Clinical Section / Original Paper

Gerontology

Gerontology 2019;65:216–228
DOI: 10.1159/000492572

Received: May 2, 2018
Accepted: July 31, 2018
Published online: September 10, 2018

# Prevalence and Associated Factors of Sarcopenia and Frailty in Parkinson's Disease: A Cross-Sectional Study

Marina Peball Philipp Mahlknecht Mario Werkmann Kathrin Marini Franziska Murr Helga Herzmann Heike Stockner Roberto de Marzi Beatrice Heim Atbin Djamshidian Peter Willeit Johann Willeit Stefan Kiechl Dora Valent Florian Krismer Gregor Karl Wenning Michael Nocker Katherina Mair Werner Poewe Klaus Seppi

Department of Neurology, Innsbruck Medical University, Innsbruck, Austria

**Keywords**
Parkinson's disease · Sarcopenia · Frailty · Prevalence · Epidemiology · Bruneck Study

**Abstract**
***Background:*** Sarcopenia and frailty are found in up to one-third of the general elderly population. Both are associated with major adverse health outcomes such as nursing home placement, disability, decreased quality of life, and death. Data on the frequency of both syndromes in Parkinson's disease (PD), however, are very limited. ***Objective:*** We aimed to screen for sarcopenia and frailty in PD patients and to assess potential associations of both geriatric syndromes with demographic and clinical parameters as well as quality of life. ***Methods:*** In this observational, cross-sectional study, we included 104 PD patients from a tertiary center and 330 non-PD controls from a population-based cohort aged >65 years. All groups were screened for sarcopenia using the SARC-F score and for frailty using the Clinical Frailty Scale of the Canadian Study of Health and Aging (CSHA CFS). Prevalence rates of sarcopenia and frailty were also assessed in 18 PD patients from a population-based cohort aged >65 years. Moreover, PD patients from the tertiary center were evaluated for motor and non-motor symptoms, quality of life, and dependency. ***Results:*** The prevalence of sarcopenia was 55.8% (95% CI: 46.2–64.9%) in PD patients from the tertiary center and 8.2% (5.7–11.7%; $p < 0.001$) in non-PD controls. Frailty was detected in 35.6% (27.0–45.2%) and 5.2% (3.2–8.1%; $p < 0.001$). Prevalence rates for sarcopenia and frailty were 33.3% (16.1–56.4%; $p = 0.004$) and 22.2% (8.5–45.8%; $p = 0.017$) in the community-based PD sample. Both sarcopenia and frailty were significantly associated with longer disease duration, higher motor impairment, higher Hoehn and Yahr stages, decreased quality of life, higher frequency of falls, a higher non-motor symptom burden, institutionalization, and higher care levels in PD patients from a tertiary center compared to not affected PD patients (all $p < 0.05$). ***Conclusions:*** Both frailty and sarcopenia are more common in PD patients than in the general community and are associated with a more adverse course of the disease. Future studies should look into underlying risk factors for the occurrence of sarcopenia and frailty in PD patients and into adequate management to prevent and mitigate them.



KARGER

E-Mail karger@karger.com
www.karger.com/ger



Klaus Seppi, MD
Department of Neurology, Innsbruck Medical University
Anichstrasse 35
AT–6020 Innsbruck (Austria)
E-Mail Klaus.Seppi@tirol-kliniken.at

## Introduction

The term sarcopenia, first implemented in 1989 [1], describes an abnormal loss of muscle mass in the elderly, and the current definition characterizes sarcopenia as a complex, multifactorial age-related loss of skeletal muscle mass and function [2]. The term frailty is used to describe increased vulnerability to stressors due to decreased reserve, resistance, and poor homeostasis with a disproportionate influence on health status and multiple organ functions [3]. The prevalence of both geriatric syndromes varies according to the definition used and depending on sex, ethnicity, age group, and geographic region. Validated screening questionnaires for easy and rapid assessment exist for both [4, 5].

The prevalence of sarcopenia using the SARC-F Score, a screening tool for sarcopenia, ranges from 4 to 34% for both sexes in the general elderly population [6–10]. The prevalence of frailty in the general elderly population was found to be 16–43% when using the Clinical Frailty Scale of the Canadian Study of Health and Aging (CSHA CFS), a screening tool for frailty [4, 11, 12]. Sarcopenia and frailty have been found more frequently in elderly individuals with chronic diseases such as chronic lung diseases (e.g., chronic obstructive pulmonary disease), cardiovascular diseases, peripheral vascular diseases, diabetes, chronic kidney disease, liver cirrhosis, and osteoporosis [13–17].

Sarcopenia and frailty are important determinants of quality of life (QoL), disability, and mortality in the elderly population [2, 3], but surprisingly there have been relatively few studies assessing the overall frequency and clinical characteristics of these conditions in Parkinson's disease (PD).

Thus, the aim of this study was to screen for sarcopenia and frailty in a large sample of PD patients and compare the prevalence rates with a control group similar in age and sex using well-established screening tools for both sarcopenia and frailty (SARC-F and CSHA CFS) [4, 5, 7, 8, 12, 18–20]. Moreover, we sought to determine potential demographic and clinical factors associated with the occurrence of sarcopenia and frailty and associations of sarcopenia and frailty with QoL in PD patients.

## Methods

*Study Participants*

In the observational, cross-sectional study, 104 patients with clinically established PD according to UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria with an age of 65 years and more [21] were recruited from our movement disorder unit from December 2016 to July 2017. For comparison, we also assessed the prevalence of sarcopenia and frailty in the general elderly population in our region using a sample from an ongoing population-based study (Bruneck Study) [22].

In 1990, Bruneck Study participants were selected as an age- and sex-stratified random sample of all inhabitants of Bruneck (i.e., 125 for each sex and 4th, 5th, 6, and 7th decade of age) and are therefore representative of the general elderly community. All 330 participants, who did not have PD and who were recruited during a follow-up assessment carried out in April 2016, were included in the present analysis as a non-PD control group. Moreover, all participants with PD ($n$ = 18) from the community-based cohort were used as a validation set for the prevalence rates of sarcopenia and frailty in PD. These patients were not included in the non-PD control group of the Bruneck Study ($n$ = 330).

*Procedures*

While several tools have been used in the past to identify sarcopenia and frailty, there is no gold standard to diagnose these syndromes [7, 18]. In the present study, we decided to use two simple and quick screening tools for their identification due to the population-based nature of the Bruneck Study. Sarcopenia was ascertained using SARC-F, a simple five-item screening questionnaire that assesses typical problems and consequences of sarcopenia: strength, assistance with walking, rising from a chair, climbing stairs, and falls [5]. Each item is scored from 0 to 2 with total score values ranging from 0 to 10 points. A score value ≥4 is predictive of sarcopenia. Thus, participants with a score value ≥4 were classified as sarcopenic (sarcopenia group) in this study [4, 7, 12, 18–20]. The SARC-F has been validated in different populations and appears to have a comparable predictive value for adverse health outcomes to operational definitions of sarcopenia [6–10, 23].

Frailty was assessed by the validated 7-item CSHA CFS which is based on information on mobility, functional capacity, comorbid diseases, and cognitive function [4]. The scale ranges from 1 (very fit) to 7 (severely frail). Participants with score values ≥5 (5: mildly frail, 6: moderately frail, 7: severely frail) were defined as being frail (frailty group) in this study [4].

To determine disease-related factors of PD possibly associated with the occurrence of sarcopenia and frailty, PD subjects underwent a standardized interview to obtain general demographic data including age at onset of PD, disease duration, drug history, and a standardized neurological examination including the MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and assessing other clinical characteristics. Non-motor symptoms were assessed by history and the MDS-UPDRS Part I. The levodopa equivalent daily dose (LEDD) was calculated using published conversion factors excluding patients that had undergone deep brain stimulation ($n$ = 14) [24]. The tremor-dominant (TD) and postural instability/gait difficulty PD phenotypes were determined, and the TD phenotype was compared to a non-TD phenotype [25]. Moreover, QoL was assessed using the 8-item Parkinson's Disease Questionnaire (PDQ-8; with lower scores indicating better QoL) [26, 27]. Information on institutionalization and level of dependency in activities of daily living were determined. Level of dependency, defined as the need for aid in activities of daily living, was self-reported by the PD patients and their relatives.

