

Handgrip strength in Parkinson's disease: A systematic review of observational studies

Força de preensão manual na doença de Parkinson: uma revisão sistemática de estudos observacionais

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Abstract

Introduction: People with Parkinson's disease may present muscle weakness. The handgrip test is used to identify upper limbs strength. There are different protocol descriptions of this assessment. Objective: To carry out a systematic review on the assessment of handgrip strength in people with Parkinson's. Methods: The review was carried out according to the PRISMA guidelines, the PubMed, SciELO, LILACS and Scopus literary databases, and registered at PROSPERO (CRD420201 9018). Quantitative analysis was performed using the Newcastle-Ottawa Scale. Twenty-seven articles were analyzed. Results: The most referenced protocol is that of the American Society of Hand Therapists. The most used instrument is the hydraulic dynamometer. Of the sixteen studies that compared handgrip strength between people with Parkinson's and healthy people, seven identified a statistically significant difference. No article was classified as unsatisfactory. Conclusion: It is not possible to affirm that handgrip strength is reduced in Parkinson's disease, when compared to healthy subjects. Protocol and instrument standardization can help comparisons between results from different studies. There are few longitudinal studies, making it difficult to understand what happens to handgrip strength as the disease progresses.

Keywords: Disability assessment. Handgrip strength. Parkinson's disease.

Resumo

Introdução: Pessoas com doença de Parkinson (DP) podem apresentar fragueza muscular. O teste de força de preensão é usado para identificar a força de membros superiores. Existem diferentes descrições de protocolos para esta avaliação. Objetivo: Realizar uma revisão sistemática na avaliação da força de preensão em pessoas com DP. Métodos: A revisão foi realizada de acordo com as diretrizes PRISMA, nos bancos de dados eletrônicos PubMed, SciELO, LILACS e Scopus e registrada na PROSPERO (CRD42020190018). Análise quantitativa foi realizada utilizando a escala Newcastle-Ottawa. Vinte e sete artigos foram analisados. Resultados: O protocolo mais referenciado é o da Sociedade Americana de Terapeutas da Mão. O instrumento mais utilizado é o dinamômetro hidráulico. Dos dezesseis estudos que compararam a força de preensão entre pessoas com DP e sujeitos saudáveis, sete identificaram diferença estatisticamente significante. Nenhum artigo foi classificado como insatisfatório. Conclusão: Não é possível afirmar que a força de preensão manual está reduzida na DP quando comparada com pessoas saudáveis. Padronização de protocolo e de instrumento podem ajudar comparações entre resultados de diferentes estudos. Existem poucos estudos longitudinais, o que torna difícil compreender o que ocorre com a força de preensão com a evolução da doença.

Palavras-chave: Avaliação de incapacidade. Força de preensão manual. Doença de Parkinson.

Introduction

Parkinson's disease (PD) is a chronic degenerative illness that generates motor and non-motor symptoms. Among the motor symptoms, people with Parkinson's (PwP) have bradykinesia associated with muscle rigidity and/or resting tremor and from the moderate stage of the disease, postural instability is included.¹ In addition to these motor symptoms, PwP can report muscle weakness.² In PD, it is still investigated whether the weakness has a central or peripheral origin, primary or secondary to the disease.³ Results reported by Friedman and Abrantes² indicate that muscle weakness would not be associated with tremor or bradykinesia (motor signals that could influence muscle strength), but to fatigue. It should be noted that the results of the research by Friedman and Abrantes²

were subjective, once the results were obtained by participants self-reporting.

Studies have objectively investigated muscle strength in PD. Jordan et al.⁴ identified that PwP achieved the same level of maximum force production in the pinch test as healthy people. Koller and Kase⁵ observed that in wrist and knee extension and flexion, PwP produced less force when compared to control group participants. However, when statistical analysis was performed to compare strength between participants in the control group and the PD group, there was no statistically significant difference for handgrip strength (HGS).⁵ Other investigations identified that PwP have lower HGS than healthy people.⁶ Therefore, it is possible to observe in the literature a divergence regarding the ability of PwP to produce force. It should be noted that this includes HGS.

Hand muscle strength can be assessed with different forms of grip, namely: lateral pinch, palmar pinch, thumb pressure, ball of thumb pressure and the use of the palm of the hand plus five fingers, usually known as manual prehension. Handgrip is a motor action present in activities of daily living (ADL) such as cooking, writing and using the telephone. HGS is, therefore, an important valence for the execution of ADL with autonomy. HGS is a parameter used in addition to identifying upper limb strength. HGS is inversely correlated with important health outcomes such as risk of mortality, length of hospital stay, locomotion mobility, and risk of falls. It is noted, therefore, that the lower the HGS, the greater the risks for individuals to have outcomes that impair their health condition.

The maintenance or reduction of handgrip strength in PwP is unclear in the literature. 4-6 Measuring handgrip strength in PwP using a dynamometer is a valid measure. However, there is disagreement as to whether handgrip strength should be assessed using the average of the measurements obtained or a measurement corresponding to the maximum voluntary contraction. This systematic review was carried out to answer the following questions: 1) What methods are used to assess HGS in PD? 2) What are instruments to assess HGS? 3) Is HGS a predictor of PD? Therefore, the main objective of this review was to analyze the methods used in observational clinical studies to measure handgrip strength in PwP, including assessment protocols and instruments, comparison with the healthy population and results obtained in the retrieved studies.

Methods

The bibliographic research was conducted by searching for articles in electronic databases (NCBI PubMed, SciELO, Scopus and LILACS) and scientific journals published until June 2024. This format allows access to current works with deep understanding of the defined theme. 12 From the collection, a qualitative evaluation of the method applied in the studies was carried out.

In order to start the research public, the study was registered with PROSPERO, under registration CRD42020190018. The study followed the PRISMA guidelines (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols). This method allows systematizing the elaboration of systematic recommendations and meta-analyses and, subsequently, meets the principle of scientific reproducibility.

To outline the search for scientific articles, the PICO strategy was used, where P (patients) were PwP, I (intervention) was HGS assessment, C (comparison) was defined as PD group or apparently healthy people (control group), and O (outcome) the HGS. The following MESH descriptors were used: Hand Strength, Parkinson Disease, Parkinson's Disease; Portuguese descriptors: Força da Mão, Doença de Parkinson; Spanish descriptors: Fuerza de la Mano, Enfermedad de Parkinson; besides Handgrip, Grip Force, Fuerza de Prensión. The descriptors were grouped into group 1: hand strength, Parkinson disease; group 2: handgrip, Parkinson disease; group 3: grip force, Parkinson disease; group 4: hand strength, Parkinson's disease; group 5: handgrip, Parkinson's disease; group 6: grip force, Parkinson's disease; group 7: força da mão, doença de Parkinson; group 8: fuerza de la mano, enfermedad de Parkinson; group 9: fuerza de prensión, enfermedad de Parkinson.

