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Research Article

Association between Calf and Thigh Circumference with Clinical and Functional Characteristics in Parkinson's Disease

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Background

Lower extremity circumference may serve as a practical screening tool for sarcopenia in older adults. However, research on calf circumference (CC) and thigh circumference (TC) in Parkinson's disease (PD) remains limited.

Objective

This study examines the relationship between CC and TC and clinical characteristics, functional performance, disease severity, quality of life, and cognitive function in PD.

Methods

This cross-sectional study involved 24 patients with PD. Clinical characteristics, functional performance tests, CC, and mid-TC were assessed. Disease severity was evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), cognitive function with the Thai Mental State Examination, and quality of life using the PD Questionnaire-8. Linear regression analysis was performed to explore relationships between lower extremity circumferences and related factors.

Results

The patients had a mean age of 64.4 years (standard deviation [SD]: 7.22), and included 11 men (45.8%). The average disease duration was four years (SD: 1.12). Based on the CC criteria, eight patients were identified as having sarcopenia. Both CC and TC were negatively correlated with UPDRS part II scores. The left and right CC also showed significant negative correlations with the Parkinson's Disease Questionnaire-8 (PDQ-8) mobility score. Specifically, left CC was associated with a β coefficient of −1.940 (95% confidence interval [CI] of B: −3.628 – −0.251, p=0.026), and right CC with a β of −1.961 (95% CI of B: −3.657 – −0.265, p=0.025).

Conclusion

The negative correlations between lower extremity circumferences and UPDRS part II and PDQ-8 mobility scores suggest that reduced muscle circumferences may indicate greater impairment in daily activities and mobility.

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1. INTRODUCTION

Parkinson's disease (PD) is a prevalent neurodegenerative disorder characterized by a progressive decline in motor function and a spectrum of non-motor symptoms that collectively impair daily living and quality of life.[1,2] The pathophysiology of PD involves the degeneration of dopaminergic neurons in the substantia nigra, leading to characteristic motor symptoms such as bradykinesia, rigidity, resting tremor, and postural instability. However, the impact of PD extends beyond motor dysfunction, affecting muscle integrity and overall physical health.[1]

The significance of sarcopenia—defined as the loss of muscle mass and strength—in individuals with PD has been previously underscored, with studies showing that its prevalence is approximately 3 times higher among patients with PD than in the general population.[3] Sarcopenia exacerbates mobility issues and is associated with increased disability, falls, PD severity, and non-motor symptoms.[4-6] Therefore, monitoring and early diagnosis of sarcopenia in PD is essential. However, diagnosis may be limited owing to a lack of measuring equipment. Lower extremity circumference is useful for assessing sarcopenia, particularly in the thighs and calves. Lower extremity circumference can be a practical and non-invasive indicator of muscle mass and function. De Luna *et al*.[7] revealed that calf circumference (CC) was independently associated with confirmed sarcopenia in patients with PD. The CC was effective in identifying patients with PD with confirmed sarcopenia, with cut-off values of <31 cm and <34 cm for women and men, respectively.[7] This finding aligns with the results of a study conducted on an elderly Thai population, which identified optimal cut-off values for sarcopenia screening as <33 cm and <34 cm (sensitivity 80.1% and 85.4%, specificity 60.5% and 70.2%) for women and men, respectively.[8] Zhang *et al*.[9] conducted a study involving 1,000 participants with an average age of 70 years and discovered a negative correlation between thigh circumference (TC) and sarcopenia. Landi *et al*.[10] discovered that a larger CC was associated with a lower frailty index and improved functional performance in older adults living in the community. In addition, Hsu *et al*.[11] discovered that a smaller CC was significantly linked to the need for assistance in daily living within 4 years. These findings suggest that lower extremity circumference could be a valuable indicator for screening sarcopenia and assessing overall health outcomes in older adults, particularly in those with PD.

However, knowledge gaps remain, particularly concerning data on CC and TC in patients with PD and related factors, especially among the Thai population. Therefore, the cross-sectional nature of the current study aimed to address this gap by exploring the associations between CC and TC and several key clinical parameters. These parameters included disease severity measured using the Unified Parkinson's Disease Rating Scale (UPDRS), cognitive function assessed via the Thai Mental State Examination (TMSE), and quality of life evaluated using the Parkinson's Disease Questionnaire-8 (PDQ-8).

2. MATERIALS AND METHODS

2.1. ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Institutional Review Board (IRB) of Maharat Nakhon Ratchasima Hospital (MNRH IRB: 67052) and the Human Research Ethics Committee of Srinakharinwirot University (SWUEC-661017). The study adhered to the ethical standards outlined in the Declaration of Helsinki, the Belmont Report, the International Conference on Harmonization in Good Clinical Practice, and relevant Thai laws and regulations. All participants provided informed consent.

2.2. STUDY DESIGN AND PARTICIPANTS

This cross-sectional study utilized baseline data from the study registered in the Thai Clinical Trials Registry 20241016001. The study enrolled 24 patients aged 50 years or older diagnosed with PD stages II and III based on the Hoehn and Yahr scale. All participants were recruited from the outpatient Neurology Unit of Maharat Nakhon Ratchasima Hospital in Thailand.

2.2.1. INCLUSION CRITERIA

Patients were included as participants if they were diagnosed with PD stages II and III based on the Hoehn and Yahr scale, had the ability to walk at least 10 m without assistance, and completed a risk assessment conducted by a neurologist.

2.2.2. EXCLUSION CRITERIA

Patients were excluded from the study if they had dementia or a previous diagnosis of anxiety or depressive disorder, a TMSE score ⩽23 points, or refused to participate in the study.