The evaluation of chronic comorbid diseases in our PD patients was performed according to the Charlson Comorbidity Index, an

**Table 1.** Baseline characteristics of PD patients and the Bruneck cohort

| | Bruneck cohort[d] ($n$ = 330) | PD cohort Innsbruck[d] ($n$ = 104) | $p$ value[c] | PD cohort Bruneck[d] ($n$ = 18) | $p$ value[c] |
|---|---|---|---|---|---|
| Sex, $n$ (%) | | | | | |
| Male | 167 (50.6) | 64 (61.5) | 0.051 | 9 (50.0) | 0.960 |
| Female | 163 (49.4) | 40 (38.5) | | 9 (50.0) | |
| Age, years | 75.3±7.3 (74.0) | 73.8±5.2 (73.8) | 0.214 | 78.7±8.1 (79.0) | 0.063 |
| SARC-F score values | 0.9±1.8 (0) | 4.3±3.0 (4.0) | <0.001 | 2.22±3.1 (1.0) | 0.032 |
| Sarcopenia[a] | | | | | |
| $n$ (%) | 27 (8.2) | 58 (55.8) | <0.001 | 6 (33.3) | 0.004 |
| 95% CI | 5.7 to 11.7% | 46.2 to 64.9% | | 16.1 to 56.4% | |
| CSHA CFS values | 2.0±1.2 (2.0) | 3.8±1.7 (4.0) | <0.001 | 3.1±1.6 (3.0) | 0.001 |
| Frailty[b] | | | | | |
| $n$ (%) | 17 (5.2) | 37 (35.6) | <0.001 | 4 (22.2) | 0.017 |
| 95% CI | 3.2 to 8.1% | 27.0 to 45.2% | | 8.5 to 45.8% | |

Data are presented as mean ± standard deviation (median), or as stated. PD, Parkinson's disease; CI, confidence interval; CSHA, Canadian Study on Health & Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia.

[a] Sarcopenia was assessed with the SARC-F score, sarcopenia: ≥4 points in the SARC-F questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] $p$ values compared to Bruneck cohort, $\chi^2$ test or Fisher's exact test for categorical variables, unpaired $t$ test for normally distributed continuous variables, Mann-Whitney U test for not normally distributed continuous variables. [d] The PD cohort Innsbruck consists of PD patients of a tertiary center. The PD cohort Bruneck combines PD cases of a population-based sample. The Bruneck cohort consists of non-PD participants.

index developed to measure overall chronic disease burden longitudinally and to predict survival [28]. Falls were assessed by standard interview, and recurrent falls were defined as more than one fall within the last year [29]. To determine the association of falls with the SARC-F, we excluded the item assessing falls in the total SARC-F score. Therefore, this modified SARC-F ranged from 1 to 8 points. The same cut-off to define sarcopenia (≥4 points) was used for this subanalysis. A handheld dynamometer (CITEC handheld dynamometer CT3002) was used to assess handgrip strength. Gait speed was measured during undisturbed straight walking at the subject's own comfortable speed over a distance of 8 m using a simple stop watch [29]. Muscle mass was not assessed in this study.

*Statistical Analysis*

Prevalence rates are given in percent of the respective category with its 95% confidence interval (95% CI), which were calculated using the modified Wald method [30]. Categorical variables are given in number and percent of the category. For continuous quantitative measures the number, the mean with its standard deviation, and the median were calculated. Thus, score values ranging from 1 to 10 points for the SARC-F score and from 0 to 7 for the CSHA CFS were provided as well as the dichotomized outcome of the assessments with the screening tools (SARC-F ≥4 as sarcopenia group and SARC-F <4 as non-sarcopenia group; CSHA CFS ≥5 as frailty group and CSHA CFS<5 as non-frailty group). The prevalence of frailty and sarcopenia in the PD and Bruneck cohort is given separately for male and female participants in number and percent of the respective category with its 95% CI. For the Bruneck PD cohort, no sex-specific analysis was performed due to its small sample size of only 18 individuals.

The $\chi^2$ test was used to assess the distribution of sarcopenia, frailty, and sex between groups (independent variable: PD cohort vs. elderly population for comparison) as well as the category distribution (independent variables: frailty and sarcopenia) of nominal variables in the PD cohort.

Mann-Whitney U tests or unpaired $t$ tests were used for group comparisons of quantitative variables depending on the scale type of the variables (see Table legends for details). Moreover, some of the quantitative variables were categorized either by tertiles (disease duration) or median (Hoehn and Yahr [H&Y] stage). We applied the $\chi^2$ test for group comparisons of these categorized variables.

The association of various outcome measures and clinical characteristics with the occurrence of sarcopenia and frailty in PD patients was assessed with an unconditional logistic regression analysis. Different regression models were assessed (model 1: unadjusted; model 2: adjusted for sex and age; model 3: adjusted for sex, age, and comorbidities; model 4: adjusted for sex, age, comorbidities, and LEDD). Associations are expressed by the odds ratio (OR) and 95% CIs. The ORs of all continuous variables (age, body mass index, Charlson Comorbidity Indices, SARC-F Score values, CSHA CFS values, disease duration, MDS-UPDRS Part I–IV and sum scores, LEDD, handgrip strength, gait velocity) were calculated for a 1 standard deviation unit change in variable levels in order to render the odds comparable. The significance level was set at two-sided $p$ value of <0.05. IBM SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA) was used to tabulate and analyze data.

**Table 2.** Sex differences in the prevalence of sarcopenia and frailty

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | Bruneck cohort[d] ($n$ = 167) | PD cohort Innsbruck[d] ($n$ = 64) | $p$ value[c] | Bruneck cohort[d] ($n$ = 163) | PD cohort Innsbruck[d] ($n$ = 40) | $p$ value[c] |
| Age, years | 74.6±7.0 (74.0) | 73.8±5.2 (73.8) | 0.469 | 76.0±7.5 (75.0) | 74.2±5.3 (74.0) | 0.451 |
| SARC-F score values | 0.53±1.2 (0.0) | 3.8±2.9 (3.5) | <0.001 | 1.3±2.2, 0.0) | 5.1±2.9 (5.0) | <0.001 |
| Sarcopenia[a] | | | | | | |
| $n$ (%) | 5 (3.0) | 32 (50.0) | <0.001 | 22 (13.5) | 26 (65.0) | <0.001 |
| 95% CI | 1.1 to 7.0% | 38.1 to 61.9% | | 9.0 to 19.7% | 49.5 to 77.9% | |
| CSHA CFS values | 1.8±1.0 (1.5) | 3.7±1.8 (3.0) | <0.001 | 2.2±1.3 (2.0) | 3.9±1.7 (4.0) | <0.001 |
| Frailty[b] | | | | | | |
| $n$ (%) | 3 (1.8) | 20 (31.3) | <0.001 | 14 (8.6) | 17 (42.5) | <0.001 |
| 95% CI | –0.4 to 5.4% | 21.2 to 43.4% | | 5.1 to 14.0% | 28.5 to 57.8% | |

Data are presented as mean ± standard deviation (median) or as stated. PD, Parkinson's disease; CI, confidence interval; CSHA, Canadian Study on Health & Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia.

[a] Sarcopenia was assessed with the SARC-F score, Sarcopenia: ≥4 points in the SARC-F Questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] $p$ values compared to Bruneck cohort, $\chi^2$ test for categorical variables, unpaired $t$ test for normally distributed continuous variables, Mann-Whitney U test for not normally distributed continuous variables. [d] The PD cohort Innsbruck consists of PD patients of a tertiary center. The PD cohort Bruneck combines PD cases of a population-based sample. The Bruneck cohort consists of non-PD participants.

## Results

### *Prevalence of Sarcopenia and Frailty in PD Compared to the General Population*

Baseline characteristics of PD patients and the Bruneck cohort are presented in Table 1. Age and sex were not significantly different. Mean SARC-F score and CSHA CFS values were significantly higher in PD patients than the Bruneck cohort (both $p < 0.001$, Table 1). The prevalence of sarcopenia (SARC-F ≥4) was 55.8% ($n$ = 58) among PD patients and 8.2% ($n$ = 27) in the group of the Bruneck cohort ($p < 0.001$). The prevalence of frailty (CSHA CFS ≥5) was 35.6% ($n$ = 37) in PD patients compared with 5.2% ($n$ = 17) among non-PD participants ($p < 0.001$; Table 1). Table 2 shows baseline characteristics of male and female participants of the PD and Bruneck cohort separately. Mean SARC-F score and CSHA CSF values were significantly higher in both male and female PD patients (both $p < 0.001$; Table 2). Fifty percent ($n$ = 32) of male PD patients and 3.0% ($n$ = 5) of male Bruneck cohort participants were sarcopenic ($p < 0.001$). The prevalence of sarcopenia among female PD patients was 65.0% ($n$ = 26) and 13.5% ($n$ = 22) in all females of the Bruneck cohort ($p < 0.001$; Table 2). The prevalence of frailty was 31.3% ($n$ = 20) among male PD patients in comparison to 1.8% ($n$ = 3) among males of the Bruneck cohort ($p < 0.001$). Female PD patients showed a prevalence of frailty of 42.5% ($n$ = 17) and females of the group of the Bruneck cohort 8.6% ($n$ = 14) ($p < 0.001$; Table 2).

The Bruneck PD cohort was not significantly different in age and sex compared to the non-PD Bruneck participants (Table 1). Mean SARC-F score and CSHA CFS values were higher in the population-based PD patients than in the community-based non-PD cohort ($p$ = 0.032 for sarcopenia, $p$ = 0.001 for frailty; Table 1). Moreover, the prevalence of sarcopenia and frailty was higher in the Bruneck PD patients compared to the non-PD Bruneck participants (Table 1).