The inclusion criteria adopted for the selection of articles were thematic correlation, articles that include individuals diagnosed with PD, articles in English, Portuguese or Spanish, full articles. Exclusion criteria were neurological diseases other than PD, articles in languages other than English, Portuguese, and Spanish; articles with abstracts only; animal studies; review articles; articles that assessed only manual pinch and/or digital force; therapeutic intervention articles; articles that performed only the kinematic evaluation; articles that only evaluated reach and grasp tasks.

Five selection phases were performed for the systematic review. In the first selection, the search took place in electronic databases to find articles for the present review with no date limit. In the second selection, the exclusion of repeated references was performed using the Mendeley software. In the third selection, all titles were read, and those relevant were selected for reading abstracts. In the fourth selection, the abstracts of all articles obtained in the third selection were read, and those relevant were chosen to full read. And in the fifth selection, the articles obtained in the fourth selection were read in full and the articles for the systematic review were chosen. Two researchers (RM and LM) were directed to identify, independently, the need or not for exclusion. In case of disagreement, a meeting was established with a third researcher (CLC) to determine the inclusion or exclusion of the article. Active searches for references were analyzed from the articles obtained in the fifth selection for the possible inclusion of new references that, perhaps, were not identified in the electronic databases. The design for the research and the storage of the identified articles were kept in a folder shared virtually between the researchers.

To perform a qualitative analysis of each study, the Newcastle Ottawa Scale (NCOS) was selected. The NCOS allows evaluating observational research through numerical scoring, with adaptations for cohort or cross-sectional studies. 14 Two researchers (RM and LM) performed their analyses, and, in case of differences in scores, meetings were held with a third researcher (CLC). Cross-sectional articles can be scored from 0 to 10, being classified as very good with a score of to 10, good from 7 to 8 points, satisfactory from 5 to 6 points, and unsatisfactory from 0 to 4 points. To assess the quality of longitudinal observational studies (cohort), the modified version of the NCOS was adopted, with a maximum of 9 points. The article was considered of high quality when it reached ≥ 7 points and of moderate quality when it reached between 5 and 6 points. 14,15

We analyzed the following variables: the HGS assessment instrument and the adopted protocol including individual positioning, grip adjustment, number of repeated measurements, contraction time, rest interval, the member evaluated and familiarization. The group of PwP and the control group (CG) were described according to the number of partici-

pants, sociodemographic (age and sex) and clinical (Hoehn and Yahr - H&Y) characteristics, and the statistical difference between them (p value), when reported in the study. The HGS results for each group were expressed as mean ± standard deviation, in the units of measurement Kg, KPa, Kgf, N or lbs.

Results

In the first search stage, 7,082 articles were identified, 5,332 were excluded, of which 5,331 were duplicates and one used the same information as a reference from a previous study by the same author, leaving 1,750 for the title reading stage. In the stage of read-

ing the titles, 1,579 references were excluded, remaining 171 for the abstracts reading. After reading the abstracts, 87 references were excluded.

In steps 2 and 3, exclusions occurred due to lack of thematic correlation of articles with the purpose of this literature review. In the fourth step, the remaining 84 articles were read in full, 59 being excluded for containing intervention, review, assessment of pinch grip and/or digital strength or kinematic assessment, and cohort that did not include individuals diagnosed with PD. An active search was also carried out in the references of the retained articles and two more studies was included that had not been reached with search strategies in the databases. Therefore, 27 articles remained for the qualitative analysis (Figure 1).16

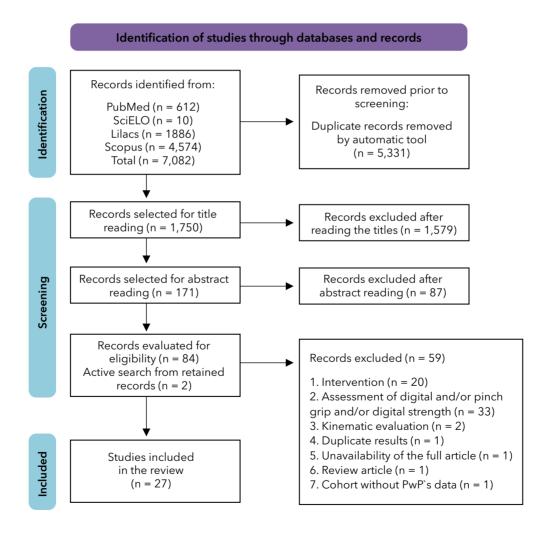


Figure 1 - Flowchart with steps for obtaining articles retained for systematic review.

Note: PwP = people with Parkinson's. Source: Page et al.16 For further information, visit: http://www.prisma-statement.org.

Regarding the method used to HGS measurement, eight articles¹⁷⁻²⁴ referenced the American Society Hand Therapists Instructions (ASHT),²⁵ while two articles^{26,27} used the Southampton protocol,²⁶ similar to the ASHT. The difference between the ASHT protocols and the Southampton protocol lies in the fact that the latter highlights the importance of standardizing encouragement during testing, describes the positioning of the lower limbs, number of attempts (three on each side) and score for use (strength maximum of six attempts performed by the participant).²⁶ The other 17 studies did not indicate reference as to the standard adopted for HGS measurement. 5,6,28-42 About the adopted body posture, 20 studies described that the evaluations were performed with the individuals sitting down, 6,17-^{24,26,27,29,30,32,34,36,37,39-41} while two articles evaluated the individuals standing^{31,33} and five articles did not describe the adopted posture. 5,28,35,38,42

For HGS measurement instruments, ten articles used manual hydraulic dynamometers, ^{18-23,26,33,36,42} six articles used digital dynamometers, ^{24,32,35,37-39} and one article used mechanical dynamometers. ³⁰ Five articles used dynamometers, but did not specify the type, that is, hydraulic, pneumatic, digital or mechanical. ^{5,27,31,34,40}

Three articles used custom electronic force sensors.^{6,28,41} Hoshiyama et al.⁶ used a plastic tube 15 centimeters long, 30 millimeters in diameter and 40 grams in mass, with a force transducer. Lafargue et al.²⁹ used two electronic sensors in a "U" format connected to a computer. Another two articles used the lowa Oral Performance Instrument (IOPI MEDICAL LLC, Woodinville, WA, USA), an instrument composed of a rubber bulb, which usually assesses tongue strength outcomes.^{17,28}

