



DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF A FERMENTED MILK CONTAINING MULTIPLE PROBIOTIC STRAINS AND PREBIOTIC FIBER FOR CONSTIPATION ASSOCIATED WITH PARKINSON'S DISEASE.

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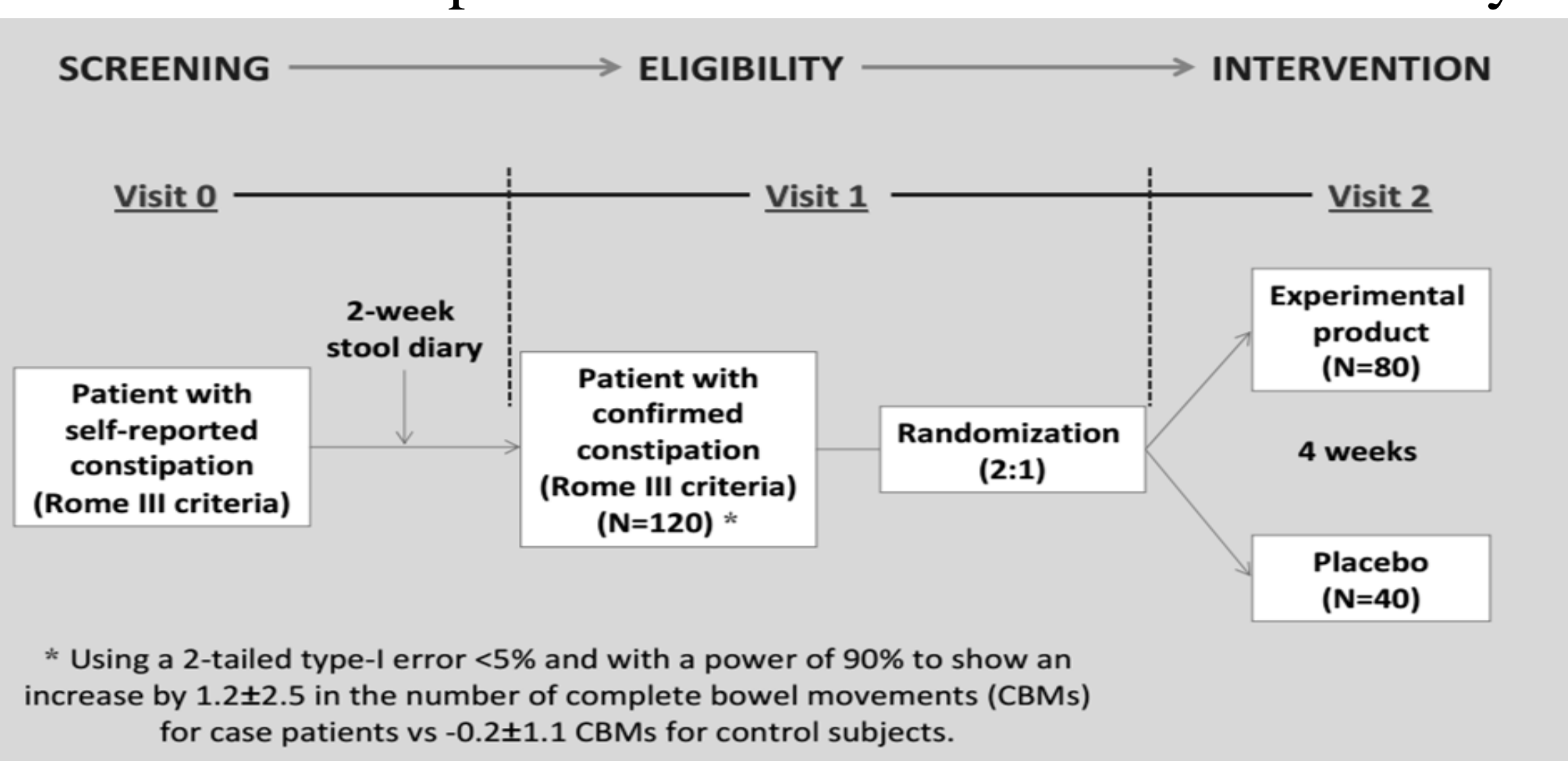
BACKGROUND & OBJECTIVE

Few treatment options have been investigated and are now available for the management of constipation in Parkinson's disease (PD). Our objective was to evaluate the efficacy of probiotics and prebiotics in PD patients with constipation.

