



# Demographic and clinical factors are associated with performance on the 6-minute walk test and the 2-minute step test in Parkinson's disease

Fatores demográficos e clínicos estão associados com o desempenho no teste de caminhada de 6 minutos e no teste de marcha de 2 minutos na doença de Parkinson

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## ABSTRACT

**Introduction:** It is still unclear whether comorbidities such as hypertension, diabetes mellitus, and dyslipidemia impact performance on the 6-minute walk test (6MWT) in Parkinson's disease (PD). Moreover, the factors associated with performance on the 2-minute step test (2MST) in PD remain unclear. **Objective:** This study aimed to analyze whether demographic factors, clinical characteristics related to PD, and comorbid conditions are associated factors with performance on the 6MWT and the 2MST in PD. **Methods:** This cross-sectional study was conducted at Associação Brasil Parkinson. 51 individuals (Hoehn & Yahr [H&Y] stages 1-4) performed the 2MST or the 6MWT twice on the same day ("on" state). An interval of at least 5 days was adopted between the assessments (2MST or 6MWT). The number of steps achieved on the 2MST, the 6MWT distance, the percentage of predicted 6MWT in healthy subjects, and the associated factors such as demographic characteristics, body mass index, H&Y stage, the Unified Parkinson's disease Rating Scale part III score, comorbidities, history of falls, and medication information were obtained. **Results:** The multiple linear regression analysis showed that the H&Y stage and age were negatively associated with 6MWT performance (adjusted  $R^2 = 0.535$ ,  $p < 0.001$ ), while only the H&Y stage was negatively associated with the percentage of predicted 6MWT ( $R^2 = 0.419$ ,  $p < 0.001$ ). Disease duration and age were negatively associated with 2MST performance, whereas male sex was positively associated with 2MST performance (adjusted  $R^2 = 0.283$ ,  $p < 0.001$ ). **Conclusion:** Advanced age and higher PD severity were associated with worse 6MWT performance, while advanced age and longer disease duration were associated with worse 2MST performance, whereas male sex was associated with better 2MST performance.

**Keywords:** Walking; Exercise test; Parkinson disease; Comorbidity.

## RESUMO

**Introdução:** Ainda não está claro se comorbidades como hipertensão, diabetes mellitus e dislipidemia influenciam o desempenho no teste de caminhada de 6 minutos (TC6M) em indivíduos com doença de Parkinson (DP). Além disso, os fatores associados ao desempenho no teste de marcha estacionária de 2 minutos (TME2M) na DP permanecem incertos. **Objetivo:** Este estudo teve como objetivo analisar se fatores demográficos, características clínicas relacionadas à DP e condições de comorbidades estão associados ao desempenho no TC6M e no TME2M em indivíduos com DP. **Métodos:** Este estudo transversal foi realizado na Associação Brasil Parkinson, com 51 indivíduos (estádios 1 a 4 de Hoehn & Yahr [H&Y]), que realizaram o TME2M ou o TC6M duas vezes no mesmo dia ("estado on"). Foram obtidos o número de passos alcançados no TME2M, a distância percorrida no TC6M, a porcentagem do valor predito para o TC6M em indivíduos saudáveis e os fatores associados, como as características demográficas, índice de massa corporal, estádios de H&Y, pontuação da parte III da Escala Unificada de Avaliação da Doença de Parkinson, comorbidades, histórico de quedas e informações sobre a medicação. **Resultados:** A análise de regressão linear múltipla mostrou que o estágio de H&Y e a idade estão negativamente associados ao desempenho no TC6M ( $R^2$  ajustado = 0,535;  $p < 0,001$ ), enquanto apenas o estágio de H&Y está negativamente associado com a porcentagem do valor predito do TC6M ( $R^2 = 0,419$ ;  $p < 0,001$ ). A duração da doença e a idade estão negativamente associados ao desempenho no TME2M e o sexo masculino está positivamente associado ao desempenho no TME2M ( $R^2$  ajustado = 0,283;  $p < 0,001$ ). **Conclusão:** Idade avançada e maior gravidade da DP estão associadas a pior desempenho no TC6M, enquanto a idade avançada e a maior duração da doença estão associadas ao pior desempenho no TME2M e o sexo masculino está associado ao melhor desempenho no TME2M.