Regarding HGS analysis, 16 articles compared the results of apparently healthy people (CG) and PwP.^{5,6,17-19,23,27-29,33,34,37,39-42} Of these 16 studies, seven pointed out that the CG participants had higher HGS than the PwP.^{6,17,27,37,39,40,42} Toktas et al.¹⁹ indicated statistically significant difference only for the right side between groups (CG and PwP), while six studies did not identify statistically significant difference in HGS between CG and PwP participants.^{5,18,28,29,33,41} Two articles did not describe the p-value in the study.^{23,34}

As for disease staging, which can vary from 1 to 5 according to the H&Y scale, ^{37,38} eight references only included PwP up to stage3, ^{5,6,18,21,27,29,30,42} seven references included up to stage 4.^{20,23,24,28,33,35,37} Only

Roberts et al.,²⁶ Paz et al.,²² and Salmon et al.⁴⁰ did not use H&Y 5 as an exclusion criterion. Six studies did not explain whether the clinical stage was used as an inclusion or exclusion criterion.^{17,19,26,32,34,36} The H&Y staging is not applicable as participation criteria for the studies by Arazi et al.,³⁹ Daniels et al.,⁴¹ and Gustafsson et al.,³¹ since this is a prediction cohort for the development of PD, therefore, PwP could not be included at the beginning of the collections.

As for the half-body evaluation, 14 articles evaluated both sides, 5,18-24,26,29,36,39,42 and eleven articles evaluated only the dominant side. 6,17,27,30-32,34,37,38,40,41 Two articles did not describe the evaluated dominance.33,35 Solomon et al.28 allowed individuals to choose the side to be tested. Of the 14 articles that evaluated both sides (right and left), eight made a comparison between them.^{5,18-21,23,26,29} Of these, only three pointed out that they had not identified a statistically significant difference between right and left sides of PwP.5,19,20 The studies by Lafarque et al.,29 Roberts et al., 26 Silva et al., 18 Villafañe et al., 23 Clael et al., 21 Kilinc et al.,²⁴ Arazi et al.,³⁹ Wong-Yu et al.⁴² did not present a comparative analysis between the HGS values of the sides. Vetrano et al.³⁶ and Paz et al.²² did not present HGS values of each side and the comparison between them. Koller and Kase⁵ observed that there was no statistically significant difference between the most affected side and less affected side by PD in individuals with hemiparkinsonism. However, the authors identified a statistically significant difference between PwP with unilateral tremor and unilateral rigidity, and individuals with unilateral tremor produced lowest HGS.⁵ Kilinc et al.²⁴ showed that PwP with postural tremor present lowest HGS, for both sides, when compared with PwP without postural tremor.

On the measurement properties (validation, reliability) of the HGS assessment, Villafañe et al.²³ evaluated the reliability of the HGS test in PwP and identified an excellent test-retest grade for both the dominant side (ICC = 0.97; p = 0.001) and the non-dominant side (ICC = 0.98; p = 0.001) in PwP, as well as for dominant (ICC = 0.99; p = 0.001) and non-dominant (ICC = 0.99; p = 0.001) CG. Silva et al.¹⁸ validated the sphygmomanometer and its reproducibility for assessing HGS in PwP. The authors identified an adequate degree of validation for the modified sphygmomanometer test and excellent reliability for the handgrip test in PwP.

Paz et al.²² investigated the correlation between HGS and the freezing phenomenon, in addition to items from section III of the UPDRS (motor exam). After the tests, the authors concluded that, only for the PwP group with freezing, HGS was a predictor of motor worsening. Kilinc et al.²⁴ examined the association between HGS and quality of life of PwP by using the Parkinson's Disease Quality of Life Questionnaire (PDQ-39). The authors showed a moderate and negative

correlation between HGS and PDQ-39 (total score and sub-parameters mobility, ADL, emotional well-being, stigma and cognition) indicating the greater HGS, the greater quality of life in PwP.²⁴

Tables 1 (observational studies) and 2 (cohort studies) contain the specification of the articles retained for analysis considering NCOS classification of the studies, instrument used to evaluate the HGS, adopted protocol, sample and results obtained in the studies.

Table 1 - Analysis of observational studies retained for the systematic review

Studies	NCOS	Instrument	Protocol	Sample	Result	
Koller and Kase (1986), ⁵ USA	6 Dynamometer (not specified)		Posture: NS; Hold time: NS; Adjustment: NS; Measurement: average of 2 trials; Member: both; Interval: NS; Familiarization: NS	PwP: 21 M (62.5 years) standard deviation not mentioned CG: 21 M (62.5 years) standard deviation not mentioned H&Y: 1-2	PwP R vs CG R: (72 ± 3 vs 75.3 ± 3); PwP L vs CG L: (79.1 ± 2.6 vs 77.7 ± 2.9) p: reports no statistically significant difference. PwP affected side vs unaffected side: (71.8 ± 3.7 vs 76.5 ± 4.2) p: reports no statistically significant difference PwP unilateral tremor vs PwP unilateral rigidity: (66.2 ± 3.8 vs 80.5 ± 4.4) p < 0.001 Unit of measurement not specified	
Hoshiyama et al. (1994), ⁶ Japan	7	Plastic tube with a transducer (diameter 30 mm, length 15 cm, mass 40 g)	Posture: sitting, looking horizontally, arm at the side of the body, forearm fixed, with the possibility of performing 45 degrees of elbow flexion; Hold time: NS; Setting: NS; Measure: plateau of 20 attempts at medium and maximum contractions; Member: dominant right; Interval: NS; Familiarization: yes	PwP: 11F/9M (57.4 ± 8.9 years) CG: 9F/11M (59.3 ± 11.51 years) p: NS H&Y: 1.95 ± 0.83	Mean contraction (N): PwP vs CG (6.1 ± 1.9 vs 6.6 ± 1.4); p: NS MVC (N): PwP vs Control (10.8 ± 2.3 vs 13.6 ± 3.5); p < 0.02	
Solomon et al. (2000), ²⁸ USA	7	Iowa Oral Performance Instrument (IOPI)	Posture: NS; Hold time: NS; Adjustment: palm of the hand; Measure: greater than 3 attempts; Member: preferred; Interval: NS; Familiarization: NS	PwP: 4F/12M (54 - 84 years) CG: 4F/12M paired with PG for sex, age, weight and height p: NS H&Y: 2.78 ± 0.73	PwP vs CG (kPa): (129.8 ± 28.3 vs 127.9 ± 27.9) p = 0.362	
O'Day et al. (2005), ¹⁷ USA	6	Iowa Oral Performance Instrument (IOPI)	Posture: sitting, shoulder adducted, elbow at 90 and forearm and wrist neutral ASHT; Hold time: 1 second; Adjustment: palm of the hand; Measure: greater than 3 maximum attempts; Member: dominant; Interval: 60 seconds; Familiarization: 1 submaximal hold	PwP: 10M (52 - 79 years) CG: 10 age-matched to PwP H&Y: NS	PwP vs CG (kPa): (108.68 ± 33.01 vs 136.34 ± 22.65) p = 0.0358	

