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Hand muscle strength in Parkinson's disease: A Sarcopenic epiphenomenon or a meaningful biomarker?

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A B S T R A C T

Introduction: Sarcopenia, the age-related loss of muscle mass and function, has been reported in Parkinson's disease (PD). While grip strength is a key marker of sarcopenia and has been linked to PD risk and progression, its relationship with underlying neurodegenerative processes remains unclear. This study examines whether grip strength is impaired in PD and reflects disease severity or dopaminergic function.
Methods: Grip strength was assessed in 147 PD patients and 35 healthy controls, alongside motor symptoms and striatal dopamine transporter (DAT) binding using [^{123}I]FP-CIT single photon emission computed tomography. Longitudinal follow-up included 84 PD patients with clinical reassessment (median 4.1 years) and 40 patients with both clinical and DAT imaging re-evaluations (median 6.2 years). Associations between grip strength, motor symptom severity and dopaminergic function were analyzed.
Results: At baseline, mean grip strength did not differ between PD patients and healthy controls, and it did not correlate with striatal DAT binding ($p > 0.37$). While striatal DAT binding declined in PD (4.2 % annually, $p < 0.001$) and was associated with worsening motor function ($p = 0.004$), grip strength was not independently associated with DAT binding decline ($p > 0.62$). However, grip strength declined alongside worsening motor symptoms ($p = 0.029$).
Conclusion: Upper limb muscle strength remains largely preserved in mild to moderate PD and does not reliably reflect dopaminergic function or disease progression. Although sarcopenia has been reported in PD, grip strength declines in parallel with motor symptom progression and DAT loss rather than directly reflecting the disease process, suggesting it is an epiphenomenon rather than an independent pathophysiological feature.

1. Introduction

Sarcopenia is a progressive skeletal muscle disorder characterized by the decline of muscle mass and function, primarily affecting the aging population [1]. It is a major contributor to frailty and is associated with an increased risk of falls, fractures, functional impairment, and mortality [2]. In Parkinson's disease (PD), the prevalence estimates of sarcopenia vary widely, ranging from 6 % to 55.5 % [3,4], reflecting inconsistencies in diagnostic criteria and the heterogeneity among studied patient populations. While muscle weakness is a recognized clinical feature of PD and sarcopenia may be associated with worse cognitive functions and quality of life in patients with parkinsonian syndromes [5], it remains unclear whether sarcopenia is a primary consequence of neurodegeneration or a secondary effect of disease-related immobility, reduced physical activity, and medication use.

A key measure of sarcopenia is hand muscle strength, typically assessed using a handgrip dynamometer, which provides a widely used, easy-to-perform, and non-invasive clinical assessment of upper limb

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muscle function [6]. In the general population, reduced grip strength appears to serve as a predictor of adverse health outcomes, including physical disability and impaired mobility [1]. In PD, low grip strength and sarcopenia have also been associated with an increased risk of developing the disease [7–10], suggesting a possible link between muscle function and the pathophysiology of neurodegeneration.

Despite these associations, it remains unclear whether grip strength is consistently reduced in PD, particularly in early disease. A review article reported impairments in mechanical muscle function in PD compared to healthy controls, but only four out of thirteen included studies specifically assessed handgrip strength, leaving its role in PD largely underexplored [11]. Additionally, while some studies indicate that PD patients have reduced grip force, especially in low-motivation tasks [12], such findings may reflect deficits in movement initiation and motivational drive due to dopaminergic dysfunction rather than intrinsic muscle weakness. Given these uncertainties, the extent to which grip strength is independently affected and whether it reflects underlying neurodegenerative processes or motor symptom severity in PD remains unresolved.

This study aimed to determine whether grip strength is impaired in PD, whether it correlates with motor symptom severity, and whether it is associated with striatal dopaminergic function. To address these questions, we examined the relationships between grip strength and MDS-UPDRS motor scores, as well as between grip strength and striatal dopamine transporter (DAT) binding, both cross-sectionally and longitudinally.