**Palavras-chave:** Caminhada; Teste de exercício; Doença de Parkinson; Comorbidade.

## Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease<sup>1</sup>. One of the significant motor alterations in PD is walking impairment, which reduces the capacity to perform activities of daily living in these individuals<sup>2,3</sup>. The 6-minute walk test (6MWT) has been widely used to evaluate walking capacity in people with PD and has been associated with health outcomes such as quality of life<sup>4,5</sup>. Although previous studies have shown that 6MWT is affected by several factors such as age, PD severity, and fall history, among others<sup>6-8</sup>, it remains unclear whether comorbidities such as hypertension, diabetes mellitus, and dyslipidemia impact 6MWT performance in people with PD. In people without PD, studies have observed a negative impact of hypertension or diabetes mellitus on functional capacity<sup>7,9,10</sup>, which may be relevant in PD. In this scenario, hypertension, diabetes mellitus, and dyslipidemia may lead to autonomic and cardiovascular dysfunctions<sup>11-13</sup> already commonly observed in individuals with PD<sup>14</sup>, which may contribute to inadequate cardiovascular responses during exercise tests and, consequently, prematurely limiting exercise tolerance in individuals with DP. However, whether these comorbidities are associated with 6MWT performance remains unclear in PD.

The 2-minute step test (2MST) has also been used as an option for assessing walking capacity in clinical settings (home care and outpatient clinics), as it has been used in some populations to assess functional capacity<sup>15,16</sup>. In addition, the 2MST has some practical advantages such as minimal space requirements (it does not require a 30-meter corridor), shorter administration time (less than 6 minutes), and greater safety, as it does not require patient displacement. During the test, the individual should march in place for two minutes while raising their knee to a height corresponding to the midpoint between the patella and the anterior superior iliac spine. The main outcome is the number of steps completed<sup>17</sup>. Although Santos et al.<sup>18</sup> observed correlations between the 2MST and the total Unified Parkinson's Disease Rating Scale (UPDRS) score, balance, gait speed and cadence and the Time Up and Go test, the factors predicting performance on the 2MST in people with PD are still not fully understood, mainly whether comorbidities also impact test performance, which may be useful when applying this test in PD rehabilitation. Thus, this study aimed to analyze whether demographic factors, clinical characteristics

related to PD, and comorbid conditions are associated factors with performance on the 6MWT and the 2MST in PD. The study hypotheses were that individuals of more advanced age, worse clinical characteristics related to PD and comorbid conditions would present worse performance on both the 6MWT and the 2MST.

## Methods

### Study design and ethical issues

The present study is a secondary analysis of data obtained from a previously published study<sup>19</sup>. This cross-sectional study follows the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist<sup>20</sup>. The study was approved by the local ethical committee (CAAE # 64690922.0.0000.5511). All participants read and signed an informed written consent form before participation.

### Recruitment and subjects

Participants were recruited from the Brazil Parkinson's Association (*Associação Brasil Parkinson*) between February and July 2023. They were recruited through verbal invitations. To participate in the present study, individuals needed to have a diagnosis of PD, H&Y stages between 1 and 4<sup>21</sup>, be aged > 45 years old, and be able to ambulate independently without the use of assistive devices or physical assistance during the tests. The exclusion criteria included: i) the presence of other neurological disorders; and ii) any health problem that restrains exercise. The characteristics of the 51 people with PD included in the present study are shown in Table 1.

### Experimental protocol

The tests were performed at Brazil Parkinson's Association. The 2MST or the 6MWT were conducted on two different days, at the same time of day, with an interval of at least 5 days between the assessments. Two trained kinesiologists conducted the tests. The same kinesiologist performed the test and retest of both tests for the same person. Participants were instructed not to exercise in the previous 24 hours, to eat a light meal 2 hours before, and to take their PD medication 30 min before the start of the sessions. At each visit, upon arrival at the institution, participants were placed at rest in the seated position for 15 minutes before the assessments. The assessments were conducted by two trained kinesiologists.

**Table 1** – Demographic and clinical characteristics of people with Parkinson's disease (n = 51).

|                                                              | Values      |
|--------------------------------------------------------------|-------------|
| Sex, male, n (%)                                             | 26 (51.0)   |
| Age, years                                                   | 67.9 (9.9)  |
| Body mass index, kg.m <sup>-2</sup>                          | 25.3 (4.3)  |
| Parkinson's disease Characteristics                          |             |
| Disease Duration, years                                      | 8.4 (5.0)   |
| Hoehn & Yahr stage, n (%)                                    |             |
| 1                                                            | 1 (2.0)     |
| 2                                                            | 20 (39.2)   |
| 3                                                            | 22 (43.1)   |
| 4                                                            | 8 (15.7)    |
| The Unified Parkinson's disease Rating Scale part III, score | 26.2 (12.6) |
| Falls history in the last year, n (%)                        | 33 (64.7)   |
| Parkinson's disease Medications use, n (%)                   |             |
| Levodopa                                                     | 47 (92.2)   |
| Dopamine Agonist                                             | 20 (39.2)   |
| Amantadine                                                   | 8 (15.7)    |
| Selegiline                                                   | 5 (9.8)     |
| Comorbid conditions, n (%)                                   |             |
| Hypertension                                                 | 18 (35.3)   |
| Dyslipidemia                                                 | 12 (23.5)   |
| Diabetes mellitus                                            | 9 (17.6)    |
| Walking capacity                                             |             |
| 2-min step test, steps                                       | 64 (23)     |
| Six-minute walk test, m                                      | 363 (133)   |
| Percentage of predicted six-minute walk test, %              | 68.3 (24.9) |

Data are means (SD) or frequency distribution.