METHODS AND PATIENTS

1 We conducted a tertiary setting, randomised, double-blind, placebo-controlled trial in PD patients with Rome III confirmed constipation after a 2-week baseline stool diary.

2 Patients (n=120) were randomly assigned (2:1) to either a fermented milk, containing multiple probiotic strains and prebiotic fiber, or placebo, once daily for 4 weeks.



	Fermented milk containing probiotics and prebiotic fibre [125 grams]	Placebo (pasteurized fermented milk) [125 grams]
Energy, kcal	75	77
Proteins, g	2.8	3.5
Carbohydrates, g	12.6	13.4
Fats, g	0.9	1.1
Fibre, g	7.8	0.26
Fructo-oligosaccharides, g	2.4	--
Calcium, mg	104	131
Phosphorus, mg	81	105
Probiotics*, CFU	250×10^9	--

The primary efficacy endpoint was the increase in the number of complete bowel movements (CBMs) per week.

The key secondary endpoints were three or more CBMs and an increase by one or more CBMs per week during week 3 and 4.

RESULTS

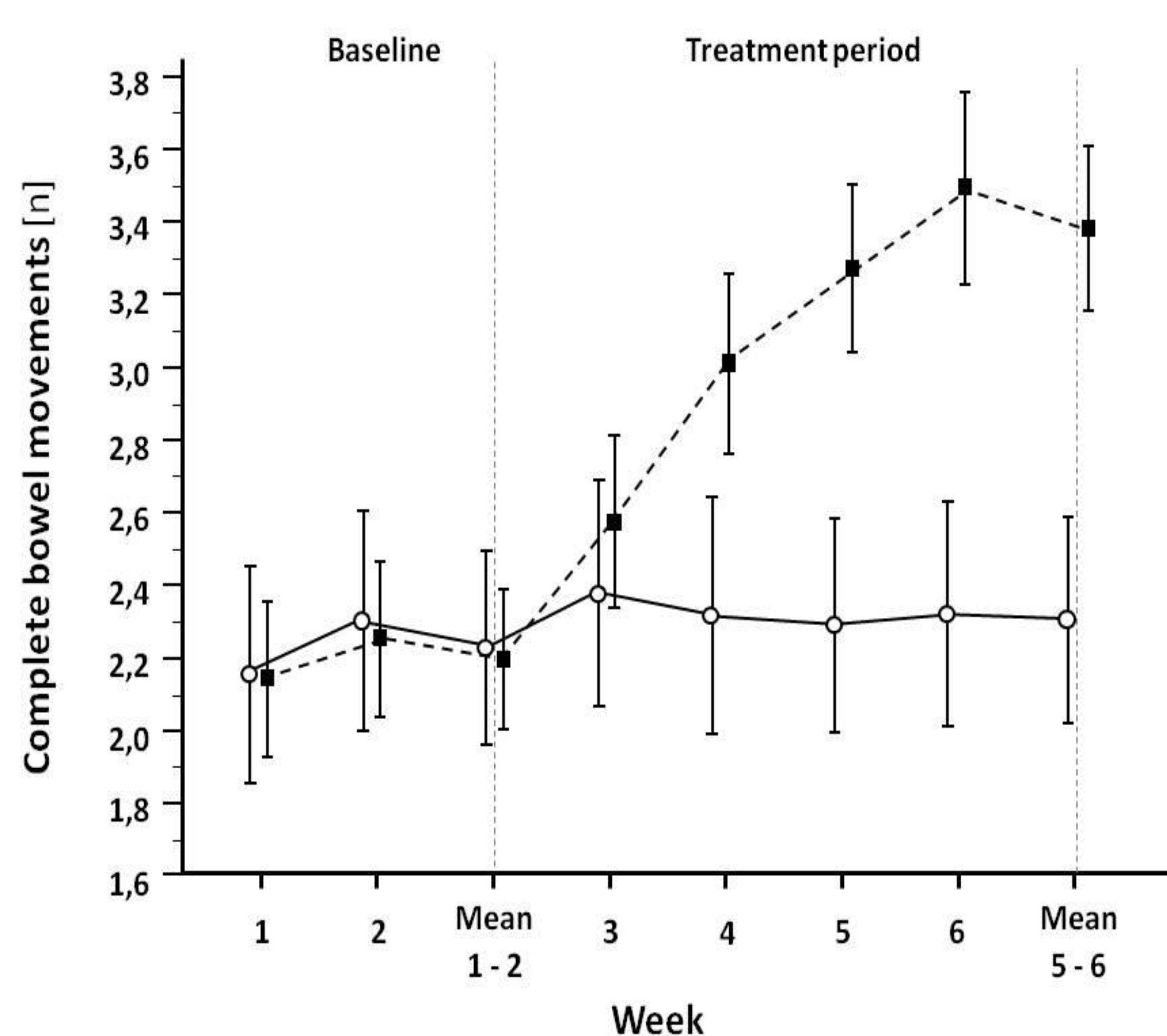


Figure. Mean number of weekly complete bowel movements (CBMs) according to intervention (■, experimental; ○, placebo) and study period.

Table. Secondary study endpoints in the randomized population^a

ENDPOINT	Experimental group (N=80)	Placebo group (N=40)	Treatment effect	P-value
Increase in CBMs ≥ 1 during week 3 and 4, % of patients	53.8 (38.9, 72.4)	25.0 (11.2, 46.0)	3.4 (1.5, 8.0) ^d	0.004
Three or more CBMs during week 3 and 4, % of patients	58.8 (43.2, 78.1)	37.5 (20.1, 61.9)	2.4 (1.1, 5.2) ^d	0.030
Mean increase in BMs ^b , n/week	0.7 (0.3, 1.0)	0.0 (-0.4, 0.3)	0.7 (0.1, 1.3) ^c	0.023
Mean increase in Stool consistency ^b , BSFS score	0.7 (0.4, 0.9)	0.1 (-0.2, 0.4)	0.6 (0.1, 1.0) ^c	0.018
Mean reduction in use of laxatives ^b , n/week	-0.8 (-1.2, -0.4)	-0.1 (-0.5, 0.2)	-0.7 (-1.3, -0.1) ^c	0.018
Treatment satisfaction (satisfied or very satisfied), % of patients	55.0 (40.0, 73.8)	17.5 (7.0, 36.1)	5.8 (2.3, 14.6) ^d	<0.001