Table 1 - Analysis of observational studies retained for the systematic review (continued)

Studies	NCOS	Instrument	Protocol	Sample	Result	
Lafargue et al. (2008), ²⁹ France	6	Two "U" shaped electronic sensors attached to the computer	Posture: sitting, with the forearm supported; Hold time: NS; Setting: NS; Measurement: MVC - 2 attempts; 10, 20, 30 and 40% MVC: 4 trials for each condition; Limb: both (more and less affected by the disease, dominant side); Interval: 10, 20, 30 and 40% MVC: 1 min. Familiarization: NS	PwP: 4F/4M (53.4 ± 14 years) CG: 8 (55.4 ± 12.7 years) matched for age, sex and handedness with PwP p: NS H&Y: 2.1 ± 3.0	MVC PwP E vs D (N): (276 ± 86 vs. 256 ± 112);	
Guimarães e Barbosa (2013), ³⁰ Brazil	7	Mechanical dynamometer (Takei Kiki Kogyio TK 1201)	Posture: sitting, with the arm extended at the side of the body; Hold time: NS; Setting: NS; Measurement: maximum strength of two attempts; Member: dominant; Interval: 1 minute; Familiarization: NS	PwP: 13F/23M (65.2 ± 11.9 years) Mild PwP: 19 (63.1 ± 10.3 years) Moderate PwP: 17 (67.6 ± 13.4 years) p = 0.259 H&Y: 1-3	Mild PwP vs Moderate PwP (kg): (31.2 ± 11.6 vs 26.6 ± 10.1) p = 0.206	
Roberts et al. (2015), ²⁶ England	6	Hydraulic dynamometer (JAMAR®)	Posture: Southampton protocol - sitting, forearm supported, except for the wrist; Hold time: NS; Adjustment: second position; Measure: greater than 3 attempts; Member: both; Interval: NS; Familiarization: NS	PwP M: 34 (71.3 ± 8.0 years) PwP F: 23 (72.6 ± 7.6 years) p = 0.53 H&Y M: 2.0 ± 2.3 H&Y F: 2.5 ± 2.3 p = 0.14	PwP M vs F (kgf): (37.9 ± 9.4 vs 22.1 ± 8.6) p < 0.0001	
Silva et al. (2015), ¹⁸ Brazil	7	Hydraulic dynamometer (JAMAR®) and aneroid sphygmomanometer. Pre-inflated to 80 mm Hg	Posture: ASHT - sitting, adducted shoulder and in neutral rotation. Elbow at 90, forearm neutral and wrist slightly extended (this is described in the article); Holding time: dynamometer: NS; sphygmomanometer: 5 seconds; Adjustment: second position (dynamometer); Measurement: average of 3 attempts; Members: both; Interval: 20 seconds between trials for the same hand, 3 minutes to perform the assessment on the opposite hand; Familiarization: 1 attempt	PwP: 14F/10M (65.5 ± 6.2 years); CG: 15F/11M (63.4 ± 7.2 years); p: NS H&Y: 2 (1-3)	Validated sphygmomanometer (intra- and inter-rater reliability, minimal detectable change) for PwP PwP (mmHg) R and L (does not describe the average of the three trials) Between PwP and CG there is no statistical difference (p > 0.05) for handgrip strength by sphygmomanometer It presents the average of each of the three attempts for PwP and CG It does not show the average dynamometer values for PwP and	

Table 1 - Analysis of observational studies retained for the systematic review (continued)

Studies	NCOS	Instrument	Protocol	Sample	Result	
Barichella et al. (2016), ³² Italy	(DynEx; Akern/MD Systems) (DynEx; Akern/MD Systems) (DynEx; Akern/MD Systems) (DynEx; Akern/MD Systems) (DynEx; Akern/MD adducted shoulder and in neutral rotation, elbow at 90, forearm and wrist in neutral position; Hold time: NS; Setting: -NS; Measurement: average of 3 attempts; Member: dominant; Interval: NS; Familiarization: NS t al. (2016), 27 5 Dynamometer (Almedic, Posture: protocol PwP: 12F/11M (66 ± 8.6)		adducted shoulder and in neutral rotation, elbow at 90, forearm and wrist in neutral position; Hold time: NS; Setting: -NS; Measurement: average of 3 attempts; Member: dominant; Interval: NS;	Other Parkinsonian syndromes: 129 Age: NS;	PwP + other Parkinsonian syndromes (kg): 20.4 ± 9.4	
Jones et al. (2016), ²⁷ Canada			PwP M vs F (kg) (38.9 vs 24.6) CG M vs F (kg) (47.4 vs 33.3); p = 0.02 (referring to the comparison between groups, regardless of gender)			
Toktas et al. (2016), ¹⁹ Turkey	7	Hydraulic dynamometer (Fabrication Enterprises Inc., White Plains, New York, USA)	Posture: sitting, adducted shoulder, elbow at 90 and forearm and wrist neutral ASHT; Hold time: 3 seconds; Adjustment: second smallest hand position; Measurement: average of three attempts; Member: both; Interval: NS; Familiarization: NS	PwP: 11F/35M (65.5 ± 9.3); CG: 10F/30M (63.4 ± 9.9); p = 0.689; H&Y: NS	PwP R vs L (unit: NS): (27.3 ± 8.2 vs 26.7 ± 8.3), p = 0.287 Control R vs L: (32.5 ± 11.7 vs 30.8 ± 12.3), p = 0.001 PwP R vs CG R, p = 0.014 PwP L vs CG L, p = 0.059	
Villafañe et al. (2016), ²³ Italy	9	Hydraulic dynamometer (JAMAR®)	Posture: sitting, adducted shoulder, elbow at 90 and forearm and wrist neutral ASHT; Hold time: 3 seconds; Adjustment: second position; Measurement: average of 3 maximum grips; Member: both; Interval: 1 minute; Familiarization: 2 to 3 attempts	PwP: 8F/7M (69.5 ± 8.6 years) CG: 9F/6M (67.5 ± 10.2 years) p = 0.49 H&Y: 1.9 ± 0.9	Validated dynamometer (dominant and non- dominant side) for PwP PwP R vs L (kgf): (25.3 ± 9.9 vs. 24.4 ± 10.3) CG R vs L (kgf): (25.9 ± 9.9 vs 24.4 ± 10.6) p: NS	
Alomari et al. (2018), ³³ USA	8	Hydraulic dynamometer	Posture: standing position, slightly bent at the waist, head in intermediate position facing forward, elbow at 90°, shoulder and wrist at 0°; Hold time: NS; Adjustment: middle portion of the middle finger at a right angle; Measurement: average of 3 attempts; Member: NS; Interval: NS; Familiarization: NS	PwP: 29 (56.9 ± 13.4 years) CG: 30 (56.3 ± 12.6 years) p = 0.460 H&Y: 2.4 ± 0.7	PwP vs CG (kg): (28.4 ± 13.1 vs 31.9 ± 10.7), p = 0.5	