### *Demographic and Clinical Associations of Sarcopenia in PD*

Tables 3 and 4 summarize baseline values and associations of sarcopenia with clinical and demographic variables in PD patients. Using univariate regression models, sarcopenia was significantly associated with a higher Charlson Comorbidity Index, higher CSHA CFS values, frailty, recurrent falls, and the non-TD phenotype of PD (Fig. 1). Sarcopenic PD patients had a significantly longer disease duration, higher H&Y stages, and higher MDS-UPDRS Part I–III and motor sum scores (Fig. 1). In ad-

**Table 3.** Clinical characteristics of sarcopenia in PD patients

| | Total | Sarcopenia[a] | | |
|---|---|---|---|---|
| | (*n* =104) | no (*n* = 46) | yes (*n* = 58) | *p* value[e] |
| *Part 1: Demographic data* | | | | |
| Sex, *n* (%) | | | | 0.134 |
| Male | 64 (61.5) | 32 (69.6) | 32 (55.2) | |
| Female | 40 (38.5) | 14 (30.4) | 26 (44.8) | |
| Age, years | 73.8±5.2 (73.8) | 73.3±5.7 (73.2) | 74.2±4.8 (74.6) | 0.366 |
| BMI | 25.1±3.6 (24.6) | 25.0±3.3 (24.5) | 25.2±3.9 (25.1) | 0.884 |
| Charlson Comorbidity Index | 0.9±1.3 (0) | 0.4±0.8 (0.0) | 1.2±1.6 (1.0) | 0.001 |
| Disease duration, years | 12.00±7.9 (10.4) | 8.6±5.8 (7.7) | 14.7±8.3 (12.9) | <0.001 |
| LEDD, mg | 842.6±537.6 (850.0) | 741.8±452.9 (799.5) | 941.2±597.8 (935.0) | 0.080 |
| *Part 2: Frailty and associated factors* | | | | |
| CSHA CFS values | 3.8±1.7 (4.0) | 2.6±1.2 (2.0) | 4.8±1.5 (5.0) | <0.001 |
| Frailty[b], *n* (%) | 37 (35.6) | 3 (6.5) | 34 (58.6) | <0.001 |
| Handgrip strength, kg | 17.7±7.5 (17.0) | 19.6±6.1 (19.8) | 16.2±8.1 (15.1) | 0.004 |
| Gait velocity, m/s | 1.2±0.4 (1.2) | 1.4±0.3 (1.3) | 1.0±0.4 (1.0) | <0.001 |
| *Part 3: Scales and questionnaires for PD* | | | | |
| PD type | | | | |
| TD/non-TD type, *n* (%) | 29 (27.9)/75 (72.1) | 24 (52.2)/22 (47.8) | 5 (8.6)/53 (91.4) | <0.001 |
| Hoehn and Yahr stage | 2.5±1.0 (2.0) | 1.9±0.8 (2.0) | 2.9±0.9 (3.0) | <0.001 |
| MDS – UPDRS Sum Score (I–III) | 68.2±28.4 (68.5) | 49.4±20.0 (47.5) | 83.0±25.1 (82.5) | <0.001 |
| MDS – UPDRS Part I | 12.7±6.9 (12.0) | 10.4±6.1 (10.0) | 14.6±7.0 (14.5) | 0.002 |
| MDS – UPDRS Part II | 17.1±9.2 (16.5) | 11.4±6.6 (11.5) | 21.5±8.6 (19.5) | <0.001 |
| MDS – UPDRS Part III | 38.4±17.5 (34.0) | 27.6±11.3 (28.0) | 46.9±16.9 (47.0) | <0.001 |
| MDS – UPDRS Motor Sum Score (Parts II & III) | 55.5±24.8 (54.0) | 39.1±16.4 (37.0) | 68.5±22.7 (66.0) | <0.001 |
| MDS – UPDRS Part IV | 4.1±4.7 (2.0) | 3.3±4.4 (1.0) | 4.7±4.9 (3.0) | 0.166 |
| *Part 4: Characteristics of PD* | | | | |
| Recurrent falls[c], *n* (%) | 48 (46.2) | 19 (35.8) | 29 (60.4) | 0.014 |
| Depression, *n* (%) | 69 (66.3) | 29 (63.0) | 40 (69.0) | 0.526 |
| Cognitive impairment, *n* (%) | 47 (45.2) | 19 (41.3) | 28 (48.3) | 0.478 |
| Dementia, *n* (%) | 19 (18.3) | 3 (6.5) | 16 (27.6) | 0.006 |
| Orthostatic hypotension, *n* (%) | 49 (47.1) | 23 (50.0) | 26 (44.8) | 0.600 |
| Apathy, *n* (%) | 43 (41.3) | 17 (37.0) | 26 (44.8) | 0.418 |
| Fatigue, *n* (%) | 58 (55.8) | 20 (43.5) | 38 (65.5) | 0.025 |
| Hallucinations, *n* (%) | 19 (18.3) | 8 (17.4) | 11 (19.0) | 0.837 |
| *Part 5: Quality of life and dependency* | | | | |
| Nursing home placement[d], *n* (%) | 6 (5.8) | 0 (0) | 6 (10.3) | 0.034 |
| Level of dependency in ADL, *n* (%) | 64 (61.5) | 18 (40.0) | 46 (79.3) | <0.001 |
| PDQ-8 SI | 25.0±16.1 (21.9) | 18.9±14.2 (14.1) | 29.8±16.1 (28.1) | 0.001 |

Data are presented as mean ± standard deviation (median) or as stated. PD, Parkinson's disease; CI, confidence interval; BMI, body mass index; TD, tremor dominant; CSHA, Canadian Study on Health & Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose; ADL, activities of daily living; PDQ-8 SI, Parkinson's Disease Questionnaire-8 Summary Index.

We did not formally adjust analyses for multiple comparisons. If adjusting for multiple comparisons, the *p* values would be set at $p < 0.008$ (0.05/6) for Part 1, $p < 0.0125$ (0.05/4) for Part 2, $p < 0.0125$ (0.05/4) for Part 3, $p < 0.006$ (0.05/8) for Part 4, and $p < 0.017$ (0.05/3) for Part 5. *p* value for MDS-UPDRS Part I–III and motor sum score was set at $p < 0.0125$ (0.05/4).

Part 1 shows baseline demographic data of sarcopenic and non-sarcopenic PD patients (age, sex, BMI, Charlson Comorbidity Index). Part 2 shows the group comparisons with respect to frailty and associated factors of both geriatric syndromes (gait velocity and handgrip strength). Part 3 shows group comparisons between sarcopenic and nonsarcopenic PD patients regarding score values of scales and questionnaires for PD. Part 4 shows clinical characteristics of PD. Part 5 represents potential consequences of disease burden and quality of life in PD patients.

[a] Sarcopenia was assessed with the SARC-F score, sarcopenia: ≥4 points in the SARC-F Questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] Recurrent falls were defined as more than one fall within the last year. For the assessment of sarcopenia, falls were excluded from the sum score (using the same cut-off). [d] Fisher's exact test. [e] $\chi^2$ test for categorical variables, unpaired *t* test for normally distributed continuous variables, Mann-Whitney U test for not normally distributed continuous variables.