## Outcomes

### • Six-minute walk test (6MWT)

The 6MWT was performed along a 30-meter corridor, as previously described<sup>22</sup>. A cone was placed at each end of the walkway to indicate where the participants had to turn. Participants were instructed to cover as much distance as possible in six min. The 6MWT distance was defined as the maximum distance achieved by the individual at the end of the test. The 6MWT was performed twice with a 15-minute interval between the assessments. The percentage of predicted 6MWT of healthy subjects with similar characteristics was calculated using the procedures previously described<sup>23</sup>. The best performance for both parameters, the 6MWT distance and percentage of predicted 6MWT, was considered for analysis of associated factors.

### • 2-min step test (2MST)

The 2MST was performed as previously described<sup>17</sup>. The 2MWT was performed twice with a 15-minute

interval between the assessments. Participants were required to march in place for 2 min. The march consisted of alternating knee elevation to the midpoint between the patella and the anterior superior iliac spine.

Participants were instructed to complete as many steps as possible during the test. An evaluator quantified the number of steps, identified by elevations of the most affected leg by PD. The best performance between the tests was considered for analysis of associated factors.

### • Potential associated factors

Demographic (i.e., sex and age), comorbidities, and clinical data were collected through a face-to-face interview. Data collected included hypertension (previous physician diagnosis or use of antihypertensive medications), dyslipidemia (previous physician diagnosis or use of lipid-lowering medications), diabetes (previous physician diagnosis or use of glucose-lowering medications), use of other medications, and history of falls in the last year (yes or no). Body mass index, disease duration, and PD severity were also assessed by the H&Y Scale by standardized guidelines<sup>21</sup> and the UPDRS part III<sup>24</sup>. Experienced physiotherapists from institution Brazil Parkinson's Association performed these assessments with an interval of up to 1 month from the walking tests.

## Statistical analysis

The software used for all analyses was the IBM SPSS Statistics (version 20.0; IBM Corp., Armonk, NY, EUA). The continuous variables were expressed as mean (standard deviation) and frequency distribution for categorical data. Univariate and multiple linear regression analyses were conducted to identify whether demographic data, comorbid conditions, H&Y stage, and UPDRS part III score were predictors of 6MWT distance, percentage of predicted 6MWT, and 2MST performance. In the univariate linear regression analysis, each variable was included in a separate regression analysis. In the multiple linear regression models, a stepwise forward technique was used to enter the covariates into the linear models, with the criteria for entry utilizing a  $p < 0.30$  and the criteria to remain in the final model utilizing a  $p < 0.05$ . Residual analysis was performed, homoscedasticity was analyzed by graphical analysis (scatter plot), and adherence to the normal distribution was tested using the Kolmogorov-Smirnov test. Multicollinearity analysis was performed assuming variance inflation factors less than five and tolerance

less than 0.20. The significance level was set at  $p < 0.05$ .

## Results

Fifty-one percent of individuals were males, most of them were in H&Y stages 2 and 3, and 64.7% reported a fall history in the last year. In addition, 92.2% of individuals were taking levodopa and 39.2% dopamine agonists. Hypertension, dyslipidemia, and diabetes were present in 35.3%, 23.5%, and 17.6% of people, respectively. One participant dropped out of the study for personal reasons and, therefore, did not perform the 6MWT on the second day. No interruptions occurred during the test execution.

The bivariate relationships between 6MWT distance, percentage of predicted 6MWT and 2MST performance, and demographic, clinical characteristics of PD, and comorbid conditions are shown in Table 2. Worse

6MWT performance was correlated with more advanced age, longer disease duration, higher H&Y stage, higher UPDRS part III score, fall history, and presence of hypertension. In addition, a lower percentage of predicted 6MWT obtained in the test was correlated with more advanced age, higher H&Y stage, higher UPDRS part III score, and higher body mass index. Finally, worse 2MST performance was correlated with more advanced age, longer disease duration, higher H&Y stage, and fall history, and better 2MST performance was correlated with male sex and higher body mass index.