Table 1 - Analysis of observational studies retained for the systematic review (continued)

Studies	NCOS	Instrument	Protocol	Sample	Result	
Falvo et al. (2018), ³⁴ USA	7 Dynamometer (not specified whether hydraulic or digital)		Posture: sitting, hand and forearm in neutral position; holding time: 3 to 5 seconds; Setting: NS; Measure: 5 sets of 30 grips at 70% maximal voluntary contraction (MVC) every 5-8 seconds; MVC: Mean of 3 attempts; Member: dominant right; Interval: 2 minutes; Familiarization: "brief"	PwP: 2F/8M (68.1 ± 8.4 years) CG: 2F/8M (68.8 ± 4.6 years) p: NS H&Y: 2.10 ± 0.32	Block 1: PwP off vs on (kg): (12.8 ± 5.8 vs 12.1± 6.1); CG (kg): 15 ± 6.1 Block 2: PwP off vs on (kg): (12.7 ± 5.3 vs 11.9 ± 6.7); CG (kg): 15.3 ± 5.4 p: NS	
Vetrano et al. (2018), ³⁶ Italy	7	Hydraulic dynamometer (North Coast Hydraulic Hand Dynamometer	Posture: sitting, wrist neutral and elbow at 90; Hold time: NS; Setting: NS; Measure: highest value of two attempts; Member: both; Interval: NS; Familiarization: NS	PwP M: 130 (73.3 ± 7.4 years) PwP F: 80 (74.4 ± 6.6) p: NS H&Y: NS	Number of people with low handgrip strength M: 97(75%) < 30 kg F: 64(80%) < 20 kg M: 75(58%) < 26 kg F: 47 (59%) < 16 kg	
Candan and Özcan, (2019), ³⁵ Turkey	5	Digital dynamometer (Fabrication Enterprises, Inc., White Plains, NY)	Posture: NS; Hold time: NS; Setting: NS; Measurement: NS; Member: NS; Interval: NS; Familiarization: two attempts	Posture: NS; PwP: 108 (69.67 ± 6.62 Hold time: NS; years) Setting: NS; H&Y: 1.89 ± 0.81 Member: NS; Interval: NS; Familiarization: two		
Clael et al. (2020), ²¹ Brazil	6	Hydraulic dynamometer (JAMAR®)	Posture: protocol adapted from ASHT; Elbow at 90; It does not mention what the adaptation was; Hold time: NS; Adjustment: hand comfort; Measure: maximum value of 3 attempts; Member: both; Interval: NS; Familiarization: NS	PwP: 29 (67.03 ± 9.47 years) H&Y: 2.03 ± 0.6	PwP R vs L (kgf): (2.62 ± 1.47 vs 27.03 ± 1.46) p: NS	
Paz et al. (2021), ²² Brazil	8	Hydraulic dynamometer (JAMAR®)	Posture: sitting, shoulder adducted, elbow at 90 and forearm and wrist neutral ASHT; Hold time: up to 10 seconds; Adjustment: second space; Measure: greater value of 3 maximum grips; Member: both; Interval: 20 seconds; Familiarization: NS	PwP: 103; FOG (65.94 ± 11.16 years), NFOG (64.52 ± 10.78 years), p = 0.512 H&Y: FOG (2.79 ± 0.78), NFOG (2.00 ± 0.82), p < 0.001	PwP FOG vs NFOG (kgf): (23.15 ± 8.92 vs 25.67 ± 10.00) p = 0.179	
Ingram et al. (2021), ³⁷ Australia	8	Digital dynamometer (JAMAR®)	Posture: sitting, elbow at 90; Hold time: NS; Adjustment: NS; Measure: greater value of 3 grips; Member: dominant; Interval: NS; Familiarization: NS	PwP: 2F/22M [68.6 (47 - 87) years] H&Y: 2.7 (1 - 4) CG: 24F/44M [68.5 (46 - 87) years]	PwP on vs CG (kg): (29.2 ± 11.1 vs 37.8 ± 12.2), p < 0.001 PwP off vs CG (kg): (29.4 ± 11.1 vs 37.8 ± 12.2), p < 0.01	

Table 1 - Analysis of observational studies retained for the systematic review (continued)