2. Methods

2.1. Participants

Part I: Cross-Sectional Study. The cross-sectional component included 147 right-handed patients diagnosed with PD and 35 right-handed age- and sex-matched healthy controls. All PD patients underwent [^{123}I]FP-CIT SPECT (DAT-SPECT) imaging as part of their diagnostic evaluation. Imaging was performed either at Turku University Hospital or the Helsinki University Medical Imaging Center, Finland, within the framework of the NMDAT project (ClinicalTrials.gov identifier: NCT02650843), as previously described [13]. Of the 147 PD patients, 106 were newly diagnosed and unmedicated, while 41 were receiving dopaminergic therapy at the time of imaging (Table 1). PD diagnoses were retrospectively validated by two movement disorder specialists, based on clinical presentation, symptom progression, response to levodopa, and DAT-SPECT findings. Healthy controls were community-dwelling elderly individuals with no prior or current clinically relevant neurological or psychiatric conditions.

Part II: Longitudinal Clinical Follow-Up. Of the 147 PD patients, 84 volunteered for longitudinal follow-up, which included repeat clinical assessments using the same standardized motor and non-motor evaluation protocols as at baseline, including grip strength. The median follow-up interval was 4.1 years (range: 1.4–7.6 years).

Part III: Longitudinal DAT Imaging Follow-Up. From the 84 PD patients participating in clinical follow-up, 40 also underwent repeat DAT-SPECT imaging, resulting in two imaging timepoints for this subgroup. The median interval between baseline and follow-up imaging was of 6.2 years (range: 2.3–7.6 years). At follow-up, patients underwent repeat clinical assessments 2–4 h before imaging, using the same standardized tests and questionnaires as in Parts I and II.

2.2. Clinical evaluation procedures

All participants underwent the clinical examinations at baseline and follow-up visits (for patients included in Parts II and III). These consisted of a clinical interview and the administration of the following tests: Part III of the International Parkinson and Movement Disorder Society's Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [14], the Mini-Mental State Examination (MMSE) [15], the Non-Motor Symptoms Scale (NMSS) [16], the Parkinson's Disease Questionnaire (PDQ-8) [17],

Table 1
Demographic and clinical characteristics of the cross-sectional cohort (Part I).

		Unmedicated PD	Medicated PD	Healthy controls	P value
Demographics	n	106	41	35	–
	Age (years)	64.1 (10.8)	66.4 (8.7)	67.7 (9.0)	0.133
	Sex (m/f)	49/57	23/18	16/19	0.529
Grip strength	Mean (kg)	30.9 (12.3)	31.7 (12.0)	35.1 (11.2)	0.193
	Right (kg)	31.6 (12.5)	32.6 (13.1)	36.2 (11.3)	0.166
	Left (kg)	30.2 (13.1)	30.9 (11.4)	34.1 (11.3)	0.273
	Asymmetry index	3.1 (11.8)	3.5 (14.3)	3.3 (5.8)	0.976
	Relative (mean:body weight)	0.40 (0.14)	0.40 (0.14)	0.44 (0.12)	0.477
	Contralateral (kg)[A]	32.1 (13.1)	32.3 (13.3)	34.5 (11.0)	0.641
	Ipsilateral (kg)[A]	29.9 (12.3)	31.1 (11.2)	35.5 (12.0)	0.066
Motor symptoms	Motor symptom duration (months)	15 [14]	30 [57]	–	0.001
	MDS-UPDRS motor score	35.0 (14.8)*	38.8 (15.8)*	6.7 (5.5)	<0.001
	UPDRS asymmetry index	−0.6 (46.1)	−4.2 (33.5)	−18.7 (50.2)	0.128
	HY stage	2 [1] *	2 [1] *	0 [0]	<0.001
Nonmotor symptoms	NMSS total	41 [49]*	36 [50]*	11 [17]	<0.001
	PDQ-8	6.3 [22.0]*	15.6 [16.0]*	3.0 [9.0]	<0.001
	MMSE	28 [3]	28 [2]	28 [2]	0.211
	BDI	6.0 [7.0]*	5.5 [11.0]*	1.0 [6.0]	<0.001
Striatal DAT binding	Caudate right (SBR)	2.22 (0.68)*†	1.86 (0.64)*	2.58 (0.28)	<0.001
	Caudate left (SBR)	2.28 (0.70)*†	1.94 (0.65)*	2.66 (0.34)	<0.001
	Caudate mean (SBR)	2.25 (0.66) *†	1.90 (0.61)*	2.62 (0.29)	<0.001
	Caudate asymmetry index	−1.56 (8.58)	−2.09 (11.90)	−1.43 (4.11)	0.935
	Putamen right (SBR)	1.47 (0.62)*†	1.15 (0.53)*	2.39 (0.31)	<0.001
	Putamen left (SBR)	1.36 (0.47)*†	1.08 (0.49)*	2.35 (0.34)	<0.001
	Putamen mean (SBR)	1.42 (0.47)*†	1.12 (0.47)*	2.37 (0.31)	<0.001
	Putamen asymmetry index	3.04 (16.63)	3.24 (18.57)	0.89 (4.08)	0.751