**Table 4.** Associations of clinical characteristics with sarcopenia

| | Sarcopenia[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | model 1 | | model 2 | | model 3 | | model 4 | |
| | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value |
| *Part 1: demographic data* | | | | | | | | |
| Sex | 0.54 (0.24 to 1.21) | 0.136 | NA | NA | NA | NA | NA | NA |
| Age (years) | 1.20 (0.81 to 1.78) | 0.363 | NA | NA | NA | NA | NA | NA |
| BMI | 1.03 (0.70 to 1.52) | 0.883 | 1.12 (0.74 to 1.69) | 0.594 | 0.96 (0.62 to 1.48) | 0.854 | 0.94 (0.61 to 1.46) | 0.792 |
| Charlson Comorbidity Index | 2.36 (1.32 to 4.24) | 0.004 | 2.69 (1.38 to 5.24) | 0.004 | NA | NA | NA | NA |
| Disease duration (years) | 2.67 (1.58 to 4.53) | <0.001 | 2.60 (1.52 to 4.42) | <0.001 | 2.45 (1.41 to 4.26) | 0.002 | 2.25 (1.24 to 4.07) | 0.008 |
| LEDD (mg) | 1.45 (0.95 to 2.21) | 0.084 | 1.53 (0.99 to 2.37) | 0.055 | 1.59 (1.01 to 2.48) | 0.044 | NA | NA |
| *Part 2: Frailty and associated factors* | | | | | | | | |
| CSHA CFS values | 6.71 (3.27 to 13.78) | <0.001 | 6.59 (3.24 to 13.40) | <0.001 | 6.29 (3.00 to 13.13) | <0.001 | 6.11 (2.88 to 12.98) | <0.001 |
| Frailty[b] | 20.31 (5.64 to 73.16) | <0.001 | 20.96 (5.63 to 77.98) | <0.001 | 18.93 (4.91 to 72.99) | <0.001 | 16.34 (4.17 to 64.06) | <0.001 |
| Handgrip strength (kg) | 0.61 (0.40 to 0.94) | 0.025 | 0.61 (0.35 to 1.05) | 0.075 | 0.60 (0.34 to 1.07) | 0.082 | 0.59 (0.33 to 1.07) | 0.080 |
| Gait velocity (m/s) | 0.38 (0.23 to 0.63) | <0.001 | 0.36 (0.20 to 0.63) | <0.001 | 0.42 (0.23 to 0.74) | 0.003 | 0.43 (0.24 to 0.79) | 0.006 |
| *Part 3: Scales and questionnaires for PD* | | | | | | | | |
| PD type | 0.09 (0.03 to 0.26) | <0.001 | 0.08 (0.03 to 0.26) | <0.001 | 0.10 (0.03 to 0.30) | <0.001 | 0.11 (0.03 to 0.35) | <0.001 |
| Hoehn and Yahr stage | 3.66 (2.11 to 6.36) | <0.001 | 4.19 (2.30 to 7.63) | <0.001 | 3.97 (2.15 to 7.33) | <0.001 | 4.41 (2.18 to 8.93) | <0.001 |
| MDS – UPDRS Sum Score (I–III) | 6.13 (3.03 to 21.41) | <0.001 | 6.34 (3.11 to 12.95) | <0.001 | 5.70 (2.77 to 11.73) | <0.001 | 6.44 (2.85 to 14.55) | <0.001 |
| MDS – UPDRS Part I | 1.97 (1.26 to 3.10) | 0.003 | 1.92 (1.21 to 3.03) | 0.005 | 1.77 (1.10 to 2.87) | 0.019 | 1.58 (0.96 to 2.60) | 0.074 |
| MDS – UPDRS Part II | 5.41 (2.68 to 10.90) | <0.001 | 5.38 (2.67 to 10.81) | <0.001 | 6.07 (2.79 to 13.19) | <0.001 | 6.55 (2.83 to 15.14) | <0.001 |
| MDS – UPDRS Part III | 5.16 (2.63 to 10.14) | <0.001 | 5.94 (2.89 to 12.21) | <0.001 | 5.16 (2.52 to 10.57) | <0.001 | 5.38 (2.43 to 11.94) | <0.001 |
| MDS – UPDRS Motor Sum Score (Parts II & III) | 6.81 (3.20 to 14.49) | <0.001 | 7.30 (3.37 to 15.78) | <0.001 | 6.49 (3.00 to 14.03) | <0.001 | 7.69 (3.16 to 18.72) | <0.001 |
| MDS – UPDRS Part IV | 1.37 (0.91 to 2.06) | 0.130 | 1.42 (0.94 to 2.15) | 0.096 | 1.37 (0.88 to 2.12) | 0.159 | 1.08 (0.65 to 1.79) | 0.769 |
| *Part 4: Characteristics of PD* | | | | | | | | |
| Recurrent falls[c] | 2.73 (1.22 to 6.12) | 0.015 | 2.85 (1.22 to 6.64) | 0.015 | 2.42 (1.01 to 5.79) | 0.048 | 4.14 (1.60 to 10.76) | 0.004 |
| Depression | 1.30 (0.58 to 2.95) | 0.526 | 1.07 (0.45 to 2.54) | 0.871 | 0.95 (0.38 to 2.37) | 0.909 | 1.00 (0.39 to 2.57) | 0.993 |
| Cognitive impairment | 1.33 (0.61 to 2.90) | 0.478 | 1.29 (0.58 to 2.91) | 0.535 | 1.10 (0.46 to 2.58) | 0.844 | 0.97 (0.40 to 2.37) | 0.945 |
| Dementia | 5.46 (1.48 to 20.12) | 0.011 | 6.27 (1.64 to 24.07) | 0.007 | 3.84 (0.92 to 16.12) | 0.066 | 3.67 (0.85 to 15.81) | 0.081 |
| Orthostatic hypotension | 0.81 (0.37 to 1.76) | 0.600 | 0.71 (0.32 to 1.59) | 0.410 | 0.61 (0.26 to 1.44) | 0.258 | 0.62 (0.25 to 1.49) | 0.281 |
| Apathy | 1.39 (0.63 to 3.06) | 0.419 | 1.26 (0.56 to 2.82) | 0.578 | 1.16 (0.49 to 2.73) | 0.739 | 1.11 (0.46 to 2.68) | 0.810 |
| Fatigue | 2.47 (1.11 to 5.47) | 0.026 | 2.34 (1.04 to 5.29) | 0.041 | 2.20 (0.93 to 5.22) | 0.074 | 1.98 (0.82 to 4.82) | 0.131 |
| Hallucinations | 1.11 (0.41 to 3.04) | 0.837 | 1.16 (0.42 to 3.20) | 0.780 | 1.14 (0.39 to 3.35) | 0.806 | 0.93 (0.31 to 2.85) | 0.904 |

PD, Parkinson's disease; OR, odds ratio; CI, confidence interval; BMI, body mass index; CSHA, Canadian Study on Health and Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose; NA, not applicable.

Model 1: binary logistic regression analysis unadjusted; model 2: binary logistic regression analysis adjusted for sex and age (in years), standard deviation (SD) corrected for continuous variables; model 3: binary logistic regression analysis adjusted for sex, age (in years, SD corrected), Charlson Comorbidity Index, SD corrected for continuous variables; model 4: binary logistic regression analysis adjusted for sex, age (in years, SD corrected), Charlson Comorbidity Index, and LEDD, SD corrected for continuous variables.

Regression analysis was not formally adjusted for multiple comparisons. If adjusting for multiple comparisons, the *p* values would be set at $p < 0.0083$ (0.05/6) for Part 1, $p < 0.0125$ (0.05/4) for Part 2, $p < 0.0125$ (0.05/4) for Part 3, and $p < 0.006$ (0.05/8) for Part 4. *p* value for MDS-UPDRS Part I–III and motor sum score was set at $p < 0.0125$ (0.05/4).

Part 1 shows baseline demographic data of sarcopenic and non-sarcopenic PD patients (age, sex, BMI, Charlson Comorbidity Index, disease duration, LEDD). Part 2 shows the group comparisons with respect to frailty and associated factors of both geriatric syndromes (gait velocity and handgrip strength). Part 3 shows group comparisons between sarcopenic and non-sarcopenic PD patients regarding score values of scales and questionnaires for PD. Part 4 shows clinical characteristics of PD.

[a] Sarcopenia was assessed with the SARC-F score, sarcopenia: ≥4 points in the SARC-F questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] Recurrent falls were defined as more than one fall within the last year. For the assessment of sarcopenia, falls were excluded in the sum score with the same cut-off.

Gerontology 2019;65:216–228
DOI: 10.1159/000492572

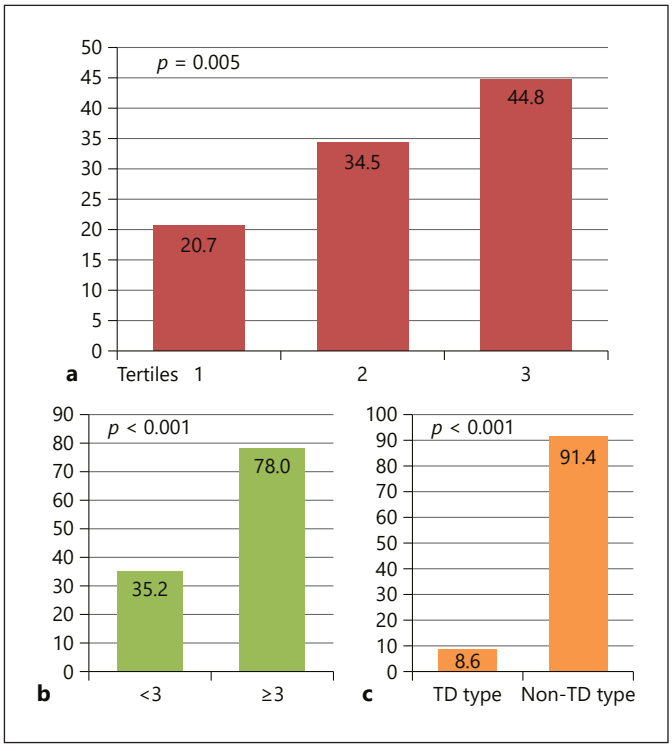


**Fig. 1.** Prevalence of sarcopenia according to disease-specific characteristics. Prevalence is given in percent. **a** Prevalence of sarcopenia according to duration of Parkinson's disease (PD). 1, disease duration tertile 1: 0.7–7.3 years; 2, disease duration tertile 2: 7.3–13.4 years; 3, disease duration tertile 3: 13.4–38.3 years. **b** Prevalence of sarcopenia according to Hoehn and Yahr stages (<3 and ≥3), separated by the median. **c** Prevalence of tremor-dominant (TD) and non-TD type of PD in sarcopenia. Figures were created using Microsoft® Excel (version 15.41).