Studies	NCOS	Instrument	Protocol	Sample	Result	
Wong-Yu et al. (2022), ⁴² China	9 Hydraulic dynamometer (JAMAR®)		Posture: NS; Hold time: NS; Adjustment: NS; Measure: greater value of 2 grips; Member: both; Interval: NS; Familiarization: one practice trial	PwP: 87F/78M (61.5 ± 8.1) H&Y: 2.4 ± 0.3 CG: 51F/31M (62.0 ± 10.2)	PwP vs CG with dominant hand (kg): (11.4 \pm 2.6 vs 14.6 \pm 2.0), p < 0.001 PwP vs CG with non- dominant hand (kg): (10.5 \pm 2.5 vs 13.8 \pm 1.8), p < 0.001	
Kilinc et al. (2023), ²⁴ Turkey	7	Digital dynamometer (JAMAR®)	Posture: sitting, elbow flexed at 90°, shoulder adducted, forearm and wrist neutral ASHT; Hold time: NS; Setting: NS; Measure: average of three measurements; Member: both; Interval: NS; Familiarization: NS	PwP: 36F/16M (67,8 ± 8,87 years) H&Y: 2 - 4	PwP R with vs without postural tremor -forehand (kg): $(48.63 \pm 18.6 \text{ vs} + 63.28 \pm 19.62)$, $p = 0.012$ PwP L with vs without postural tremor - forehand (kg): $(48.96 \pm 21.34 \text{ vs} + 62.77 \pm 19.32)$, $p = 0.016$ PwP R with vs without postural tremor - hand (kg): $(47.58 \pm 17.3 \text{ vs} + 63.34 \pm 19.88)$, $p = 0.008$ PwP L with vs without postural tremor - hand (kg): $(48.90 \pm 19.83 \text{ vs} + 62.41 \pm 20.17)$, $p = 0.023$	
Pereira et al. (2023), ³⁸ Brazil	7	Digital dynamometer (JAMAR®)	Posture: NS; Hold time: NS; Setting: NS; Measure: average of three maximum grips; Member: dominant; Interval: NS; Familiarization: NS	PwP: 27F/33M (≥ 60 years) H&Y: 1 - 4	PwP with dynapenic abdominal obesity vs obesity or dynapenia (kgf): 14.3 (12.2 - 15.83) vs 21.1 (18.4 - 23.87), p = 0.001	
Arazi et al. (2023), ³⁹ Iran	9	Digital dynamometer (Saehan, model SH5003, Saehan Co, South Korea)	Posture: sitting, hand flexed at 90° along the vertical axis, wrists in slight extension; Hold time: NS; Setting: NS; Measure: average of three measurements; Member: both; Interval: 30s; Familiarization: was taught how to use a dynamometer	PwP M: 117 (61.66 ± 11.28 years) H&Y: 2.31 ± 0.69 CG M: 156 (61.86 ± 6.29 years)	PwP R vs CG R (kg): (30.71 ± 9.85 vs 32.85 ± 6.07), p = 0.02 PwP L vs CG L (kg): (29.85 ± 9.46 vs 31.73 ± 4.86), p = 0.03	
Salmon et al. (2023), ⁴⁰ Australia	7	Handheld dynamometer (Saehan)	Posture: sitting; Hold time: NS; Setting: NS; Measure: average of three maximum grips; Member: dominant; Interval: NS; Familiarization: NS	PwP: 10F/20M (69 ± 8 years) H&Y: 1.1 ± 0.7 CG: 9F/15M (69 ± 6 years)	PwP vs CG (N): (286 ± 69 vs 359 ± 66), p< 0.001	
Daniels et al. (2024), ⁴¹ USA	6	Force transducer (SM-50, Interface Inc., Scottsdale, AZ, USA)	Posture: sitting, elbow supported by an armrest; Hold time: 3s; Setting: NS; Measure: greater value of 3 maximal isometric grips contractions; Member: dominant or more affected; Interval: 60s; Familiarization: NS	PwP: 6F/16M (66.5 ± 11.3 years) CG: 6F/11M (69.3 ± 7.7 years) H&Y: NS	PwP vs CG (N): (370.7 ± 133.0 vs 373.3 ± 126.3), p = 1.0	

Note: ASHT = American Society of Hand Therapists; H&Y = Hoehn and Yahr; NCOS = Newcastle-Ottawa Scale (0 to 10 points); PwP = people with Parkinson's; F = female; M = male; L = left; R = right; CG = control group; PG = group of people with Parkinson's disease; FOG = freezing group; NFOG = non-freezing group; NS = not stated; p = p-value.

Table 2 - Analysis of retained cohort studies for the systematic review

Studies	NCOS	Instrument	Protocol	Sample	Result PG (N): 615 ± 98	
Gustafsson et al. (2015), ³⁰ Sweden	7	Dynamometer (model not specified)	Posture: standing, arm vertical and elbow flexed at 90°; Hold time: NS; Setting: NS; Measure: three attempts. If the third was greater, the test would continue until the value stopped increasing; Member: dominant; Interval: NS; Familiarization: NS	n = 1,317,713 (18.3 ± 0.8 years)		
Combs-Miller and Moore (2019), ²⁰ USA	Miller and 7 Hydraulic dynamometer Postu 2019), ²⁰ (JAMAR®) adduct elbow at 9 and wrist Hold t se Adjustn pr Measure of 3 ma normaliz		Posture: sitting, adducted shoulder, elbow at 90 and forearm and wrist neutral ASHT; Hold time: 3 to 5 seconds; Adjustment: second position; Measurement: mean of 3 maximum grips normalized with body weight; Member: both; Interval: NS; Familiarization: NS	PG: 74 (66.7 ± 8.4 years) H&Y: NS	Dominant vs non-dominant (lbs): 0.46 ± 0.13 vs 0.43 ± 0.12; p > 0.05	

Note: ASHT = American Society of Hand Therapists; H&Y = Hoehn and Yahr; NCOS = Newcastle-Ottawa Scale (0 to 9 points); PG = group of people with Parkinson's disease; lbs = pounds; N: Newton; NS = not stated; p = p-value.

Table 3 details variables that can impact the results of strength tests, such as body posture, contraction time, instrument adjustment, HGS analysis, evaluated upper limb, interval between attempts and familiarization with the strength test protocol. Informing how such variables are controlled also contributes to the interpretation of the results obtained, as well as to the reproducibility of the applied methods. Of the 27 studies analyzed, only three mentioned how all these variables were applied during collections. 17, 18,23

Among the indicated variables, the HGS analysis (if one attempt, if maximum value reached, if average value of several attempts) was the most described, appearing in 26 of the 27 articles. Only Candan and Özcan³⁵ did not describe whether, for data analysis, they used the maximum value or the average of attempts and how many attempts were performed by the participants. The body posture adopted was described by 81.5% (n = 22) of the articles. Only Koller and Kase,⁵ Candan and Özcan,³⁵ Solomon et al.,²⁸ Wong-Yu et al.,⁴² and Pereira et al.,³⁸ did not indicate the participants' position for the HGS assessment. The grip time was indicated by 29.3% (n = 8) of the articles.^{17-20,22,23,26,33} The instrument adjustment was described in 42.1% of

the articles that used a manual dynamometer. $^{18-23,25,32}$ Hoshiyama et al., 6 Solomon et al., 28 O'Day et al., 17 Lafargue et al., 29 and Daniels et al., 41 used instruments in which there is no application of grip adjustment for different hand sizes. The interval between attempts was reported in 37% (n = 10) studies. 17,18,22,23,26,28,29,33,39,41 Familiarization with the HGS test was the least frequently reported information in the studies, being presented in only 29.6% (n = 8) of the articles analyzed. 6,17,18,23,33,34,39,42

Familiarization was the least addressed and without standardization element between studies. Hoshiyama et al.⁶ only indicated that it was performed, without indicating the protocol. O'Day et al.¹⁷ guided the performance of a submaximal grip. Silva et al.¹⁸ performed a previous attempt. Arazi et al.³⁹ taught the participants how to use a dynamometer to measure maximum HGS. Villafañe et al.²³ allowed two to three attempts before the execution was counted. Wong-Yu⁴² allowed one practice trial before the test trials. Candan and Özcan³⁵ reported that a brief familiarization was performed. The low number of reports and the lack of standardization make it difficult to analyze whether familiarization generates bias in the results obtained, either for improvement or for worsening.