Values are presented as n, median [IQR], or mean (SD). P-values were calculated using chi-square/Fisher's exact tests, one-way ANOVA, or Kruskal-Wallis tests. [A] In relation to predominant side of striatal DAT deficit. Missing data: contralateral and ipsilateral grip strength (unmedicated PD: n = 1, HC: n = 1) motor symptom duration (unmedicated PD: n = 6; medicated PD: n = 1), UPDRS asymmetry index (HC: n = 2), PDQ-8 (unmedicated PD: n = 10; medicated PD: n = 1 and BDI score (unmedicated PD: n = 10; medicated PD: n = 1). * Significantly different from healthy controls or † medicated PD patients (Bonferroni-corrected pairwise $p < 0.05$).

and the Beck Depression Inventory (BDI) [18]. All examiners had successfully completed the MDS-UPDRS Training Program and Exercise. Among the PD patients, one individual had missing data for the MDS-UPDRS motor score. The Part I examinations were conducted between 2014 and 2019, Part II between 2016 and 2022, and Part III between 2021 and 2022.

2.3. Evaluation of grip strength

Grip strength was assessed in all phases of the study using a hydraulic Jamar hand dynamometer (Model 5030J1; Performance Health, Chicago, USA) for maximal voluntary isometric grip force [19]. The assessment was conducted following standardized protocols to ensure reliability and reproducibility across all study participants.

Participants were seated with their elbow flexed at 90°, the forearm in a neutral position, and the wrist slightly extended. Before the test, each participant was given one practice trial to familiarize themselves with the device and testing procedure. This was followed by two maximal-effort test trials per hand, performed with a 3- to 5-s sustained contraction. A rest period was allowed between trials to minimize fatigue. The highest recorded value from the two trials was used for analysis. Grip strength was measured in both hands to assess potential asymmetry in muscle function. Testing was conducted at baseline and follow-up visits under identical conditions to allow for longitudinal comparisons. Additionally, assessments were performed at the same time of day for each participant whenever possible.

2.4. Ethics and informed consent

The study received approval from the Ethics Committee of Turku University Hospital (decision No. 3/1801/2021) and was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants involved in Parts I, II, and III.

2.5. SPECT imaging and image preprocessing

Participants received an injection of 185 MBq of the radiopharmaceutical [^{123}I]FP-CIT 3 h prior to SPECT imaging. To minimize radiation exposure to the thyroid, they were given either 250–300 mg of potassium perchlorate or potassium iodide tablets (130 mg) 30–60 min before the radiopharmaceutical injection. For Part I, SPECT imaging was performed using one of six SPECT/CT devices, all of which were calibrated in advance using a striatal phantom (RSD, Radiology Support Devices, Inc., Long Beach, USA) following a published calibration procedure [20,21]. In Part III, all follow-up images were acquired using a single device (Symbia T6 Series SPECT/CT, Siemens Healthineer, Erlangen, Germany). The SPECT images were reconstructed with HybridRecon Neurology version 3.0.1 (Hermes Medical Solutions AB, Stockholm, Sweden) using a three-dimensional (3D) ordered-subsets expectation maximization (OSEM) algorithm. The imaging protocol adhered to the recommendations of the European Association of Nuclear Medicine (EANM) [22].