The multivariate analysis indicated that higher H&Y stage and more advanced age were associated with worse 6MWT performance. The model explained 53.5% of the variance in 6MWT performance. Higher H&Y stage was associated with a lower percentage of predicted 6MWT. The model explained 41.9% of the variance in

**Table 2** – Bivariate relationship between 6-min walk test distance, percentage of predicted 6-min walk test, and 2-min step test and demographic, Parkinson's disease clinic, and comorbid conditions data of people with Parkinson's disease.

| Variables                                                    | 6-min walk test, m<br>(n = 50) |         | % predicted 6-min walk test<br>(n = 50) |         | 2-min step test, n<br>(n = 51) |         |
|--------------------------------------------------------------|--------------------------------|---------|-----------------------------------------|---------|--------------------------------|---------|
|                                                              | r                              | p value | r                                       | p value | r                              | p value |
| Demographic data                                             |                                |         |                                         |         |                                |         |
| Age, years old                                               | -0.572                         | < 0.001 | -0.473                                  | < 0.001 | -0.346                         | 0.006   |
| Sex, women= 0; men= 1                                        | 0.226                          | 0.057   | 0.157                                   | 0.138   | 0.309                          | 0.014   |
| Anthropometry data                                           |                                |         |                                         |         |                                |         |
| Body mass index, kg.m <sup>-2</sup>                          | 0.165                          | 0.126   | 0.235                                   | 0.050   | 0.267                          | 0.029   |
| Parkinson's disease clinic data                              |                                |         |                                         |         |                                |         |
| Disease duration, years                                      | -0.380                         | 0.003   | -0.224                                  | 0.059   | -0.412                         | 0.001   |
| Hoehn & Yahr stage                                           | -0.684                         | < 0.001 | -0.647                                  | < 0.001 | -0.383                         | 0.003   |
| The Unified Parkinson's Disease Rating Scale part III, score | -0.335                         | 0.009   | -0.274                                  | 0.027   | -0.172                         | 0.113   |
| Falls history in the last year, no = 0; yes = 1              | -0.266                         | 0.031   | -0.187                                  | 0.097   | -0.309                         | 0.014   |
| Comorbid conditions                                          |                                |         |                                         |         |                                |         |
| Diabetes mellitus, no= 0; yes= 1                             | 0.041                          | 0.389   | 0.001                                   | 0.496   | 0.131                          | 0.179   |
| Hypertension, no= 0; yes= 1                                  | -0.254                         | 0.038   | -0.161                                  | 0.133   | 0.004                          | 0.489   |
| Dyslipidemia, no= 0; yes= 1                                  | -0.057                         | 0.346   | -0.077                                  | 0.296   | 0.036                          | 0.400   |

$p < 0.05$ .

**Table 3** – Multiple regression models predicting 6-min walk test, percentage of predicted 6-min walk test and 2-min step test in people with Parkinson's disease.

| Dependent variables                  | Independent variables   | B (SE)           | b      | p value |
|--------------------------------------|-------------------------|------------------|--------|---------|
| 6-min walk test, m (n= 50)           | Hoehn & Yahr stage      | -96.499 (19.778) | -0.534 | < 0.001 |
|                                      | Age, years old          | -4.398 (1.458)   | -0.330 | 0.004   |
| % predicted 6-min walk test (n = 50) | Hoehn & Yahr stage      | -21.920 (3.726)  | -0.647 | < 0.001 |
|                                      | Disease duration, years | -1.593 (.552)    | -0.350 | 0.006   |
| 2-min step test, steps (n = 51)      | Age, years old          | -0.698 (.279)    | -0.301 | 0.016   |
|                                      | Sex                     | 11.538 (5.500)   | 0.253  | 0.041   |

B (SE): regression coefficient (error standard); b: standardized coefficients.  $p < 0.05$ . F: F-statistic; R: correlation coefficient; R<sup>2</sup>: coefficient determination; SEE: standard error of estimate.

F = 29.156; R = 0.744; R<sup>2</sup> = 0.554; adjusted R<sup>2</sup> = 0.535; SEE = 90.706 m

F = 34.615; R = 0.647; R<sup>2</sup> = 0.419; SEE = 19.179 %

F = 7.591; R = 0.571; R<sup>2</sup> = 0.326; adjusted R<sup>2</sup> = 0.283; SEE = 19.468 steps

the percentage of predicted 6MWT. Longer disease duration and more advanced age were associated with worse 2MST performance, whereas male sex was associated with better 2MST performance. The model explained 28.3% of the variance in 2MST performance (Table 3).

## Discussion

The main findings of the present study were: 1) Hypertension, dyslipidemia, and diabetes were not associated with 6MWT and 2MST performance; 2) H&Y stage and age were negatively associated with 6MWT performance; 3) H&Y stage was negatively associated with the percentage of predicted 6MWT; and 4) Disease duration and age were negatively associated with worse 2MST performance, whereas male sex was positively associated with better 2MST performance in people with PD.

The average 6MWT distance covered by our individuals was 363 (133) m, which is close to that observed by Kobayashi et al.<sup>25</sup>, who observed an average of 341 (111) m, and lower than Canning et al.<sup>6</sup>, who observed the average of 546 (103) m, which may be attributed to variations in inclusion criteria among studies. The lower average age and PD severity (only H&Y stages 1-3) observed in Canning et al.'s study<sup>6</sup> may have influenced the discrepancy between results. In the current study, H&Y stage and age were the factors associated with 6MWT performance. It has been suggested that the aging process increases vulnerability and loss of dopaminergic neurons and, consequently, impairment of motor control in this population<sup>26</sup>. Data from the current study corroborated with previous studies such as Falvo et al.<sup>27</sup> and Üğüt et al.<sup>8</sup>, who also identified that H&Y stage and age were associated with 6MWT performance in people with PD.