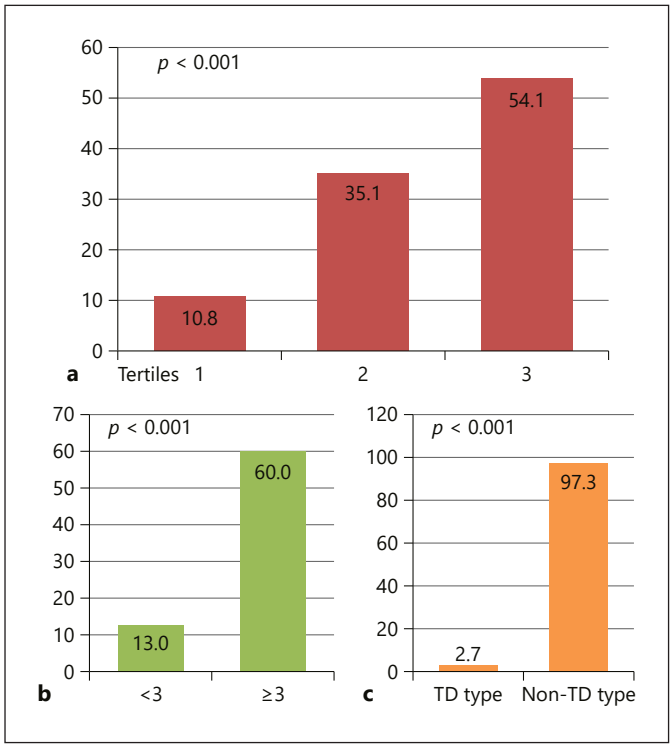


**Fig. 2.** Prevalence of frailty according to disease-specific characteristics. Prevalence is given in percent. **a** Prevalence of frailty according to duration of Parkinson's disease (PD). 1, disease duration tertile 1: 0.7–7.3 years; 2, disease duration tertile 2: 7.3–13.4 years; 3, disease duration tertile 3: 13.4–38.3 years. **b** Prevalence of frailty according to Hoehn and Yahr stages (<3 and ≥3), separated by the median. **c** Prevalence of tremor-dominant (TD) and non-TD type of PD in frailty. Figures were created using Microsoft® Excel (version 15.41).

dition, the sarcopenia group was more likely to be demented and to suffer from fatigue (Tables 3, and 4). When adjusting for the covariates sex, age, comorbidities, and LEDD, multivariate logistic regression analysis showed significant associations of sarcopenia with higher CHSA CFS values, frailty, longer disease duration, higher H&Y stages, higher MDS-UPDRS Part II and III and motor sum scores, higher LEDD, recurrent falls, and the non-TD phenotype of PD (Tables 3 and 4). Handgrip strength and gait velocity were lower in the sarcopenia group, and gait velocity showed a significantly negative association with sarcopenia in a multivariate regression model after adjustment for age, sex, comorbidities, and LEDD (Tables 3 and 4). Moreover, sarcopenic PD patients were more often in a nursing home, required more help than the non-sarcopenia group, and had higher PDQ-8 score values (Tables 3 and 4).

*Demographic and Clinical Associations of Frailty in PD*

The baseline characteristics and evaluation of associated factors for frailty in PD patients are shown in Tables 5 and 6. In univariate regression models, frailty was significantly associated with older age, a higher Charlson Comorbidity Index, higher SARC-F score values and therefore sarcopenia, recurrent falls, and the non-TD type of PD (Fig. 2). The disease duration was significantly longer, the H&Y stage was higher, the LEDD was higher, and all MDS-UPDRS scores and the motor sum score were higher among frail compared with non-frail PD patients (Fig. 2). In addition, cognitive impairment, dementia, fatigue, and hallucinations were independently associated with frailty (Tables 5 and 6). When adjusting for sex, age, comorbidities, and LEDD, the multivariate logistic regression analysis revealed significant associa-

**Table 5.** Clinical characteristics of frailty in PD patients

| | Total | Frailty[b] | | |
|---|---|---|---|---|
| | (*n* = 104) | no (*n* = 67) | yes (*n* =37) | *p* value[e] |
| *Part 1: Demographic data* | | | | |
| Sex, *n* (%) | | | | 0.244 |
| Male | 64 (61.5) | 44 (65.7) | 20 (54.1) | |
| Female | 40 (38.5) | 23 (34.3) | 17 (45.9) | |
| Age, years | 73.8±5.2 (73.8) | 72.9±5.4 (73.3) | 75.4±4.6 (76.2) | 0.022 |
| BMI | 25.1±3.6 (24.6) | 25.4±3.7 (24.6) | 24.5±3.5 (21.6) | 0.203 |
| Charlson Comorbidity Index | 0.9±1.3 (0) | 0.6±1.0 (0.0) | 1.4±1.7 (1.0) | 0.004 |
| Disease duration, years | 12.00±7.9 (10.4) | 9.6±6.3 (8.3) | 16.5±8.5 (16.4) | <0.001 |
| LEDD, mg | 842.6±537.6 (850.0) | 754.2±508.7 (700.0) | 1,035.2±557.4 (1,137.5) | 0.021 |
| *Part 2: Sarcopenia and associated factors* | | | | |
| SARC-F score values | 4.3±3.0 (4.0) | 2.8±2.1 (3.0) | 7.1±2.1 (8.0) | <0.001 |
| Sarcopenia[a], *n* (%) | 58 (55.8) | 24 (35.8) | 34 (91.9) | <0.001 |
| Handgrip strength, kg | 17.7±7.5 (17.0) | 19.6±6.8 (18.6) | 13.8±7.4 (12.8) | <0.001 |
| Gait velocity, m/s | 1.2±0.4 (1.2) | 1.3±0.4 (1.3) | 0.9±0.4 (0.9) | <0.001 |
| *Part 3: Scales and questionnaires for PD* | | | | |
| PD type | | | | |
| TD/non-TD type, *n* (%) | 29 (27.9)/75 (72.1) | 28 (41.8)/39 (58.2) | 1 (2.7)/36 (97.3) | <0.001 |
| Hoehn and Yahr stage | 2.5±1.0 (2.0) | 2.0±0.8 (2.0) | 3.3±0.9 (3.0) | <0.001 |
| MDS – UPDRS Sum Score (I–III) | 68.2±28.4 (68.5) | 54.5±21.0 (52.0) | 93.0±22.6 (93.0) | <0.001 |
| MDS – UPDRS Part I | 12.7±6.9 (12.0) | 11.1±6.4 (10.0) | 15.7±6.8 (16.0) | 0.001 |
| MDS – UPDRS Part II | 17.1±9.2 (16.5) | 12.7±6.2 (14.0) | 25.0±8.5 (25.0) | <0.001 |
| MDS – UPDRS Part III | 38.4±17.5 (34.0) | 30.7±13.6 (31.0) | 52.3±15.1 (52.0) | <0.001 |
| MDS – UPDRS Motor Sum Score (Parts II & III) | 55.5±24.8 (54.0) | 43.4±17.9 (43.0) | 77.3±20.5 (77.0) | <0.001 |
| MDS – UPDRS Part IV | 4.1±4.7 (2.0) | 3.1±3.9 (1.0) | 5.9±5.6 (5.0) | 0.009 |
| *Part 4: Characteristics of PD* | | | | |
| Recurrent falls[c], *n* (%) | 48 (46.2) | 23 (35.4) | 25 (69.4) | 0.001 |
| Depression, *n* (%) | 69 (66.3) | 42 (62.7) | 27 (73.0) | 0.288 |
| Cognitive impairment, *n* (%) | 47 (45.2) | 23 (34.3) | 24 (64.9) | 0.003 |
| Dementia, *n* (%) | 19 (18.3) | 4 (6.0) | 15 (40.5) | <0.001 |
| Orthostatic hypotension, *n* (%) | 49 (47.1) | 32 (47.8) | 17 (45.9) | 0.859 |
| Apathy, *n* (%) | 43 (41.3) | 26 (38.8) | 17 (45.9) | 0.479 |
| Fatigue, *n* (%) | 58 (55.8) | 32 (47.8) | 26 (70.3) | 0.027 |
| Hallucinations, *n* (%) | 19 (18.3) | 8 (11.9) | 11 (29.7) | 0.025 |
| *Part 5: Quality of life and dependency* | | | | |
| Nursing home placement[d], *n* (%) | 6 (5.8) | 1 (1.5) | 5 (13.5) | 0.022 |
| Level of dependency in ADL, *n* (%) | 64 (61.5) | 29 (43.9) | 35 (94.6) | <0.001 |
| PDQ-8 SI | 25.0±16.1 (21.9) | 20.7±15.7 (18.8) | 32.8±14.0 (31.3) | <0.001 |

Data are presented as mean ± standard deviation (median) or as stated. PD, Parkinson's disease; CI, confidence interval; BMI, body mass index; TD, tremor dominant; CSHA, Canadian Study on Health & Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose; ADL, activities of daily living; PDQ-8 SI, Parkinson's Disease Questionnaire-8 Summary Index.

We did not formally adjust analyses for multiple comparisons. If adjusting for multiple comparisons, the *p* values would be set at $p < 0.008$ (0.05/6) for Part 1, $p < 0.0125$ (0.05/4) for Part 2, $p < 0.0125$ (0.05/4) for Part 3, $p < 0.006$ (0.05/8) for Part 4, and $p < 0.017$ (0.05/3) for Part 5. *p* value for MDS-UPDRS Part I–III and motor sum score was set at $p < 0.0125$ (0.05/4).