2.6. Image analyses

The reconstructed SPECT images for both parts I and III of the study were analyzed using BRASS analysis software (version 2.6, Hermes Medical Solutions AB, Stockholm, Sweden). Specific binding ratios (SBRs) of DAT were calculated for each of the six subregions of the striatum: the left and right anterior putamen, posterior putamen, and caudate (regions of interest, ROIs). The occipital cortex was used as the reference tissue for these calculations. The SBRs were determined using the following formula:

$$SBR = (SBR_{caudate\ or\ putamen} - SBR_{occipital})/SBR_{occipital}. \quad (1)$$

To determine the mean level of DAT binding in the putamen, the SBRs of the anterior and posterior putamen were averaged. For the Part II analysis, baseline and follow-up DAT images were reconstructed simultaneously using identical preprocessing parameters. Age, sex, and MDS-UPDRS motor scores or changes in MDS-UPDRS motor scores were included as covariates in the analyses. In Part III, both absolute changes and yearly adjusted changes in DAT binding were examined.

2.7. Statistical analyses

Statistical analysis was conducted using IBM SPSS Statistics (version 29, SPSS Inc., Chicago, IL, USA). The normality of variables was assessed through histograms and Shapiro-Wilk tests. Data are presented as mean (SD), median [IQR], or n. Group differences were evaluated using chi-square or Fisher's exact tests for categorical variables, and Mann-Whitney U tests or independent samples t-tests for continuous variables. Differences in demographic and clinical characteristics between baseline and follow-up were analyzed using McNemar's test for binary variables and the Wilcoxon signed-rank test or paired-samples *t*-test for continuous variables. A linear regression model was used in Part I to identify predictors of mean putamen DAT binding. In Part II, an ANCOVA model was employed to examine the relationship between changes in grip strength and changes in MDS-UPDRS motor scores, with baseline age and sex as covariates. In Part III, an ANCOVA model was applied to assess the association between changes in putamen DAT binding, grip strength, and MDS-UPDRS motor score, with baseline age and sex included as covariates. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Cross-sectional analysis (Part I)

The demographic and clinical characteristics of the study cohort are presented in Table 1. Grip strength did not differ between PD patients and healthy controls (Fig. 1). In both the unmedicated PD group and healthy controls, grip strength was on average 1.4–2.1 kg higher in the dominant (right) hand compared to the non-dominant hand (unmedicated PD: $p = 0.045$; HC: $p = 0.002$). A similar trend was observed in the medicated PD group, but the difference did not reach statistical significance ($p = 0.056$).

Healthy controls showed the highest, and the medicated PD group the lowest DAT binding values ($p < 0.001$; Table 1, Fig. 1). Grip strength was not associated with putamen DAT binding in any of the three groups, even when adjusting for age, sex and MDS-UPDRS motor scores ($p > 0.37$; Fig. 1, Supplementary Table 1). Similarly, MDS-UPDRS motor scores were not predictive of putamen DAT binding in any group ($p > 0.05$, Supplementary Table 1). However, in the unmedicated PD group, a significant negative association was observed between age and putamen DAT binding ($\beta = -0.013$, $p = 0.013$).

3.2. Clinical longitudinal analysis (Part II)

The demographic and clinical characteristics of the longitudinal PD cohort are summarized in Table 2. Mean grip strength remained stable during the follow-up period, with no significant changes observed ($p = 0.69$). In contrast, the levodopa equivalent daily dose (LEDD) increased significantly at the follow-up visits ($p < 0.001$), and MDS-UPDRS motor scores showed decline over time ($p = 0.013$). However, PD-related quality of life deteriorated, as reflected by an increase in PDQ-8 scores ($p < 0.001$).

