nineteen of 195 total individuals in the HDFIT study were excluded from this study due to valid physical activity data not being available at baseline. Table 1 contains the descriptive data of the 176 individuals. The mean age of the population was 52 ± 15 years, 71% were males, 57% were white and 35% were used public transportation to go to the dialysis clinic. Approximately 35% of the individuals had diabetes mellitus, 17% coronary artery disease and 8% congestive heart failure. The vascular access in 85% of the individuals was an arteriovenous fistula. The mean weight before and after HD was 78 ± 16 Kg and 75 ± 15 Kg, whereas body mass index was 26.7 ± 4.9 Kg/m². The mean age of the population was 52 ± 15 years, 71% were males, 57% were white and 35% were used public transportation to go to the dialysis clinic. Approximately 35% of the individuals had diabetes mellitus, 17% coronary artery disease and 8% congestive heart failure. The vascular access in 85% of the individuals was an arteriovenous fistula. The mean weight before and after HD was 78 ± 16 Kg and 75 ± 15 Kg, whereas body mass index was 26.7 ± 4.9 Kg/m². The mean Kt/V for the population was 1.5 ± 0.4.

The mean potassium measurement was 5.2 ± 0.8 mmol/L, phosphorus was 1.7 ± 0.45 mmol/L, calcium was 2.2 ± 0.17 mmol/L and parathyroid hormone (PTH) was 37.8 ± 31.5 PMol/L. The mean albumin measurement was 40.3 ± 4 g/L, haemoglobin 112 ± 17 g/L, ferritin 359 ± 345 ng/mL and transferrin saturation index 30 ± 17%.

Accelerometer determined physical activity found individuals took a mean of 5258 ± 3540 steps per 24 hours after HD and 953 ± 617 in the first 2 hours after HD. Among the SF-36 components, the physical component summary (PCS) score was 60.8 ± 19.9 points and the mental component summary (MCS) score was 66.7 ± 22.3 points. Physical Functioning presented a mean score of 68.3 ± 25.4 points and Emotional Wellbeing score of 72.9 ± 19.3 points. The General Health component score was 49.3 ± 17.5 points, Pain score was 70.6 ± 25.4 points, and Vitality score was 63.3 ± 21.2 points. The mean Role Physical score was 55 ± 39.7 points, while the Emotional Role score was 55.6 ± 43.1 points and Social Role score was 73.9 ± 25.1 points.

In univariate analysis, both vitality and physical functioning were correlated to daily steps, \( r = 0.34 \) (\( P < .001 \)) and \( r = 0.39 \) (\( P < .001 \)), respectively. In the 2-hour post-HD period, Vitality was not correlated to step counts \( (r = 0.23; P = .20) \), yet Physical Functioning was \( (r = 0.32; P < .001) \).

DRT was up to 30 minutes in 57.6% of the individuals, from 30 to 60 minutes in 16.2% of individuals, from 60 to 120 minutes in 9.4% of individuals, from 120 to 240 minutes in 7.9% of individuals and no participant reported DRT of more than 240 minutes. DRT was not associated with post-HD weight (\( P = .13 \)), haemoglobin levels (\( P = .47 \)), calcium (\( P = .42 \)), potassium (\( P = .13 \)), phosphorus (\( P = .88 \)), PTH (\( P = .86 \)) or albumin (\( P = .86 \)). More years of schooling did not vary significantly among the three subgroups of DRT (\( P = .29 \)), while the use of public transportation showed an association with longer DRT (\( P = .02 \)).

There was no correlation between the number of steps in 24 hours after HD and DRT (\( r = −0.09, P = .44 \)). There was no significant difference between the number of steps in the first 2 hours after HD stratified from 0 to 30 minutes (\( P = .55 \)), 30 to 60 minutes (\( P = .10 \)), 60 to 90 minutes (\( P = .12 \)), 90 to 120 minutes (\( P = .61 \)) post-HD.