Table 3 - Analysis of the presence or absence of information regarding handgrip strength (HGS) in the retained studies for systematic review

Studies	Posture	СТ	Adjustment	HGSA	ULS	Interval	FAM
Koller and Kase (1986), ⁵ USA							
Hoshiyama et al. (1994), ⁶ Japan							
Solomon et al. (2000), ²⁸ USA							
O'Day et al. (2005), ¹⁷ USA							
Lafargue et al. (2008), ²⁹ France							
Guimarães and Barbosa (2013), ³⁰ Brazil							
Gustafsson et al. (2015), ³¹ Sweden							
Roberts et al. (2015), ²⁶ England							
Silva et al. (2015), ¹⁸ Brazil							
Toktas et al. (2016), ¹⁹ Turkey							
Jones et al. (2016), ²⁷ Canada							
Villafañe et al. (2016), ²³ Italy							
Barichella et al. (2016), ³² Italy							
Alomari et al. (2018), 33 USA							
Falvo et al. (2018), ³⁴ USA							
Vetrano et al. (2018), ³⁶ Italy							
Candan and Özcan. (2019), ³⁵ Turkey							
Combs-Miller and Moore (2019), ²⁰ USA							
Clael et al. (2020), ²¹ Brazil							
Paz et al. (2021), ²² Brazil							
Ingram et al. (2021), ³⁷ Australia							
Wong-Yu et al. (2022), ⁴² China							
Kilinc et al. (2023), ²⁴ Turkey							
Pereira et al. (2023), ³⁸ Brazil							
Arazi et al. (2023), ³⁹ Iran							
Salmon et al. (2023), ⁴⁰ Australia							
Daniels et al. (2024), ⁴¹ USA							

Note: CT = contraction time; GSA = handgrip strength analysis; ULS = upper limb side; FAM = familiarization; green = information reported in the study; red = information missing in the study; yellow = variable analysis is not applicable due to the used instrument.

Of the articles retained for the systematic review, only two are cohort. Gustafsson et al.³¹ followed up with 1,317,713 individuals. The aim of the study was to identify whether HGS at 18 years old would be a predictor of PD. Thirty years after collection, it was identified that 977 participants were diagnosed with PD and that they had lower HGS. The study reached the conclusion that there was motor decline 30 years before the clinical

diagnosis of PD. Combs-Miller and Moore²⁰ performed a 2-year follow-up with PwP to identify whether HGS would be a predictor of motor decline caused by the disease. According to the results, this variable was not a predictor, unlike others, such as exercise habits.

According to the NCOS analysis of cross-sectional studies, only Villafañe et al.,²³ Wong-Yu et al.⁴² and Arazi et al.³⁹ rated very good (9 points). Of the others, 14 arti-

cles were classified as good (7 to 8 points), 5,6,18,19,22,24, 29, 31-33,35,37,38,40 while eight were classified as satisfactory (5 to 6 points). 17,21,25-28,34,41 No article was classified as unsatisfactory (0 to 4 points). Of the two longitudinal observational studies, both were considered of high quality, as they achieved 7 points. 20,30

In general, the articles obtained a good classification, considering that none was considered unsatisfactory, based on the NCOS. However, there are gaps that, once filled, would help the interpretation and reproducibility of methods and results, as shown in Table 3.

Discussion

The present study aimed to conduct a systematic review of HGS in people with PD to answer the following questions: 1) What methods are used to assess HGS in PD? 2) What is the reliability/validity of the instruments to test the HGS? 3) What are the advantages/disadvantages of using the HGS test in clinical practice? 4) Is HGS a predictor of PD?

Of the twenty-two studies that described the participants position for the HGS assessment, 33.4% adopted the position recommended by the ASHT. 17-24 The ASHT guides a body position to be standardized during the evaluation, namely: sitting, shoulder adducted and in neutral rotation, elbow flexed at 90 degrees and forearm and wrist in neutral position.²⁵ Few studies retained for the systematic review adopted the Southampton protocol (7.4%).^{26,27} It proposes that the assessment occurs in a chair that allows forearm support and that there be a standardization of encouragement given to the assessed person with the following words: "I want you to squeeze as hard as you can for as long as you can until I say stop. Squeeze, squeeze, squeeze, stop (when the needle stops rising)."26 The encouragement given during maximal evaluations can affect the final result. Jung and Hallbeck⁴⁵ identified that the use of verbal encouragement contributed positively to peak strength during the handgrip test.

Although most studies describe the positioning of the participants, some do not. Body posture can impact the HGS result. Xu et al.⁴⁶ determined that the HGS was higher in the standing position when compared to the sitting position. However, they did not identify a statistically significant difference when the

elbows were flexed at 90 degrees or fully extended while the participants were seated. In a study conducted by our research group, we verified HGS in PwP in three different positions, namely: 1) Sitting posture with flexed elbow (ASHT); 2) Standing posture with extended elbow; 3) Standing posture with flexed elbow. Our study did not show statistically significant differences in the measurement of HGS for PD in the three different positions (unpublished data).

The evaluated limb varied across studies. PD is characterized by unilateral motor involvement and, with the progression of the disease, both sides will be affected.1 However, only 15% of the studies compared the HGS between the two hands of PwP. The analysis between the sides can help in decision-making about treatment in clinical practice as well as to elucidate whether the HGS is related to the motor alteration that occurs due to PD. Cooperation would be interesting to carry out a multicenter study to enable the analysis of the HGS considering the side most affected by the disease, ensuring a reduction in bias risk by gender, age group and clinical stage of PD. Multicentric studies allow for the recruitment of more people, making it possible to have a more representative sample of the population with PD.

As for the instruments used, the manual hydraulic dynamometer Jamar® has an excellent grade in the test-retest of HGS in PwP, being, therefore, an adequate tool for this evaluation. The hydraulic dynamometer, as well as the digital dynamometer, has the advantage of being applicable in clinical practice due to the relative low cost, reliability and reproducibility. Solomon et al. and O'Day et al. The used the lowa Oral Performance Instrument (IOPI), which has been validated for HGS in healthy people. However, there are no validation or reliability studies for HSG in PwP. Silva et al. validated the modified sphygmomanometer test for the assessment of HGS in PwP, presenting a low-cost alternative that is recurrently used by health professionals.