Part 1 shows baseline demographic data of frail and non-frail PD patients (age, sex, BMI, Charlson Comorbidity Index). Part 2 shows the group comparisons with respect to sarcopenia and associated factors of both geriatric syndromes (gait velocity and handgrip strength). Part 3 shows group comparisons between frail and non-frail PD patients regarding score values of scales and questionnaires for PD. Part 4 shows clinical characteristics of PD. Part 5 represents potential consequences of disease burden and quality of life in PD patients.

[a] Sarcopenia was assessed with the SARC-F score, sarcopenia: ≥ 4points in the SARC-F Questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] Recurrent falls were defined as more than one fall within the last year. For the assessment of sarcopenia, falls were excluded from the sum score (using the same cut-off). [d] Fisher's exact test. [e] $\chi^2$ test for categorical variables, unpaired *t* test for normally distributed continuous variables, Mann-Whitney U test for not normally distributed continuous variables.

**Table 6.** Associations between clinical characteristics and frailty

| | Frailty[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | model 1 | | model 2 | | model 3 | | model 4 | |
| | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value |
| *Part 1: Demographic data* | | | | | | | | |
| Sex | 0.61 (0.27 to 1.40) | 0.245 | NA | NA | NA | NA | NA | NA |
| Age (years) | 1.10 (1.01 to 1.19) | 0.025 | NA | NA | NA | NA | NA | NA |
| BMI | 0.76 (0.50 to 1.16) | 0.202 | 0.86 (0.55 to 1.34) | 0.493 | 0.73 (0.45 to 1.18) | 0.202 | 0.71 (0.43 to 1.16) | 0.173 |
| Charlson Comorbidity Index | 1.90 (1.21 to 2.98) | 0.005 | 1.76 (1.10 to 2.81) | 0.019 | NA | NA | NA | NA |
| Disease duration (years) | 2.68 (1.63 to 4.39) | <0.001 | 2.62 (1.58 to 4.34) | <0.001 | 2.43 (1.47 to 4.02) | 0.001 | 2.16 (1.30 to 3.60) | 0.003 |
| LEDD (mg) | 1.67 (1.06 to 2.64) | 0.027 | 1.89 (1.15 to 3.12) | 0.013 | 1.97 (1.17 to 3.31) | 0.010 | NA | NA |
| *Part 2: Sarcopenia and associated factors* | | | | | | | | |
| SARC-F score values | 10.50 (4.54 to 24.28) | <0.001 | 13.32 (4.86 to 36.45) | <0.001 | 12.89 (4.66 to 35.62) | <0.001 | 11.84 (4.29 to 32.64) | <0.001 |
| Sarcopenia[a] | 20.31 (5.64 to 73.16) | <0.001 | 22.06 (5.76 to 84.48) | <0.001 | 19.28 (4.91 to 75.68) | <0.001 | 16.87 (4.18 to 68.14) | <0.001 |
| Handgrip strength (kg) | 0.38 (0.22 to 0.66) | 0.001 | 0.31 (0.15 to 0.63) | 0.001 | 0.29 (0.14 to 0.61) | 0.001 | 0.30 (0.14 to 0.63) | 0.002 |
| Gait velocity (m/s) | 0.27 (0.15 to 0.50) | <0.001 | 0.28 (0.15 to 0.54) | <0.001 | 0.30 (0.15 to 0.59) | <0.001 | 0.31 (0.15 to 0.62) | 0.001 |
| *Part 3: Scales and Questionnaires for PD* | | | | | | | | |
| PD type | 0.04 (0.01 to 0.30) | 0.002 | 0.02 (0.00 to 0.21) | 0.001 | 0.03 (0.00 to 0.25) | 0.002 | 0.03 (0.00 to 0.31) | 0.003 |
| Hoehn and Yahr stage | 6.21 (3.02 to 12.78) | <0.001 | 7.56 (3.35 to 17.07) | <0.001 | 7.34 (3.23 to 16.72) | <0.001 | 7.47 (3.04 to 18.39) | <0.001 |
| MDS – UPDRS Sum Score (I–III) | 10.36 (4.13 to 26.02) | <0.001 | 11.54 (4.25 to 31.31) | <0.001 | 11.21 (4.08 to 30.83) | <0.001 | 10.99 (3.88 to 31.15) | <0.001 |
| MDS – UPDRS Part I | 2.03 (1.30 to 3.19) | 0.002 | 2.07 (1.29 to 3.32) | 0.003 | 1.95 (1.19 to 3.18) | 0.008 | 1.70 (1.02 to 2.84) | 0.042 |
| MDS – UPDRS Part II | 10.86 (4.07 to 28.97) | <0.001 | 12.72 (4.33 to 37.36) | <0.001 | 14.17 (4.51 to 44.56) | <0.001 | 13.50 (4.22 to 43.14) | <0.001 |
| MDS – UPDRS Part III | 5.60 (2.85 to 11.01) | <0.001 | 6.93 (3.14 to 15.30) | <0.001 | 6.48 (2.95 to 14.22) | <0.001 | 5.75 (2.58 to 12.81) | <0.001 |
| MDS – UPDRS Motor Sum Score (Parts II & III) | 9.95 (4.04 to 24.51) | <0.001 | 12.96 (4.50 to 37.30) | <0.001 | 12.49 (4.32 to 36.12) | <0.001 | 11.89 (4.06 to 34.87) | <0.001 |
| MDS - UPDRS Part IV | 1.82 (1.20 to 2.76) | 0.005 | 2.04 (1.30 to 3.18) | 0.002 | 2.00 (1.26 to 3.16) | 0.003 | 1.55 (0.93 to 2.59) | 0.091 |
| *Part 4: Characteristics of PD* | | | | | | | | |
| Recurrent falls[c] | 4.15 (1.73 to 9.93) | 0.001 | 4.85 (1.91 to 12.31) | 0.001 | 4.15 (1.60 to 10.77) | 0.003 | 3.43 (1.27 to 9.26) | 0.015 |
| Depression | 1.61 (0.67 to 3.87) | 0.290 | 1.26 (0.50 to 3.18) | 0.627 | 1.27 (0.48 to 3.33) | 0.632 | 1.40 (0.50 to 3.94) | 0.525 |
| Cognitive impairment | 3.53 (1.52 to 8.20) | 0.003 | 3.33 (1.39 to 8.01) | 0.007 | 3.30 (1.34 to 8.15) | 0.010 | 3.40 (1.32 to 8.78) | 0.011 |
| Dementia | 10.74 (3.22 to 35.83) | <0.001 | 11.95 (3.32 to 43.07) | <0.001 | 9.70 (2.57 to 36.67) | 0.001 | 11.26 (2.78 to 45.56) | 0.001 |
| Orthostatic hypotension | 0.93 (0.42 to 2.08) | 0.859 | 0.79 (0.34 to 1.84) | 0.586 | 0.70 (0.29 to 1.68) | 0.422 | 0.71 (0.29 to 1.79) | 0.472 |
| Apathy | 1.34 (0.60 to 3.02) | 0.480 | 1.20 (0.52 to 2.78) | 0.677 | 1.20 (0.50 to 2.85) | 0.687 | 1.18 (0.48 to 2.93) | 0.718 |
| Fatigue | 2.59 (1.10 to 6.06) | 0.029 | 2.26 (0.94 to 5.43) | 0.068 | 2.17 (0.88 to 5.35) | 0.094 | 1.84 (0.72 to 4.72) | 0.202 |
| Hallucinations | 3.12 (1.12 to 8.66) | 0.029 | 3.44 (1.20 to 9.87) | 0.022 | 3.66 (1.23 to 10.85) | 0.019 | 3.16 (1.02 to 9.83) | 0.046 |

PD, Parkinson's disease; OR, odds ratio; CI, confidence interval; BMI, body mass index; CSHA, Canadian Study on Health and Aging; CFS, Clinical Frailty Scale; SARC-F, a simple five-item questionnaire for sarcopenia; MDS-UPDRS, Movement Disorder Society-Unified Parkinson´s Disease Rating Scale; LEDD, levodopa equivalent daily dose; NA, not applicable.

Model 1: binary logistic regression analysis unadjusted; model 2: binary logistic regression analysis adjusted for sex and age (in years), standard deviation (SD) corrected for continuous variables; model 3: binary logistic regression analysis adjusted for sex, age (in years, SD corrected), Charlson Comorbidity Index, SD corrected for continuous variables; model 4: binary logistic regression analysis adjusted for sex, age (in years, SD corrected), Charlson Comorbidity Index, and LEDD, SD corrected for continuous variables.

Regression analysis was not formally adjusted for multiple comparisons. If adjusting for multiple comparisons, the *p* values would be set at $p < 0.0083$ (0.05/6) for Part 1, $p < 0.0125$ (0.05/4) for Part 2, $p < 0.0125$ (0.05/4) for Part 3, and $p < 0.006$ (0.05/8) for Part 4. *p* value for MDS-UPDRS Part I–III and motor sum score was set at $p < 0.0125$ (0.05/4).