The results for the multivariate linear regression models are presented in Table 2 and Figure 1. The multivariable analysis confirmed DRT was not associated with the physical activity captured by the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD or % (count)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>176</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.48 ± 14.9</td>
</tr>
<tr>
<td>% Male</td>
<td>71.59 (126)</td>
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<tr>
<td>% White</td>
<td>56.82 (100)</td>
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<td>% Higher education</td>
<td>19.32 (34)</td>
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<tr>
<td>% Public transportation</td>
<td>34.66 (61)</td>
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<td>% Fistula</td>
<td>84.66 (149)</td>
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<tr>
<td>Kt/V</td>
<td>1.53 ± 0.4</td>
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<tr>
<td>Post HD SBP (mmHg)</td>
<td>148.66 ± 23.2</td>
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<tr>
<td>Post HD weight (kg)</td>
<td>75.26 ± 15.5</td>
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<tr>
<td>Body mass index (Kg/m²)</td>
<td>26.7 ± 4</td>
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<tr>
<td>Potassium (mmol/L)</td>
<td>5.18 ± 0.78</td>
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<tr>
<td>Phosphorus (mmol/L)</td>
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<tr>
<td>PTH (pmol/L)</td>
<td>357.05 ± 297.03</td>
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<td>Calcium (mmol/L)</td>
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<td>Albumin (g/L)</td>
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<td>Haemoglobin (g/L)</td>
<td>111.7 ± 16.8</td>
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<tr>
<td>Ferritin (ng/ml)</td>
<td>359.21 ± 345.26</td>
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<tr>
<td>TSAT (%)</td>
<td>30.02 ± 17</td>
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<td>24 hour post-HD steps</td>
<td>5258.49 ± 3540.22</td>
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<td>2 hour post-HD steps</td>
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<td>Physical component summary</td>
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<tr>
<td>Mental component summary</td>
<td>66.73 ± 22.3</td>
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<td>Physical functioning</td>
<td>68.31 ± 25.42</td>
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<td>Emotional wellbeing</td>
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<td>General health</td>
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<tr>
<td>Pain</td>
<td>70.57 ± 25.43</td>
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<tr>
<td>Role emotional</td>
<td>55.62 ± 43.09</td>
</tr>
<tr>
<td>Role physical</td>
<td>55 ± 39.66</td>
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<tr>
<td>Social role</td>
<td>73.93 ± 25.1</td>
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<td>Vitality</td>
<td>63.3 ± 21.16</td>
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accelerometer neither in the 2-hour post-HD period nor in the 24-hour post-HD period, but vitality was associated with physical activity in the 24-hour post-HD period. Physical Functioning, on the other hand, was associated with physical activity in both the early (2-hour) and later (24-hour) post-HD periods in the multivariable models.

3 | DISCUSSION

In this cross-sectional analysis of baseline data from a randomized controlled trial that included assessments of fatigue and granularly measured physical activity in the protocol, Vitality scores were associated with step counts in the 24-hour post-HD period. In contrast, DRT was not associated with physical activity captured by the accelerometer in the period immediately (2 hours) after the HD session.

Fatigue has been recognized as an important symptom from a HD patient’s perspective. Ninety percent of ESRD patients reported they would agree to undergo dialysis more frequently if it would increase in their energy level, while only 19% would accept increasing the frequency of sessions to increase their survival by 3 years. The high prevalence and impact of fatigue on health and quality of life of individuals may explain why this is one of four priority outcomes for HD individuals, but the recognition, stratification and management remain a challenge. Most importantly, patient reported fatigue captured in quality of life assessment has been associated with poor outcomes in HD patients. In this sense, it could be that physical inactivity is a potential mediator of the association between chronic fatigue and worse outcomes. In fact, data from randomized controlled trials of exercise interventions among ESRD seems to support this, considering that improvements in fatigue were not shown after exercise interventions. In light of the association we reported, the most plausible structural relation between chronic fatigue and reduced physical activity would be that the latter contributes to the former among ESRD patients.

Few previous studies explored the associations between objective physical activity and fatigue dimensions, including general fatigue assessed by the SF-36 and DRT. In a cross-sectional analysis of 48 adult HD patients, Sheshadri et al reported lower Vitality was associated to daily step counts measured by a pedometer. We therefore confirm these results in a broader population using an accelerometer, which is known to be a reference method for measuring step counts. Remarkably, we have shown Vitality scores associate only to the 24-hour period after HD, which suggests that post-HD fatigue may not be the main contributing factor to general fatigue in this population. These results should be confirmed in further investigations. On the other hand, Physical Function was associated with steps taken within 2 hours of HD and 24 hours post-HD. This is consistent with previous literature in non-CKD individuals that showed Physical Function is associated with objectively measured physical levels.

DRT did not show associations with objective physical activity as measured by accelerometer. To the best of our knowledge this is the first study to compare patient reported DRT with measured physical activity. However, a previous study found post-HD fatigue, not assessed by the DRT question, to be associated to physical activity measured by accelerometry, among 26 HD individuals. Several factors may explain the lack of associations. Given the DRT question assesses how the patient feels, is fatigued by, and ultimately tolerates the HD treatment, it might be capturing attributes of fatigue not specifically related to physical fatigue. DRT captures both mental and physical factors related to HRQOL and it may be possible that in more functional populations the mental subdomain might explain a greater proportion of the information provided by the question. Another possibility is that DRT may have restricted content validation among ESRD individuals, which may further limit a broader implementation of this metric in clinical studies. Finally, although our individuals are relatively functional compared to wider ESRD populations, the physical activity among these individuals remain low, which could compromise the detection of any association of DRT and daily steps. Reflecting on the inclusion criteria for the HDFIT trial, our study cohort descriptive differs from that of other studies. Vitality, Physical Functioning and Physical Role were found to be relatively preserved in this group of stable ESRD individuals, which may further limit a broader implementation of measured physical activity with Physical Functioning and Fatigue, including DRT. We analysed granular data on step counts, which included measures in reference to the dialysis treatments, thereby we were able to test the hypothesis that DRT would associate more strongly to changes in physical activity in the early period after dialysis. However, our study also has some limitations. The cross-sectional design may have limited inferences for the association between subjective and objective measures for physical activity. Given individuals included in the study did not have any limitations in ambulation nor mobility, and were younger than the overall population, these findings may only be generalizable to individuals with similar characteristics. Additionally, we cannot rule out limitations in accelerometer fidelity, as patients could have missed wearing the device for specific periods.
Moreover, we did not include sub analyses based on dialysis shifts or distance from the clinic, which could be potentially effect modifiers of step counts and fatigue associations. The specific contribution of fatigue and DRT to a sedentary life, and most importantly its association with poor outcomes associated with low physical activity profiles deserves further investigation.