The results of ANCOVA analysis (Supplementary Table 2) demonstrated that a greater increase in MDS-UPDRS motor scores over time was associated with a greater decline in grip strength, after adjusting for baseline age and sex (all PD patients: $p = 0.029$, medicated at baseline: $p = 0.003$). These findings suggest a relationship between progressive

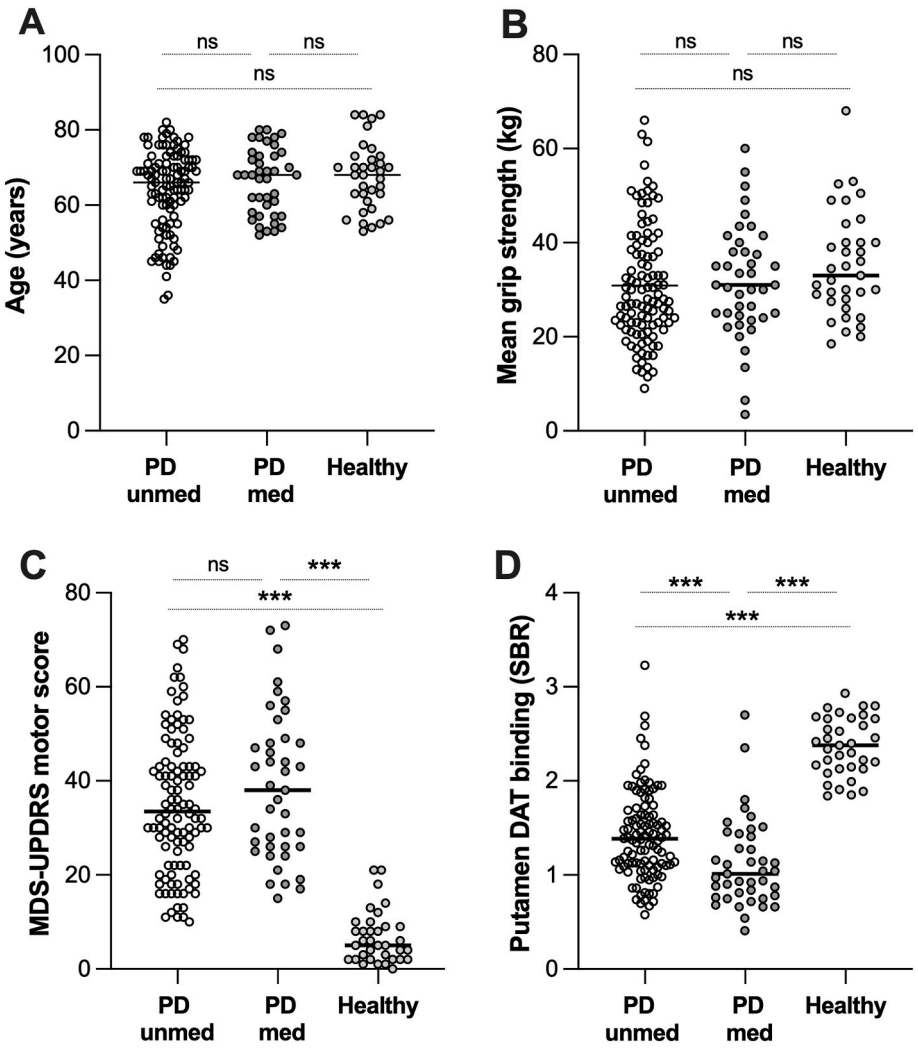

Fig. 1. Group Differences in Age, Mean Grip Strength, MDS-UPDRS Motor Score, and Putamen DAT Binding.
(A) Age distribution across unmedicated PD patients, medicated PD patients, and healthy controls.
(B) Mean grip strength comparison among the three groups, demonstrating no significant differences.
(C) MDS-UPDRS motor scores, demonstrating greater motor impairment in PD groups compared to healthy controls.
(D) Putamen DAT binding levels, showing significantly reduced striatal dopaminergic function in PD patients, with the lowest values observed in the medicated group.
***P < 0.001, ns = not significant.

motor impairment and reduced grip strength over time, particularly in more advanced patients receiving dopaminergic therapy.