Part 1 shows baseline demographic data of frail and non-frail PD patients (age, sex, BMI, Charlson Comorbidity Index, disease duration, LEDD). Part 2 shows the group comparisons with respect to sarcopenia and associated factors of both geriatric syndromes (gait velocity and handgrip strength). Part 3 shows group comparisons between frail and non-frail PD patients regarding score values of scales and questionnaires for PD. Part 4 shows clinical characteristics of PD.

[a] Sarcopenia was assessed with the SARC-F score, sarcopenia: ≥4 points in the SARC-F questionnaire. [b] Frailty was assessed with the CSHA CFS, frailty: ≥5 points in the CSHA CFS. [c] Recurrent falls were defined as more than one fall within the last year. For the assessment of sarcopenia, falls were excluded in the sum score with the same cut-off.

tions of frailty with higher SARC-F score values, sarcopenia, longer disease duration, the non-TD type of PD, higher H&Y stages, higher MDS-UPDRS Part I–III and motor sum scores, higher LEDD, and recurrent falls. Cognitive impairment, dementia, and hallucinations also remained associated with frailty after adjustment for sex, age, and comorbidities (Tables 5 and 6). Handgrip strength and gait velocity were lower in the frailty group and showed an inverse association with frailty in multivariate regression models after adjustment for age, sex, comorbidities, and LEDD (Tables 5 and 6). Furthermore, frail PD patients were more frequently institutionalized and dependent, and had higher PDQ-8 sum score values (Tables 5 and 6).

## Discussion

Previous studies attempting to assess the prevalence of frailty and sarcopenia in PD samples have yielded inconsistent results of 32.6% for frailty and ranging from 6.6 to 40.7% for sarcopenia [31–33]. Discrepancies were most likely due to significant differences in patient selection and methods used [31–33]. In our study, we found that both sarcopenia and frailty were significantly more common in PD patients compared with the general elderly population. The prevalence rates of sarcopenia and frailty in our general population-based sample were within previously reported ranges, contributing to the validity of the screening tools used [4, 6–12]. The prevalence rates of sarcopenia and frailty were slightly lower in the community-based PD cohort compared to the PD cohort recruited in the tertiary center. However, their 95% CIs overlapped, supporting the high prevalence rates of sarcopenia and frailty in PD.

Both sarcopenia and frailty were associated with clinical characteristics of advanced PD, in particular longer disease duration, higher H&Y stages, higher motor impairment and non-motor burden including dementia, falls, reduced QoL, as well as institutionalization. This is in keeping with findings of previous studies assessing sarcopenia and frailty in PD patients [31–33]. In addition, sarcopenia and frailty were associated with a non-TD presentation. Similar to observations in non-PD populations [2, 3], PD subjects with sarcopenia and frailty had reductions in gait velocity and handgrip strength compared to those without. Grip strength is known to be reduced in PD patients and to correlate with age, UPDRS motor scores, and H&Y stages [34]. Interestingly, there was a positive association of frailty with hallucinations in our PD cohort, and we found common risk factors for the development of both [35] in our PD cohort as well.

Altered neuromuscular control resulting in gait difficulties, a lower gait velocity, and falls has been described in PD patients and is also associated with sarcopenia and frailty [36]. A high frequency of falls was more commonly reported by PD patients with both sarcopenia and frailty compared to those without, underlining the importance of screening for falls in PD. PD patients with both frailty and sarcopenia more commonly presented with a non-TD phenotype, which appears consistent with faster disease progression and faster rate of cognitive decline in non-TD versus TD patients [37, 38]. Overall, sarcopenia and frailty in our study were associated with motor and non-motor milestones of advanced PD. Progressive disability in PD is driven by the evolution of treatment-resistant motor symptoms such as freezing of gait, postural instability, and recurrent falls, as well as by increasingly prevalent and bothersome non-motor symptoms which are a major determinant of QoL, and of institutionalization [38]. Indeed, QoL was significantly impaired in PD patients with both sarcopenia and frailty, and affected patients were more commonly institutionalized. A potential drawback of our study is the lack of adjustment for multiple comparisons. However, main outcomes of our study would largely survive adjustment for multiple comparisons as indicated in the legends of Tables 3–6.

Our assessment has several strengths including the relatively large cohort of consecutively recruited PD patients and a cohort of elderly participants comparable in age and sex, representing a typical elderly western population with respect to demographic and lifestyle characteristics as well as comorbidities. Sarcopenia, frailty, and PD-related motor and non-motor symptoms were carefully and comprehensively evaluated according to established questionnaires and rating scales. There are, however, limitations to this study. While the Bruneck cohort was population-based, the PD cohort was recruited in a university hospital. Thus, the prevalence of sarcopenia and frailty in PD as well as their clinical and demographic associations are representative for tertiary center PD patients in more advanced disease stages [39]. Therefore, the prevalence rates may not be generalizable to the overall PD population. However, our results were reproducible in an unselected PD population (Bruneck PD cohort) with sarcopenia and frailty being significantly more prevalent in PD patients compared to non-PD subjects similar in age and sex, which adds further strength to our study (Table 1).

The cross-sectional nature of the present study did not allow for a prospective assessment of risk factors for sarcopenia and frailty in PD. A prospective follow-up examination of our well-described PD cohort may give additional information on the association of sarcopenia and frailty with potential clinical milestones in PD as well as nursing home placement and mortality. Moreover, this would aid in assessing the effect size of the influence of the three syndromes on each other. Symptoms of PD may overlap with characteristics of sarcopenia and frailty, but this also applies to other chronic neurological and non-neurological diseases in which the geriatric syndromes have been assessed so far (e.g., stroke, cardiovascular diseases, cancer, or osteoporosis) [13, 16, 17, 33, 40]. As PD could be seen as a paradigmatic disease for frail and sarcopenic elderly, an insight into the underlying pathophysiology could be provided by prospective long-term studies.

Finally, as the SARC-F score and the CSHA CFS are screening tools, a positive screening should ideally lead to further examination to confirm the diagnosis of sarcopenia and frailty. The absence of a gold standard for the diagnosis and the need for additional measurements to assess sarcopenia and frailty limit evaluation in clinical routine [33]. Moreover, the application of these screening tools does not allow determining different stages of sarcopenia, and the assessment of associations of different stages of frailty with PD is beyond the scope of this paper. While sarcopenia is defined by the loss of muscle mass and a constraint in one functional criterion such as muscle strength or physical performance (e.g., gait velocity), severe sarcopenia is defined as impairment in all three criteria [2]. Two models are currently proposed to determine frailty: the cumulative deficit model [4] and the physical phenotype model of frailty [1]. The latter is the most widely used definition and includes unintentional weight loss, weakness, exhaustion, low gait velocity, and low weekly energy expenditure [3]. Accordingly, frailty is defined as an impairment in three or more categories, while a prefrail stage is characterized by fulfilling one or two criteria [3]. The aim of our study was to screen for the two geriatric syndromes in PD patients and to compare their prevalence with a control group. We did not assess muscle mass in this study, but found that gait speed and handgrip strength were positively associated with sarcopenia and frailty in our study. This adds to the validity of the screening tools used in this study to assess both geriatric syndromes in PD patients. The advantage of using screening tools in patients is the easy and rapid identification of people at risk, which may then be followed by targeted application of additional assessments. Future research studies should examine the feasibility of the use of screening tools for sarcopenia and frailty in PD patients and use the operational criteria to determine these geriatric syndromes in PD populations. As there are different stages of sarcopenia and frailty, future studies should also assess their prevalence in PD as this might have major implications for rehabilitation approaches.

To the best of our knowledge, there is no controlled study reporting on the prevalence and clinical associations of sarcopenia and frailty in PD. Our study suggests that both sarcopenia and frailty are common in PD patients and are associated with more advanced disease stages, higher motor impairment and non-motor burden, falls, reduced QoL, as well as institutionalization. Importantly, sarcopenia and frailty seem to be a typical finding in advanced PD patients. The results of our study should increase awareness among clinicians of the high prevalence and disease burden of sarcopenia and frailty in PD. Those at risk for sarcopenia and frailty according to the screening tools should be further assessed to confirm the diagnosis. Moreover, future studies should identify risk factors for sarcopenia and frailty in PD to discover feasible therapeutic options for prevention and mitigation of both.


## Acknowledgment

We want to thank all participants who voluntarily consented to enclose information for this evaluation.


## Statement of Ethics

The study protocols were approved by the local ethics committees. All participants gave written informed consent. The interviews and examinations were carried out in accordance to the principles expressed in the Declaration of Helsinki. The authors certify that they comply with ethical guidelines for authorship and publishing of the journal.

## Disclosure Statement

Marina Peball, Philipp Mahlknecht, Mario Werkmann, Kathrin Marini, Franziska Murr, Helga Herzmann, Heike Stockner, Roberto de Marzi, Beatrice Heim, Atbin Djamshidian, Peter Willeit, Johann Willeit, Stefan Kiechl, Dora Valent, Florian Krismer, Gregor K. Wenning, Michael Nocker, Katherina Mair, Werner Poewe, and Klaus Seppi declare that they have no conflict of interest.