In summary, we observed that higher patient perceived Physical Functioning and Vitality were associated with HD individuals living a more physically active life. Surprisingly, patient perceived DRT was not associated with physical activity levels, for reasons yet to be investigated. These patterns of patient reported fatigue perceptions and measured physical activity partially validate (against accelerometer-measured physical activity) the SF-36 fatigue assessment. Findings also indicate that there might be limitations in the interpretation of the DRT assessment tool. Since physical activity is an important component of a healthy life, our results may partially explain the associations between fatigue and poor outcomes in HD individuals.

ACKNOWLEDGEMENTS
The HDFIT trial was a multi-centre investigator-initiated study, whereby the site investigators and principal investigator were not being monetary funded for the conduct of study activities. This project was supported by (a) the study investigators, (b) the proponent institution Pontifícia Universidade Católica do Paraná, (c) the outpatient dialysis centres and (d) Fresenius Medical Care. The steering committee was composed of nephrologists representing site institutions and supporting affiliates. Investigators were involved in the design of the protocol and performed medical oversight and the coordination of data collection during the trial. The principal investigator provided medical oversight of the conduct of the trial at all sites under the guidance of the steering committee and coordinated the trial management. The proponent institution Pontifícia Universidade Católica do Paraná supported the trial with infrastructure for study management through use of the university’s ACRO, hosting of the REDCap electronic case report form on the university’s server and use of the university’s central Ethics Review Board and Research Council. The outpatient dialysis centres permitted clinical research at the clinics and supported the trial with their clinical staff who performed data collection and the conduct of study procedures under the oversight of the site investigators and local trial leadership. Fresenius Medical Care provided the sites with the infrastructure for the conduct of the trial including HDF machines, dialysis supplies for study participants, body composition monitor machines in clinics without them. In addition, they provided some staff for site monitoring. Fresenius Medical Care

FIGURE 1  Forest plot of regression coefficients of physical functioning, Vitality and DRT for step counts as outcome in multiple regression model. PRO, patient reported outcome
provided a monetary award to PUCPR's ACRO (EPICENTER) that performed the central management, data acquisition and monitoring. Fresenius Medical Care and the subsidiary company Renal Research Institute provided support from statistical experts to assist in the analysis of trial data under the oversight of the steering committee. Fresenius Medical Care has supported three investigator meetings, as well as three steering committee meetings. The leadership of Fresenius Medical Care reviewed and approved the protocol prior to commencement. The steering committee members (Supplementary Appendix C) who represent supporting institutions reviewed and approved the research design, protocol, addendums and changes to the protocol, analyses and this publication of study data, as well as provided oversight of the trial conduct and safety.

We would like to acknowledge and thank the site investigators, participating dialysis centers and staff conducting this trial (Supplementary Appendix A); the EPICENTER ACRO staff and affiliates managing the trial (Supplementary Appendix B); and the external advisory committee members Bernard Canaud, MD, PhD, Cristina Marelli, MD and Rodrigo S. Reis, PhD, MSc.

CONFLICT OF INTEREST
J. L., M. G., J. W. L., M. H. are students at Pontifícia Universidade Católica do Paraná. J. W. L., A. B. L. B. are employees of Fresenius Medical Care. M. H. is an employee of Renal Research Institute, a wholly owned subsidiary of Fresenius Medical Care North America. MEFC is employee by Federal University of São Paulo, and receives research grants, consulting fees and honoraria from Baxter Healthcare and Fresenius Medical Care. A. L. C. N. C. E. P. F. receive consulting fees and speaker honorarium from Fresenius Medical Care. C. E. P. F. receives lecture fees and travel support from Fresenius Medical Care, Alexion, Baxter and Astra Zeneca, and is employed by Pontifícia Universidade Católica do Rio Grande do Sul. R. P. F., T. P. M. are employed by Pontifícia Universidade Católica do Paraná. R. P. F., C. E. P. F., T. P. M., M. E. F. C are recipients of scholarships from the Brazilian Council for Research (CNPq). R. P. F. is employed by Arbor Research Collaborative for Health, and receives research grants, consulting fees and honoraria from Astra Zeneca, Novo Nordisc, Akebia and Fresenius Medical Care.

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REFERENCES


SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.