A novelty of this study is the analysis of 6MWT performance as a percentage of predicted compared with healthy controls of similar age, sex, and body mass index. The use of relative values allows for an objective estimation of the degree of walking impairment caused by the disease. It also enables more appropriate comparisons among studies involving individuals with different proportions of men and women and different age distributions. In this current study, the mean performance of the individuals was  $68.3 \pm 24.9\%$  of the average performance of healthy individuals, indicating a 32% reduction in performance. The results revealed that the H&Y stage was the unique factor associated with the percentage of predicted 6MWT performance. This

association reinforces the idea that the primary factor linked to 6MWT performance is the clinical condition of people with PD. The slight discrepancy with the results for absolute 6MWT may be explained by the inclusion of age in the calculation of the percentage of predicted<sup>23</sup>, adjusting the results for this factor.

In contrast to UPDRS part III scores, H&Y stage was associated with both 6MWT performance and the percentage of predicted 6MWT performance. Although this result may initially seem unexpected, it corroborates with previous studies<sup>8,25</sup> that also observed only an association between H&Y stage and 6MWT performance in individuals PD. One possible explanation is that the H&Y scale encompasses balance and gait impairments,<sup>21</sup> which are determinant factors of 6MWT performance. In contrast, UPDRS part III scores encompass impairments involving the entire body, including alterations in facial expression, difficulties in finger performance tasks, impairment in hand movements, among others,<sup>24</sup> which may have less influence on 6MWT performance.

The average of 2MST observed in this study was 64 (23) steps. Lima et al.<sup>28</sup> observed an average of 2MST over 75 steps in people with PD. Evaluating the factors associated with performance in 2MST may help understand the impact of different factors on test performance. The results of this study revealed that disease duration, age, and sex were associated with 2MST performance. Interestingly, in contrast to 6MWT performance, H&Y was not associated with 2MST performance. These results suggest that characteristics of the 2MST (e.g., marching in place with a clear visual cue, no change in direction, examiners remaining close, greater feeling of security, possibility of leaning on the support nearby, among others) may have mitigated the impact of different levels of motor severity evaluated with the H&Y scale. On the other hand, sex and age were associated with 2MST performance. Previous studies<sup>8,29,30</sup> have reported that women and individuals of more advanced age with PD have lower cardiorespiratory capacity and lower limb strength compared to men and younger individuals, making it possible to speculate that these two components are required during the maintenance of knee elevation.

Studies have reported a prevalence of hypertension, diabetes mellitus and dyslipidemia ranging from 14-69%, 10-10.4%, and 3-20.3%, respectively, in individuals with PD<sup>3,31-33</sup>. In the current study, the prevalence was 35.3%, 17.6%, and 23.5%, respectively, confirming

a substantial proportion of individuals with PD presenting these comorbid conditions. In people without PD, studies have reported a deleterious impact of comorbidities such as hypertension and diabetes mellitus on functional capacity<sup>7,9,10</sup>. Individuals with PD may present alterations in the muscle metaboreflex and reduced sympathetic activity, which may result in lower vasoconstriction and peripheral vascular resistance and a blunted increase in heart rate and systolic blood pressure during exercise test, compromising adequate blood supply during the test in these individuals<sup>14</sup>. In addition, mitochondrial dysfunction<sup>34</sup>, which is also commonly present in these individuals, may also lead to deleterious alterations in aerobic energy utilization, further limiting test performance. In this context, hypertension, diabetes mellitus, and dyslipidemia may also lead to metabolic, autonomic, and cardiovascular dysfunctions<sup>11-13,35,36</sup>, which might potentiate the metabolic, autonomic, and cardiovascular impairments inherent to PD, and consequently, increase exercise intolerance in these individuals. Contrary to the study hypothesis, this phenomenon was not observed in people with PD in the current study, suggesting that the functional impairments caused by PD are not overcome by these comorbid conditions, highlighting the severe consequences of PD on functional performance.

As practical applications for this study, both tests have been widely used to evaluate walking capacity in different populations and have been associated with health outcomes. The application of these tests has the advantage of not requiring specific equipment. In the current study, individuals of more advanced age and higher PD severity were associated with worse 6MWT performance, while advanced age and longer disease duration were associated with worse 2MST performance, whereas male sex was associated with better 2MST performance. Therefore, these factors should be considered when using and interpreting the results of the 6MWT and the 2MST in PD.