## Funding Sources

The Bruneck Study was supported by the "Pustertaler Verein zur Prävention von Herz- und Hirngefässerkrankungen," the Gesundheitsbezirk Bruneck, the mayor of Bruneck, and the "Assessorat für Gesundheit," Province of Bolzano, Italy. The 10-year follow up was supported by the Austrian Society of Neurology (ÖGN). Furthermore, the Bruneck Study was supported by the excellence initiative (Competence Centers for Excellent Technologies – COMET) of the Austrian Research Promotion Agency FFG: "Research Center of Excellence in Vascular Ageing – Tyrol, VASCage" (K-Project No. 843536) funded by the BMVIT, BMWFW, Wirtschaftsagentur Wien, and Standortagentur Tirol. Kathrin Marini and Philipp Mahlknecht are partially supported by a grant from the Tyrolean Science Fund (TWF).

## Author Contributions

1. Research project: A, conception; B, organization; C, execution
2. Statistical analysis: A, design; B, execution; C, review and critique
3. Manuscript: A, writing of the first draft; B, review and critique.

*MP*: 1A, 1B, 1C, 2A, 2B, 3A. *PM*: 1A, 1B, 1C, 2A, 2B, 2C, 3B. *KS*: 1A, 1B, 2A, 2B, 2C, 3B. *MW*, *KM*, *FM*, *HH*, *HS*, *RD*, *BH*, *AD*, *MN*, *KM*: 1B, 1C, 3B. *FK*: 2C, 3B. *DV*: 3B. *PW*, *JW*, *SK, GKW*: 1C, 3C, 3B. *WP*: 1A, 2C, 3B.

## References

1 Rosenberg IH, Roubenoff R: Stalking sarcopenia. Ann Intern Med 1995;123:727–728.
2 Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinkova E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People: Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412–423.
3 Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group: Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–M156.
4 Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A: A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.
5 Malmstrom TK, Morley JE: SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J Am Med Dir Assoc 2013;14:531–532.
6 Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE: SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle 2016;7:28–36.
7 Wu TY, Liaw CK, Chen FC, Kuo KL, Chie WC, Yang RS: Sarcopenia screened with SARC-F questionnaire is associated with quality of life and 4-year mortality. J Am Med Dir Assoc 2016;17:1129–1135.
8 Kemmler W, Sieber C, Freiberger E, von Stengel S: The SARC-F Questionnaire: diagnostic overlap with established sarcopenia definitions in older German men with sarcopenia. Gerontology 2017;63:411–416.
9 Woo J, Leung J, Morley JE: Validating the SARC-F: a suitable community screening tool for sarcopenia? J Am Med Dir Assoc 2014;15:630–634.
10 Woo J, Leung J, Morley JE: Defining sarcopenia in terms of incident adverse outcomes. J Am Med Dir Assoc 2015;16:247–252.
11 Theou O, Brothers TD, Mitnitski A, Rockwood K: Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. J Am Geriatr Soc 2013;61:1537–1551.
12 Kelly S, O'Brien I, Smuts K, O'Sullivan M, Warters A: Prevalence of frailty among community dwelling older adults in receipt of low level home support: a cross-sectional analysis of the North Dublin Cohort. BMC Geriatr 2017;17:121.
13 Angulo J, El Assar M, Rodriguez-Manas L: Frailty and sarcopenia as the basis for the phenotypic manifestation of chronic diseases in older adults. Mol Aspects Med 2016;50:1–32.
14 Musso CG, Jauregui JR, Macias Nunez JF: Frailty phenotype and chronic kidney disease: a review of the literature. Int Urol Nephrol 2015;47:1801–1807.
15 Montano-Loza AJ: Clinical relevance of sarcopenia in patients with cirrhosis. World J Gastroenterol 2014;20:8061–8071.
16 Meza-Junco J, Montano-Loza AJ, Baracos VE, Prado CM, Bain VG, Beaumont C, Esfandiari N, Lieffers JR, Sawyer MB: Sarcopenia as a prognostic index of nutritional status in concurrent cirrhosis and hepatocellular carcinoma. J Clin Gastroenterol 2013;47:861–870.
17 Binkley N, Buehring B: Beyond FRAX: it's time to consider "sarco-osteopenia." J Clin Densitom 2009;12:413–416.
18 Tan LF, Lim ZY, Choe R, Seetharaman S, Merchant R: Screening for frailty and sarcopenia among older persons in medical outpatient clinics and its associations with healthcare burden. J Am Med Dir Assoc 2017;18:583–587.
19 Tanaka S, Kamiya K, Hamazaki N, Matsuzawa R, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Matsunaga A, Masuda T, Ako J: Utility of SARC-F for assessing physical function in elderly patients with cardiovascular disease. J Am Med Dir Assoc 2017;18:176–181.
20 Ida S, Nakai M, Ito S, Ishihara Y, Imataka K, Uchida A, Monguchi K, Kaneko R, Fujiwara R, Takahashi H, Murata K: Association between sarcopenia and mild cognitive impairment using the Japanese version of the SARC-F in elderly patients with diabetes. J Am Med Dir Assoc 2017;18:809 e809–809 e813.
21 Hughes AJ, Daniel SE, Kilford L, Lees AJ: Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–184.
22 Wenning GK, Kiechl S, Seppi K, Muller J, Hogl B, Saletu M, Rungger G, Gasperi A, Willeit J, Poewe W: Prevalence of movement disorders in men and women aged 50–89 years (Bruneck Study cohort): a population-based study. Lancet Neurol 2005;4:815–820.
23 Cao L, Chen S, Zou C, Ding X, Gao L, Liao Z, Liu G, Malmstrom TK, Morley JE, Flaherty JH, An Y, Dong B: A pilot study of the SARC-F scale on screening sarcopenia and physical disability in the Chinese older people. J Nutr Health Aging 2014;18:277–283.
24 Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE: Systematic review of levodopa dose equivalency reporting in Parkinson's disease. Mov Disord 2010;25:2649–2653.
25 Stebbins GT, Goetz CG, Burn DJ, Jankovic J, Khoo TK, Tilley BC: How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: comparison with the unified Parkinson's disease rating scale. Mov Disord 2013;28:668–670.

26 Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N: The PDQ-8: Development and validation of a short-form Parkinson's disease questionnaire. Psychol Health 1997;12:805–814.
27 EuroQol Group: EuroQol – a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.
28 Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383.
29 Mahlknecht P, Kiechl S, Bloem BR, Willeit J, Scherfler C, Gasperi A, Rungger G, Poewe W, Seppi K: Prevalence and burden of gait disorders in elderly men and women aged 60–97 years: a population-based study. PLoS One 2013;8:e69627.
30 Agresti A, Coull BA: Approximate is better than "exact" for interval estimation of binomial proportions. Am Stat 1998;52:119–126.
31 Ahmed NN, Sherman SJ, Vanwyck D: Frailty in Parkinson's disease and its clinical implications. Parkinsonism Relat Disord 2008;14:334–337.
32 Barichella M, Pinelli G, Iorio L, Cassani E, Valentino A, Pusani C, Ferri V, Bolliri C, Pasqua M, Pezzoli G, Frazzitta G, Cereda E: Sarcopenia and dynapenia in patients with parkinsonism. J Am Med Dir Assoc 2016;17:640–646.
33 Vetrano DL, Pisciotta MS, Laudisio A, Lo Monaco MR, Onder G, Brandi V, Fusco D, Di Capua B, Ricciardi D, Bernabei R, Zuccala G: Sarcopenia in Parkinson disease: comparison of different criteria and association with disease severity. J Am Med Dir Assoc 2018;19:523–527.
34 Roberts HC, Syddall HE, Butchart JW, Stack EL, Cooper C, Sayer AA: The association of grip strength with severity and duration of Parkinson's: a cross-sectional study. Neurorehabil Neural Repair 2015;29:889–896.
35 Zhu K, van Hilten JJ, Putter H, Marinus J: Risk factors for hallucinations in Parkinson's disease: results from a large prospective cohort study. Mov Disord 2013;28:755–762.
36 Pickering RM, Grimbergen YA, Rigney U, Ashburn A, Mazibrada G, Wood B, Gray P, Kerr G, Bloem BR: A meta-analysis of six prospective studies of falling in Parkinson's disease. Mov Disord 2007;22:1892–1900.
37 Jankovic J, Kapadia AS: Functional decline in Parkinson disease. Arch Neurol 2001;58:1611–1615.
38 Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, Schrag AE, Lang AE: Parkinson disease. Nat Rev Dis Primers 2017;3:17013.
39 Hobson DE, Lix LM, Azimaee M, Leslie WD, Burchill C, Hobson S: Healthcare utilization in patients with Parkinson's disease: a population-based analysis. Parkinsonism Relat Disord 2012;18:930–935.
40 Ryan AS, Ivey FM, Serra MC, Hartstein J, Hafer-Macko CE: Sarcopenia and physical function in middle-aged and older stroke survivors. Arch Phys Med Rehabil 2017;98:495–499.