Treatment continuation (likely or very likely to continue), % of patients	56.3 (41.0, 75.3)	30.0 (15.5, 52.4)	3.0 (1.3, 6.7) ^d	0.008

Abbreviations: CBMs, complete bowel movements; BMs, bowel movements; BSFS, Bristol Stool Form Scale

^a Numbers in parentheses are 95% CIs

^b Mean change during week 3 and 4 of treatment period

^c According to a generalized linear regression model (data are reported as mean difference between the experimental and placebo groups)

^d According to a logistic regression model (data are reported as odds between the experimental and placebo groups)

For the primary endpoint, the consumption of a fermented milk containing probiotics and prebiotics resulted in a higher increase in the number of CBMs (mean, 1.2 [95%CI, 0.8 to 1.6]) than placebo (0.1 [95%CI, -0.4 to 0.6]) (mean difference, 1.1 [95%CI, 0.4 to 1.8]; $P=0.002$).

For the key secondary endpoints, a higher number of patients in the probiotics-prebiotics group versus the placebo group reported three or more CBMs ($P=0.030$; 58.8% vs. 37.5%; OR=2.4 [95%CI, 1.1 to 5.2]) and an increase by one or more CBMs ($P=0.004$; 53.8% vs. 25.0%; OR=3.5 [95%CI, 1.8 to 8.1]) during week 3 and 4.

CONCLUSIONS

The consumption of a fermented milk containing multiple probiotic strains and prebiotic fiber was superior to placebo in improving constipation in PD patients.



SARCOPENIA AND DYNAPENIA IN PATIENTS WITH PARKINSONISM

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RATIONALE

To estimate prevalence of sarcopenia and dynapenia in Parkinson's disease (PD) outpatients and to investigate their association with the features of the disease.

METHODS

Consecutive patients (N=364) aged ≥ 65 years, affected by parkinsonian syndromes and attending a specialised tertiary care center were included.

Skeletal muscle mass (SMM), as well as strength and gait speed (GS) were assessed by bioimpedence analysis, handgrip dynamometry, and the 4-meter walking test, respectively.