3.3. Longitudinal analysis with follow-up DAT imaging (Part III)

The demographic and clinical characteristics of the PD cohort with follow-up DAT imaging are presented in Table 3. Grip strength remained stable during the follow-up period, with no significant changes observed ($p = 0.86$). In contrast, MDS-UPDRS motor scores significantly declined over time ($p = 0.009$), and LEDD increased ($p < 0.001$). As expected, striatal DAT binding declined bilaterally ($p < 0.001$), consistent with progressive nigrostriatal dopaminergic degeneration (Supplementary Figure 2).

Results from ANCOVA analysis (Supplementary Table 3) indicated that the annual change in putamen DAT binding was not significantly associated with the annual change in grip strength, after adjusting for baseline age, sex and the annual change in MDS-UPDRS motor score ($p > 0.62$). However, a greater annual decrease in putamen DAT binding was significantly associated with a greater annual increase in MDS-UPDRS motor scores, even after controlling for baseline age and sex ($p = 0.004$).

4. Discussion

This study investigated the relationship between handgrip strength, motor symptoms, and dopaminergic function in PD using both cross-sectional and longitudinal approaches. The findings demonstrate that, at group-level, grip strength is not decreased in PD and remains stable over time up to 6 years and, even as motor symptoms, striatal DAT binding, and quality of life progressively deteriorate. Although individually motor function decline was associated with grip strength reduction, there was no independent association between grip strength and dopaminergic neurodegeneration, indicating that hand muscle strength is not a reliable biomarker of PD dopaminergic progression. Taken together, these results suggest that grip strength loss in advanced disease represents an epiphenomenon of overall motor decline rather than a direct measure of disease pathology.

Table 2
Demographic and clinical characteristics of the longitudinal PD cohort (Part II, n = 84).

		Baseline	Follow-up	P value
Demographics	Age (years)	63.6 (10.7)	67.8 (10.6)	<0.001
	Sex (m/f)	43/41		
Grip strength	Mean (kg)	32.5 (12.1)	32.0 (11.5)	0.691
	Right (kg)	33.4 (12.9)	32.5 (11.3)	0.486
	Left (kg)	31.6 (11.9)	31.6 (12.0)	0.948
	Relative (mean:body weight)	0.41 (0.15)	0.40 (0.13)	0.538
Motor symptoms	LEDD (mg)	0 [52]	475 [387]	<0.001
	MDS-UPDRS motor score	34.1 (13.6)	29.7 (16.0)	0.013
	HY stage	2 [1]	2 [0]	0.465
Nonmotor symptoms	NMSS total	38 [42]	46 [46]	0.124
	PDQ-8	9.4 [22.0]	19.0 [25.0]	<0.001
	MMSE	28 [2][a]	28 [3][b]	0.007
	BDI	6.0 [8.0]	7.0 [6.0]	0.167

Median [IQR] time interval between examination = 49 months (4.1 years) [44]. Median [IQR] motor symptom duration at baseline = 17 months [26]. Values are median [IQR], mean (SD) or *n*. P-values are from related-samples Wilcoxon signed rank tests or paired-samples *t*-tests. Missing values for PDQ-8 (baseline n = 2, follow-up n = 4) and BDI score (baseline n = 3, follow-up n = 5).
[a] Mean (SD): 27.9 (1.9).
[b] Mean (SD): 27.0 (2.9).

4.1. Grip strength is preserved in PD

The relative preservation of grip strength in PD challenges the assumption that muscle weakness or sarcopenia is a universal feature of the disease, despite recent evidence suggesting that reduced grip strength may be associated with increased risk of developing PD [7,9,10]. Unlike motor symptoms such as bradykinesia, postural instability, and gait disturbances, which progressively worsen, grip strength remained unchanged over the 6-year follow-up period. While previous studies have reported reduced muscle strength and impaired physical function in PD compared to elderly controls [3,11], these studies have assessed muscle function using diverse criteria, including gait speed and skeletal muscle mass index, suggesting that muscle weakness in PD could primarily affect the lower extremities and trunk rather than the upper limbs.