This study had some limitations. First, this is a cross-sectional study, which limits the causal relationship of the associations; Second, participants were recruited from a single center, which may limit the generalizability of the findings to other centers; Third, the number of falls in the last year was not assessed due to the difficulty participants may have had in accurately reporting the exact number of falls. Finally, measures of balance, freezing of gait, and cognitive, among other factors that may predict test performance were not included. In conclusion,

comorbid conditions were not associated with 6MWT and 2MST performance in PD. However, advanced age and higher PD severity were associated with worse 6MWT performance, while advanced age and longer disease duration were associated with worse 2MST performance, whereas male sex was associated with better 2MST performance. These results suggest that the functional impairments caused by PD are not outweighed by other health conditions, highlighting the impact of PD severity, age, and sex on functional performance. Therefore, these factors should be considered when using and interpreting the results of 6MWT and 2MST in PD.

### Conflict of interest

The authors declare no conflict of interest.

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### Author's contributions

Kanegusuku H: Conceptualization; Methodology; Software; Validation; Formal analysis; Investigation; Supervision; Project administration; Visualization; Writing – original draft; Approval of the final version. Silva-Batista C: Validation; Investigation; Visualization; Writing – review & editing; Approval of the final version. Guelfi ETN: Conceptualization; Methodology; Validation; Investigation; Resources; Project administration; Writing – review & editing; Approval of the final version. Rogatto FBT: Validation; Investigation; Data curation; Visualization; Writing – review & editing; Approval of the final version. Lima VFS: Validation; Investigation; Data curation; Visualization; Funding acquisition; Writing – review & editing; Approval of the final version. Farah BQ: Validation; Investigation; Visualization; Writing – review & editing; Approval of the final version. Correia MA: Conceptualization; Methodology; Validation; Investigation; Resources; Supervision; Project administration; Visualization; Writing – review & editing; Approval of the final version.

### Declaration regarding the use of artificial intelligence tools in the article writing process

The authors used artificial intelligence tool ChatGPT for English language review.

### Availability of research data and other materials

The datasets generated during the study are available from the corresponding author upon reasonable request.

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# Reviewers' assessment

The reviews of this article were originally conducted in Portuguese. This version has been translated using ChatGPT and subsequently reviewed by the Chief Editors.

## Reviewer A

Anonymous

### Format

- Does the article comply with the manuscript preparation rules for submission to the Revista Brasileira de Atividade Física e Saúde?

Yes

- Regarding formal aspects, is the manuscript well structured, containing the sections: introduction, methods, results, and discussion (with the conclusion as part of the discussion)?

Partially

- Is the language appropriate, and is the text clear, precise, and objective?

Partially

- Was any indication of plagiarism observed in the manuscript?

No

#### Suggestions/Comments:

- The text lacks specificity.
- The Conclusion is separated from the Discussion.

### Abstract

- Are the abstract and the abstract in English adequate (containing: objective, information about the study participants, variables studied, main results, and a conclusion) and do they reflect the content of the manuscript?

Yes

#### Suggestions/Comments:

- No comment

### Introduction

- Was the research problem clearly stated and delimited?

No

- Is the research problem adequately contextualized in relation to existing knowledge, moving from the general to the specific?

No

- Are the reasons justifying the need for the study (including the authors' assumptions about the problem) well established in the writing?

No

- Are the references used to support the presentation of the research problem current and relevant to the topic?

Partially

- Was the objective clearly presented?

No

#### Suggestions/Comments:

- 1. The study rationale provided in the introduction does not reveal in meaningful way why this study is needed or how it advances the field.
- 1.1 For example, the authors need to provide better justification for why assessing hypertension, diabetes, and dyslipidemia matter in this population. Because they are treatable? Because they are added burden to the central and peripheral nervous systems? Please elaborate.
- 1.2 In addition, there is a difference between assessing functional capacity via 2-min step test and walking capacity. Stepping in place does not replace the need for an actual walking test, unless the patient is unable to walk.
- 1.3 "Additionally, examiners can remain nearby throughout the test, which differs from the 6MWT." Under good research practices, individuals with risk of falls such as people with PD should always be accompanied during walking tests. I am confident that in most laboratories studying PD that is the case. I would remove this from the test.
- 1.4 In a quick literature search there were two studies investigating the 2-min step test in PD. Please revise the statement "no study has explored the factors associated with performance in the 2MST in people with PD".
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- 2. The study objective lacks specificity. What is the focus here?
- 3. What are the study hypotheses?