Based on these assessments sarcopenia was diagnosed using the EWGSOP criteria. Dynapenia was defined as handgrip strength <30 and <20 in men and woman, respectively.

RESULTS

In total, 235 patients (64.6%) had a diagnosis of idiopathic PD. Low SMM index was recorded in 27 patients. Due to gait disturbances and postural instability, GS could not be measured in 98 patients and was found to be reduced in 61.3% of those assessed. Prevalence of sarcopenia and dynapenia were 6.6% and 75.5%, respectively. Sarcopenia tended to be higher in patients unable to perform GS assessment and was unrelated to the type of parkinsonian syndrome. It was associated with older age, longer disease duration, more severe disease and higher disability in activities of daily living, as assessed by disease-specific clinical rating scale. Dynapenia was directly associated with parkinsonism other than PD, older age and disability, while regular physical therapy appeared to be a preventive factor. However, it was unrelated to disease duration and severity. Finally, the disability score of activities of daily living was inversely correlated with handgrip strength and GS.

Table 1 Characteristics of the Study Population

Characteristic	Overall population (N=364)
Male gender, N (%)	194 (53.3)
Age (years), Mean (SD)	72.8 (5.6)
Disease duration (years), Mean (SD)	8.5 (5.6)
Parkinson's disease, N (%)	235 (64.6)
UPDRS part II (score), Mean (SD)	17.6 (6.7)
UPDRS part III (score), Mean (SD)	26.3 (10.0)
Hohen-Yahr stage ≥3, N (%)	2.8 (0.7)
Dysphagia (SDQ score ≥11), N (%)	38 (10.4)
Mini Mental State Examination (score), Mean (SD)	25.6 (4.0)
Regular physical therapy, N (%)	140 (38.5)
Protein redistribution diet, N (%)	80 (22.0)
Body mass index (kg/m ²), Mean (SD)	26.1 (4.3)
Calf circumference (cm), Mean (SD)	36.5 (3.6)
Recent weight loss (≥10% in 6 months), N (%)	17 (4.7)

Fig. 1 Assessment of sarcopenia according to EWGSOP algorithm and diagnostic criteria. HG, handgrip; MM, muscle mass