One possible explanation for this preservation is that grip strength relies primarily on corticospinal pathways [23], which are mostly spared in PD [24]. In contrast, gait and postural control depend more heavily on basal ganglia circuits, which are directly impaired by dopamine depletion [25]. Additionally, frequent use of upper limbs in daily activities may contribute to the maintenance of grip strength, whereas lower limb strength may decline due to decreased mobility and physical activity [26]. A systematic review further supports the notion that muscle strength deficits are more pronounced in the lower limbs and trunk compared than in the upper extremities in PD [11]. Moreover, PD-related motor impairments appear to be more severe in proximal rather than distal muscle groups [27]. This suggests that grip strength, a measure of distal upper limb function, may be less affected by PD-related neurodegeneration than larger, weight-bearing muscle groups, and alternative measures focusing on dynamic motor control instead of hand static force may better capture motor dysfunction in PD [28].

Table 3
Demographic and clinical characteristics of the longitudinal PD cohort with DAT imaging (Part III, n = 40).

		Baseline	Follow-up	P value
Demographics	Age (years)	63.6 (9.6)	69.1 (9.5)	<0.001
	Sex (m/f)			–
Grip strength	Mean (kg)	32.2 (11.9)	31.7 (11.5)	0.855
	Right (kg)	33.2 (12.2)	32.3 (11.2)	0.724
	Left (kg)	31.2 (12.4)	31.1 (12.2)	0.992
	Relative (mean:body weight)	0.40 (0.14)	0.40 (0.14)	0.933
	Contralateral (kg)[A]	33.5 (13.0)	31.6 (12.1)	0.466
	Ipsilateral (kg)[A]	31.1 (11.7)	31.3 (11.4)	0.950
Motor symptoms	LEDD (mg)	0 [238]	530 [454]	<0.001
	MDS-UPDRS motor	35.0 (14.3)	29.2 (17.1)	0.009
	HY stage	2 [1]	2 [0]	0.012
Nonmotor symptoms	NMSS total	38 [34]	46 [49]	0.152
	PDQ-8	6.3 [18.8]	16.0 [29.5]	0.010
	MMSE	28 [2]	28 [3]	0.068
	BDI	5.0 [8.0]	6.0 [5.0]	0.711
Striatal DAT binding (SBR)	Caudate right	2.01 (0.46)	1.46 (0.33)	<0.001
	Caudate left	2.14 (0.53)	1.54 (0.38)	<0.001
	Caudate mean	2.08 (0.44)	1.50 (0.31)	<0.001
	Putamen right	1.21 (0.33)	0.88 (0.27)	<0.001
	Putamen left	1.26 (0.42)	0.95 (0.28)	<0.001
	Putamen mean	1.23 (0.28)	0.91 (0.24)	<0.001

Median [IQR] time interval between examination = 75 months (6.2 years) [32]. Median [IQR] motor symptom duration at baseline = 18 months [25]. Values are median [IQR], mean (SD) or *n*. *P* values are from related-samples Wilcoxon signed rank tests or paired-samples *t*-tests. [A] In relation to predominant side of striatal DAT deficit. Missing values for contralateral and ipsilateral grip strength (baseline n = 1, follow-up n = 1), PDQ-8 (baseline n = 1) and BDI score (baseline n = 1, follow-up n = 1).

4.2. Grip strength is not associated with dopaminergic function

Our findings indicate that grip strength is not directly linked to dopaminergic function in PD, either cross-sectionally or longitudinally. Over time, changes in grip strength were not associated with alterations in striatal DAT binding, reinforcing the notion that grip strength does not serve as a direct marker of nigrostriatal dopaminergic loss. In contrast, increasing MDS-UPDRS motor scores were associated with greater reductions in DAT binding. This finding aligns with previous studies showing that striatal presynaptic dopaminergic loss is associated with worsening bradykinesia and other core motor symptoms [29]. Consequently, previous reports linking reduced grip strenght to an increased risk of levodopa-induced dyskinesia [30], may reflect a greater overall disease burden and more advanced disease stage rather than a direct association with dopaminergic dysfunction. The lack of correlation between grip strength and DAT binding suggests that muscle strength in early to moderate PD may be maintained through compensatory neural mechanisms, explaining its relative preservation despite progressive striatal dopaminergic degeneration.