Hoshiyama et al.,⁶ Lafargue et al.,²⁹ and Daniels et al.⁴¹ used electronic dynamometers with force transducers associated with a computer, characterizing a laboratory research. Because they are devices with more complex technology, they may present greater difficulty in accessing manufacturers and distributors, higher cost, and greater difficulty in application due to the use of specific equipment and programs. Labora-

tory research is important to investigate information that common instruments are not able to obtain, such as the force curve applied during HGS, and help to deepen knowledge, without necessarily being applied in practice.

The instruments variety can result in different force values, with different measurement units (kgf, Newton, Kg.Pa), which makes it difficult to compare studies that used different tools. The standardization of the instrument used, with the consequent standardization of the measurement units, may help professionals from different countries to interpret and compare the results obtained by each study.

The instrument setting also varied among the studies. Despite the ASHT guiding dynamometer adjustment in the second adjustment space, 25 some articles did not follow this guideline. A larger or smaller grip can change the resistance arm, the power arm and, consequently, the HGS. Hamilton et al. 49 observed that, when performing the HGS test with healthy people in the five possible adjustment spaces, the individuals had the greatest force production in the second adjustment. PwP may present the striatal hand phenomenon, characterized by flexion of the metacarpophalangeal joint, 43 which may make handgrip difficult in different positions.

Based on the recruited studies, it is not possible to state that PwP have lower HGS compared to healthy people. Of the studies retained for systematic review that compared PwP with CG, 43.7% (n = 7) identified that PwP had statistically lower HGS than CG, while 37.5% (n = 6) did not observe a statistically significant difference between groups. This fact shows that muscle weakness is not necessarily a characteristic of PD, although PwP present this complaint.² Gustafsson et al.31 identified low HGS in people who were diagnosed with PD 30 years after the assessment, while Combs-Miller and Moore²⁰ did not identify HGS as a predictor of motor decline. Therefore, it is not yet clear in the literature whether muscle weakness, when as-sessed by hand grip, is a motor sign of PD. More cohort studies are needed to better understand whether HGS is correlated with the development of PD.

The NCOS allows articles evaluation through three domains, namely: selection, comparability and results. In the field of participant selection, only Paz et al.²² were scored for sample size and its mathematical

justification. The sample calculation is important to understand the representation of the results in the studied population. Despite PD being the second most common neurodegenerative disease in the world,⁵¹ recruiting PwP to participate in research may not be simple, due to the motor fluctuation characteristic of the disease⁵² and possible locomotion difficulties, often dependent on a caregiver.⁵³ The difficulty in recruitment generates limitations to understand the HGS in the clinical subtypes of the disease, tremordominant, rigid-akinetic and postural instability-gait disorder,⁵⁴ and in the clinical stages of the H&Y scale, since it would require the inclusion of more individuals for the ideal representation of each subgroup.

H&Y staging allows understanding in which stage of PD the person is. Elaborated in 1967,43 it was modified and included stages 1.5 and 2.5,44 where: stage 1 indicates people with only unilateral involvement; stage 1.5, unilateral and axial involvement; stage 2, bilateral disease without balance deficit; stage 2.5, mild bilateral disease, with recovery on the push test; stage 3, mild to moderate disease, with some postural instability and still able to live independently; stage 4, severe disability, still able to walk or stand unassisted; and stage 5, confined to bed or wheelchair unless assisted. Only Guimarães and Barbosa³⁰ compared the HGS between PwP in stages up to 1.5 (mild), 2 and 3 (moderate), but they did not observe a statistically significant difference between the groups, indicating that with the progression of the disease, until the stage 3, it is possible that no loss of HGS will occur. In a recent publication, Salmon et al.⁵⁵ identified that PwP in the early stage of PD (H&Y 1) had 20% less HGS than apparently healthy people. This result reinforces the importance of investigating the relationship between the clinical status of PwP and muscle strength.

One fourth of the studies excluded PwP with H&Y 4 or 5 from recruitment. 5,6,18,21,27,29,30,42 This fact reinforces the difficulty of accessing PwP in a more severe state of the disease. However, as the HGS test is of low motor complexity and can be performed sitting down, an effort in future research to increase knowledge about HGS in advanced stages of PD would be interesting. It is possible to observe the same scarcity of information in the literature on therapeutic intervention studies. The way in which the articles presented the H&Y studied groups value is also noteworthy.

Goetz et al.⁵⁷ advised that the best way to analyze the H&Y of the PwP group would not be through the average of the participants, but through the median. Only Silva et al.¹⁸ presented the median value.

Familiarization with HGS assessment, regarding form, volume, and intensity, is hardly mentioned in articles on the subject, whether in PwP or healthy population. Mehmet et al.⁵⁸ identified the description of warming up in only two articles out of 34 on HGS for the elderly, while the present study identified the description of familiarization in only eight out of 20 articles. The effect of familiarization on the test result is still not a consensus in the literature and may be biased by the effect of learning to perform or muscle wasting in the main evaluation phase. Wallerstein et al.⁵⁹ observed that three familiarization sessions generated a statistically significant difference for the elderly in the peak torque test during knee extension. Hibbert et al.60 suggest a minimum of three familiarizations prior to the test to reduce possible statistical errors in participants with no experience in the performed task. For PwP, prior attempts to assess maximal strength may not be recommended due to disease characteristics. PwP may experience fatigue due to low dopamine. Familiarization, depending on how it is performed, may result in greater fatigue before the tests are performed.

Conclusion

The most performed method among the analyzed studies for the evaluation of HGS in PwP is the protocol recommended by ASHT. The frequently used instrument was the Jamar® dynamometer, validated for PD. The HGS test, when applied with a hydraulic dynamometer, is quick and easy to apply, not requiring great expertise from the evaluator, who will obtain an important measure correlated to the ADL. Although some PwP report muscle weakness and reduced muscle strength, it is still not possible to state that HGS is the primary motor sign of disease involvement. Future studies on the subject are recommended, especially with approaches that compare sides and the different stages of the disease, in addition to cohort studies. Therefore, we recommend conducting a multicenter study to reach a larger sample size, allowing the stratification of participants according to H&Y stages without statistical loss.

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Authors' contributions

ROM, LTM, AELS, TSRP and CLC made the search and screening of the articles. ROM, LTM, AELS and TSRP produced manuscript tables. TSRP, CLC and VLSB provided the mentorship for ROM and LTM. All authors contributed to manuscript revision and approved the final version of the manuscript.

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