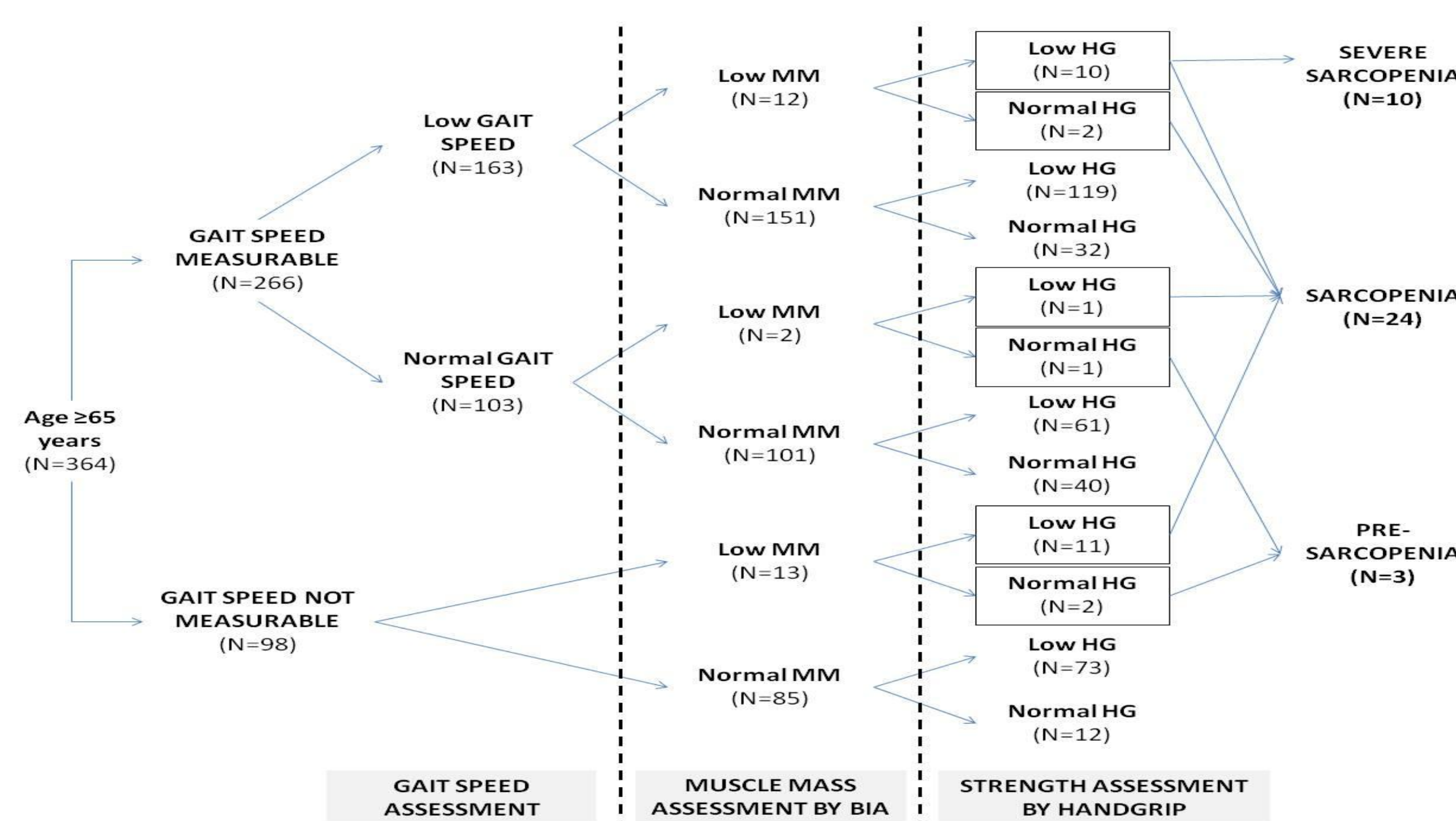


Fig. 2. Correlation between disability in activities of daily living (UPDRS part II) and measures of functional status (Plot A, handgrip strength; Plot B, 4-meter course gait speed). Trend lines are for the Pearson partial correlation (overall study population [sex-adjusted]; continuous line) or correlation in gender strata (-, men; B, women; dashed lines).