4.3. Implications for clinical practice and research

In clinical settings, grip strength measurement does not appear to provide meaningful information on disease progression during the early years of PD. Given that grip strength remains largely stable while motor symptoms progressively worsen, it is unlikely to serve as a reliable standalone marker for tracking neurodegeneration or monitoring disease progression in routine practice. However, if grip strength is assessed early in the disease course, it could establish a baseline reference, which may become relevant over the long term. In advanced PD, a measurable decline in grip strength could reflect disease progression to a stage where hand function is increasingly compromised, warranting additional clinical support or rehabilitative interventions to preserve functional independence.

For clinical trials and research, these findings suggest that grip strength is unlikely to be a suitable primary or secondary endpoint for assessing disease progression or treatment efficacy. Instead, studies should prioritize more sensitive motor outcomes, such as MDS-UPDRS motor scores, postural stability assessment, proximal muscle strength, or gait parameters, which better reflect the underlying neurodegenerative process and its functional impact.

5. Limitations

Several limitations should be considered when interpreting these findings. While the longitudinal component included a moderate sample size, which was sufficient to detect significant associations with motor function, it may have lacked the power to identify more subtle changes in grip strength over time. Moreover, as the cohort primarily consisted of early-stage, mostly unmedicated PD patients at baseline, the findings may not be generalizable to more advanced disease stages, where muscle function may be more severely affected due to cumulative neurodegeneration and long-term medication effects. In addition, follow-up data were not available for healthy controls, which limits the ability to perform direct longitudinal comparisons between PD patients and controls. Additionally, grip strength alone does not provide a comprehensive assessment of overall muscle function, as it excludes lower limbs and trunk strength measurements, which may be more affected in PD and more functionally relevant for disease progression. Importantly, while grip strength is a widely used clinical indicator of muscle function and a core component in the operational definition of sarcopenia, it is not by itself diagnostic of the condition. Comprehensive sarcopenia assessment requires additional measures of muscle mass and/or performance. Grip strength was selected in this study for its practicality and clinical relevance, particularly in settings where more comprehensive muscle function testing is not feasible. Finally, this study relied on static grip strength measurements, which may fail to capture deficits in dynamic motor control, fine motor coordination, or repetitive force modulation, all of which can be impaired in PD. Despite these limitations, this study provides valuable long-term insights into the relationship between upper limb muscle strength, motor symptom progression, and striatal dopaminergic function in PD.

6. Conclusion

While grip strength is preserved and does not directly correlate with dopaminergic function, it declines in parallel with worsening motor symptoms, suggesting that it reflects general motor dysfunction rather than disease-specific neurodegeneration. These findings emphasize the need for alternative motor assessments that better capture PD-related deficits. Ultimately, grip strength is not a suitable marker for assessing dopaminergic function or tracking disease progression in PD, but it may still serve as a convenient complementary proxy for general motor function monitoring in clinical practice.

CRediT authorship contribution statement

Emmi K. Saarinen: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Tomi Kuusimäki:** Writing – review & editing, Investigation. **Kalle Niemi:** Writing – review & editing, Visualization, Investigation. **Tommi Noponen:** Writing – review & editing, Investigation. **Elina Jaakkola:** Writing – review & editing, Investigation. **Elina Myller:** Writing – review & editing, Investigation. **Mikael Eklund:** Writing – review & editing, Investigation. **Simo Nuuttila:** Writing – review & editing, Investigation. **Toni Ihalainen:** Writing – review & editing, Investigation. **Kirsi Murtomäki:** Writing – review & editing, Investigation. **Tuomas Mertsalmi:** Writing – review & editing, Investigation. **Reeta Levo:** Writing – review & editing, Investigation. **Tero Vahlberg:** Writing – review & editing, Investigation, Formal analysis. **Juho Joutsa:** Writing – review & editing, Investigation. **Filip Scheperjans:** Writing – review & editing, Investigation. **Valtteri Kaasinen:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request from qualified investigators for research purposes. Access will be granted in accordance with institutional and ethical guidelines.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2025.108021.

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