## Methods

- Are the methodological procedures, in general, appropriate for studying the research problem?  
Yes
- Are the methodological procedures adopted for conducting the study sufficiently detailed?  
Partially
- Was the procedure adopted for selecting or recruiting participants appropriate for the problem studied and described in a sufficient, clear, and objective manner?  
Partially
- Were information provided about the instruments used for data collection, their psychometric properties (e.g., reproducibility, internal consistency, and validity), and, when relevant, about the operational definition of variables?  
Yes
- Is the data analysis plan appropriate and adequately described?  
Yes
- Were the inclusion and/or exclusion criteria for sample participants described and appropriate for the study?  
Yes
- Did the authors provide clarification about the ethical procedures adopted for conducting the research?  
Yes

### Suggestions/Comments:

- 1. Page 4, lines 19-20: "The 2MST or 6MWT were conducted in two days, at the same time of day, with an interval of at least 5 days between the assessments." Please provide an explanation for why two days of testing and why 5 days between assessments.
- 2. Page 6, line 1: How were comorbidities determined? Self-report? Based on formal diagnosis from medical history? Based on concomitant medications? Please specify.

## Results

- Is the use of tables and figures appropriate and does

it facilitate adequate presentation of the study results?

Yes

- Is the number of illustrations in the article in accordance with the journal's manuscript submission guidelines?  
Yes
- Are the number of participants at each stage of the study, as well as the number and reasons for losses and refusals, presented in the manuscript?  
Partially
- Are the characteristics of the participants presented and sufficient?  
Yes
- Are the results presented appropriately, highlighting the main findings and avoiding unnecessary repetition?  
Yes

### Suggestions/Comments:

- 1. Page 7, line 1: When initiating a sentence use text, i.e. "Fifty-one percent were males", followed by numeric representations.
- 2. Page 7, lines 3-4: What was the percentage of people with diabetes?

## Discussion

- Are the main findings of the study presented?  
Partially
- Are the study limitations and strengths presented and discussed?  
Yes
- Are the results discussed in light of the study limitations and the existing knowledge on the topic?  
Yes
- Are the potential contributions of the main study findings to scientific development, innovation, or real-world intervention discussed by the authors?  
No

### Suggestions/Comments:

- 1. Page 8, lines 1-4: Are these really the main findings of the study? There is no novelty in these associations. How about the comorbidities? Wasn't this the focus of the study? Shouldn't the main findings be whether or not comorbidities show added effect on walking and functional capacity in people with PD?
- 2. Page 9, lines 13-17: My interpretation is that, from a contribution point of view, this is the most important information from this article.

## Conclusion

- Was the study conclusion presented appropriately and is it consistent with the study objective?  
No
- Is the study conclusion original?  
No

### Suggestions/Comments:

- The lack of specificity in the objects has consequences for the conclusion. The conclusion does not show how this study advances the field. The associations found are known and expected in this population.

## References

- Are the references up to date and sufficient?  
Partially
  - Is most of the reference list composed of original research articles?  
Yes
  - Do the references comply with the journal's standards (quantity and format)?  
Yes
  - Is citation in the text adequate, that is, do the statements in the text cite references that actually substantiate such statements?  
Partially
- Suggestions/Comments:**
- The study should elaborate more on the assessment of comorbidities based on previous research.

## Comments to the authors

### Introduction

- 1. The study rationale provided in the introduction does not reveal in meaningful way why this study is needed or how it advances the field.
- 1.1 For example, the authors need to provide better justification for why assessing hypertension, diabetes, and dyslipidemia matter in this population. Because they are treatable? Because they are added burden to the central and peripheral nervous systems? Please elaborate.
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with risk of falls such as people with PD should always be accompanied during walking tests. I am confident that in most laboratories studying PD that is the case. I would remove this from the test.

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- 2. The study objective lacks specificity. What is the focus here?
- 3. What are the study hypotheses?

### Methods

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- 2. Page 6, line 1: How were comorbidities determined? Self-report? Based on formal diagnosis from medical history? Based on concomitant medications? Please specify.

### Results

- 1. Page 7, line 1: When initiating a sentence use text, i.e. "Fifty-one percent were males", followed by numeric representations.
- 2. Page 7, lines 3-4: What was the percentage of people with diabetes?

### Discussion

- 1. Page 8, lines 1-4: Are these really the main findings of the study? There is no novelty in these associations. How about the comorbidities? Wasn't this the focus of the study? Shouldn't the main findings be whether or not comorbidities show added effect

on walking and functional capacity in people with PD?

- 2. Page 9, lines 13-17: My interpretation is that, from a contribution point of view, this is the most important information from this article.

### Conclusion

- The lack of specificity in the objects has consequences for the conclusion. The conclusion does not show how this study advances the field. The associations found are known and expected in this population.

### Minor comment

- There are minor language mistakes in the manuscript that can be easily addressed by additional proof-reading.

## Final decision

- Reject

## Reviewer B

Anonymous

## Comments to the authors

### General comments

- This manuscript addresses an interesting and clinically relevant topic regarding factors associated with functional walking performance in people with Parkinson's disease (PD). The inclusion of both the 6-minute walk test (6MWT) and the 2-minute step test (2MST) is valuable, particularly because evidence regarding the 2MST in PD is still limited.
- However, the manuscript presents important conceptual, methodological, and interpretative issues that should be addressed before publication. In its current form, the main novelty proposed in the introduction (i.e., the role of comorbidities such as hypertension, diabetes mellitus, and dyslipidemia) is not sufficiently supported by the results and discussion sections. Ultimately, the main findings reinforce already well-established associations between PD severity, aging, and functional performance.
- In addition, the manuscript would benefit from substantial English language revision, as several sections contain grammatical inaccuracies, unclear phrasing, repetitive wording, and inconsistencies in terminology and interpretation.