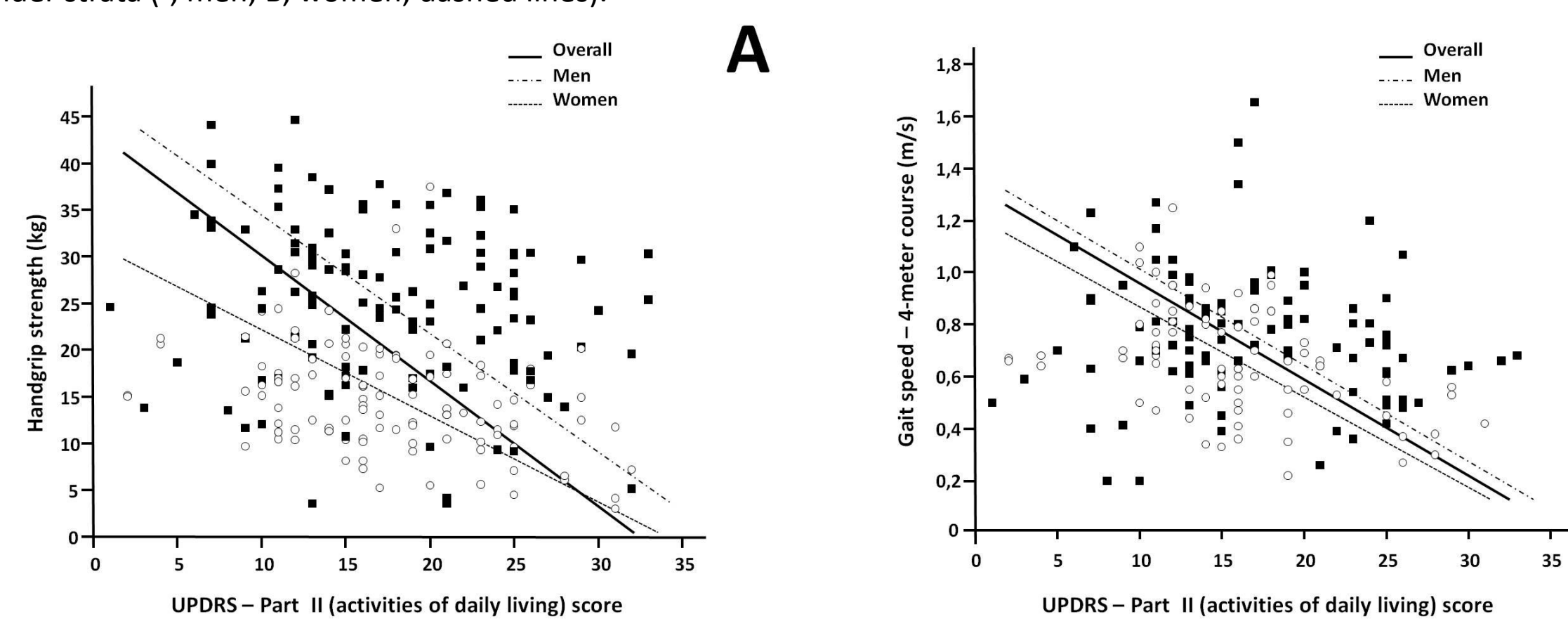


Table 2 Prevalence of Sarcopenia and Dynapenia in the Overall Study Population and Predefined Subgroups

Population or sub-group	N	Sarcopenia		Dynapenia	
		N	% (95%CI)	N	% (95%CI)
Overall	364	24	6.6 (4.3-9.7)	275	75.5 (70.8-79.9)
Females	170	14	8.2 (4.6-13.4)	138	81.2 (74.5-86.8)
Males	194	10	5.1 (2.5-9.3)	137	70.6 (64.0-77.3)
Parkinson's disease	235	14	6.0 (3.3-9.8)	166	70.6 (64.4-76.4)
Other parkinsonism	129	10	7.8 (3.8-13.8)	109	84.5 (77.1-90.3)
Gait speed measurable	266	13	4.9 (2.6-8.2)	191	71.8 (66.0-77.1)
Gait speed not measurable	98	11	11.2 (5.7-19.2)	72	73.5 (63.6-81.9)

Table 3 Characteristics of the Study Population by Diagnosis of Sarcopenia

Characteristic	Sarcopenia (N=24)	No sarcopenia (N=340)	P-value ^a
Male gender, N (%)	10 (41.7)	184 (54.1)	0.291
Age (years), Mean (SD)	75.2 (4.7)	72.6 (5.6)	0.026
Disease duration (years), Mean (SD)	10.8 (5.8)	8.3 (5.6)	0.040
Parkinson's disease, N (%)	14 (58.3)	221 (65.0)	0.514
UPDRS part II (score), Mean (SD)	21.2 (10.8)	17.4 (6.4)	0.049
UPDRS part III (score), Mean (SD)	27.0 (10.7)	26.2 (10.0)	0.697
Hohen-Yahr stage, N (%)	3.1 (0.9)	2.8 (0.7)	0.048
Dysphagia (SDQ score ≥11), N (%)	3 (12.5)	35 (10.3)	0.728
Mini Mental State Examination (score), Mean (SD)	25.5 (4.4)	25.6 (4.0)	0.90
Regular physical therapy, N (%)	8 (33.3)	132 (38.8)	0.669
Protein redistribution diet, N (%)	3 (12.5)	77 (22.6)	0.315
Body mass index (kg/m ²), Mean (SD)	20.8 (2.8)	26.5 (4.2)	<0.001
Calf circumference (cm), Mean (SD)	30.7 (1.2)	36.9 (3.3)	<0.001
Recent weight loss (≥10% in 6 months), N (%)	2 (8.3)	15 (4.4)	0.616

Abbreviations: UPDRS, Unified Parkinson's Disease Rating Scale (Part II: Activities of daily living; Part III: Motor examination); SDQ, Swallowing Disturbance Questionnaire. ^a For comparison between groups by Student's t-Test or Fisher's exact test or gender-adjusted linear regression (*).

CONCLUSIONS

Impaired functional status is a prominent feature of this patient population, independently of disease duration and severity. Sarcopenia is mainly related to advancing disease and, due to a significant sparing of SMM, is an infrequent condition, likely to play a minor role in disability

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