### Major comments

#### 1. Use of the term "older people"

- The authors frequently use the term "older people" throughout the discussion and conclusion. However, the inclusion criteria allowed participants aged >45 years, meaning that not all participants can be considered older adults. The terminology should be revised throughout the manuscript to avoid conceptual inaccuracies.

#### 2. Lack of clarity regarding the novelty of the study

- The introduction emphasizes the importance of evaluating comorbidities such as hypertension, diabetes mellitus, and dyslipidemia. However, these variables are minimally discussed in the discussion and conclusion sections. Since the main findings indicate that age and PD severity are associated with poorer walking performance (findings already widely established in the literature) the manuscript should better clarify:
  - What is truly novel in this study,
  - Why assessing comorbidities is clinically relevant,
  - What additional contribution this study provides beyond previous studies.
- The discussion regarding comorbidities should be substantially expanded.

#### 3. Title is too broad

- The title "Factors associated with the performance in gait tests in Parkinson's disease" is very broad and nonspecific. A more focused title reflecting the specific tests and variables evaluated would improve clarity.

#### 4. Hypothesis is missing

- The introduction does not clearly state the study hypothesis. The authors should explicitly present their hypotheses at the end of the introduction.

#### 5. Inclusion of participants with Hoehn & Yahr stage 4

- Participants with H&Y stage 4 were included, but important methodological details are missing. Please clarify:
  - Whether all participants were independently ambulatory,
  - Whether assistive devices were allowed,
  - Whether participants required physical assistance during the tests,
  - Whether any interruptions occurred during test execution.
- This is particularly important because H&Y stage 4 is typically associated with substantial mobility limitations.

#### 6. Repetition of exhaustive functional tests

- The authors performed the 6MWT and 2MST twice with a 15-minute interval between attempts. Please justify:
- Why both tests were repeated,
- Whether fatigue effects were considered.
- Since the 6MWT is a physically demanding test, residual fatigue may influence performance.

#### **7. Percentage of predicted 6MWT lacks clinical justification**

- The rationale for using the “percentage of predicted 6MWT” remains unclear throughout the manuscript. The authors should better explain:
- The clinical meaning of this variable,
- Why it is relevant in PD,
- How it adds information beyond absolute walking distance.

#### **8. Lack of detail regarding clinical assessments**

- The manuscript does not clearly describe:
- Who performed the H&Y, UPDRS, hypertension, diabetes mellitus, and dyslipidemia assessments,
- Whether raters were trained,
- When these assessments were performed relative to the walking tests.
- These methodological details should be clarified.

#### **9. Overrepetition of table results**

- Several paragraphs in the Results section simply repeat the information already presented in the tables. The authors should prioritize interpretation and synthesis rather than reproducing table values in the text. For example, instead of repeating correlations numerically, the text could emphasize the clinical interpretation of the findings.

#### **10. Unexpected lack of association with UPDRS III**

- The absence of UPDRS III in the final regression models is interesting and deserves further discussion. Considering that participants with H&Y stage 4 were included, one would expect higher UPDRS III scores and stronger associations with functional performance. The authors should discuss possible explanations for this finding.

#### **11. Interpretation of sex differences in the 2MST is confusing**

- The discussion states that “older men who have

higher disease duration were associated with worse 2MST performance,” but Table 3 suggests better performance in men (positive beta coefficient). Additionally, the explanation regarding lower cardio-respiratory fitness and strength in women appears inconsistent with the reported results. This section should be revised for consistency and clarity.

#### **12. Limitations section**

- The statement regarding exclusion of H&Y stage 5 participants should not necessarily be considered a limitation, since individuals at this stage may not be able to safely or adequately perform the proposed tests.
- More relevant **limitations** would include:
- Cross-sectional design,
- Absence of freezing of gait assessment,
- Lack of balance evaluation,
- Lack of cognitive measures,
- Potential selection bias from a single-center sample.

#### **Minor comments**

- “people without DP” should be corrected to “people without PD”.
- Several grammatical and stylistic issues are present throughout the manuscript.
- The manuscript would benefit from professional English editing.
- Falls history should be better described: Was this variable binary (yes/no)?; Were recurrent fallers identified?; How many falls were considered?
- Table 2 reports n=50 for the 6MWT analysis, while the total sample was n=51. The missing participant and reason for exclusion should be explicitly reported.
- The description of the 2MST contains inconsistent terminology (“walk on the spot” versus marching in place).

#### **Final decision**

- Substantial revisions required