2.3. DATA COLLECTION AND MEASUREMENTS

Before data collection, participants in the "on period" of their PD medication received detailed instructions on testing procedures. Appointments were scheduled between 8:00 am and 11:00 am at the fitness center of Nakhon Ratchasima Rajabhat University to ensure consistency. Participants were advised to wear light, comfortable clothing and remove metal objects. The controlled testing environment was set at approximately 23 – 25°C. The sessions included the following activities: (i) completion of a structured neurological assessment and questionnaire, (ii) assessment of body composition, and (iii) measurement of CC and TC under controlled conditions.

2.3.1. NEUROLOGICAL ASSESSMENT AND QUESTIONNAIRES

A neurologist assessed all patients using a coded system to ensure anonymity. The following instruments were used to evaluate cognitive status, disease severity, and quality of life:

(i) TMSE: The cognitive status of patients with PD was assessed using the TMSE, a validated instrument for evaluating cognitive function. The TMSE consists of six subtests covering the areas of orientation (6 points), registration (3 points), attention (5 points), calculation (3 points), language (10 points), and memory (3 points), resulting in a maximum score of 30 points. A score above 23 points indicates normal cognitive function, whereas lower scores indicate potential cognitive impairment.[12]

(ii) UPDRS: The UPDRS has been used to measure disease severity and functional impairment in patients

with PD. This comprehensive scale is divided into four parts. Part I evaluated mentality, behavior, and mood, Part II on activities of daily living (ADLs), Part III on motor examination, and Part IV on complications of therapy.[13]

(iii) PDQ-8: The PDQ-8 was administered to assess the quality of life in patients with PD. This short questionnaire contains eight questions on mobility, ADLs, emotional well-being, stigma, social support, cognition, communication, and physical complaints. The PDQ-8 is widely used and a valid measure of the quality of life in PD.[14]

2.3.2. BODY COMPOSITION ASSESSMENT AND PATIENT CHARACTERISTICS

Body composition was assessed using a digital body composition scale (Omron HBF-375 Karada Scan, Japan). The measurements obtained included body mass, body mass index, body fat percentage, skeletal muscle mass, visceral fat, and basal metabolic rate. Blood pressure was recorded using a blood pressure monitor (Omron HEM-7143T1, Japan). Systolic and diastolic blood pressure readings were taken after a 10-min rest period to ensure precision.

2.3.3. CIRCUMFERENCE MEASUREMENT

Measuring mid-TC and CC is a simple and reliable method for assessing muscle mass and nutritional status. Accurate techniques include consistent anatomical landmarks and standardized positioning to ensure precision. These anthropometric assessments are essential in clinical practice and research for assessing sarcopenia and related disorders (Figure 1).

CC was measured following a four-step procedure:[7,8,10]

(i) Positioning: Participants stood upright with their feet shoulder-width apart and their weight evenly distributed. This posture ensured a consistent and relaxed posture

(ii) Landmark identification: The widest part of the calf was located, typically midway between the ankle and knee

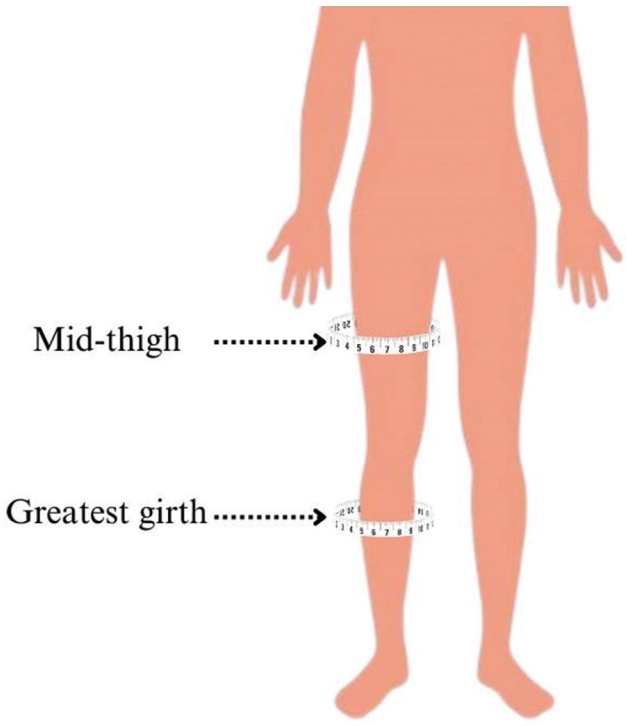

Figure 1. Circumference measurement

(iii) Measurement method: A non-elastic tape was used to measure the circumference at the widest point of the calf. The tape was placed horizontally, snug against the skin, without compressing the tissue

(iv) In this study, patients with PD and sarcopenia were defined based on CC with values of <33 cm and <34 cm (sensitivity 80.1% and 85.4%, specificity 60.5% and 70.2%) for women and men, respectively.

TC measurement was taken using the following steps:[15]

(i) Positioning: The participant stood upright with legs slightly apart and the weight evenly distributed on both feet

(ii) Landmark identification: The inguinal crease (where the thigh meets the pelvis) and the proximal edge of the patella (the top of the kneecap) were located. The distance between the points was measured, and the center point on the skin was marked

(iii) Measurement procedure: A non-elastic measuring tape was wrapped horizontally around the middle of the thigh. The tape ran perpendicular to the longitudinal axis of the thigh and was laid flat without compressing the underlying tissue.

2.4. FUNCTIONAL PERFORMANCE TEST

2.4.1. FIVE-TIMES SIT-TO-STAND TEST

A 5-times sit-to-stand test was employed to evaluate lower extremity strength, balance, and fall risk. Participants sat in a chair, and when the outcome assessor said "GO," they were tasked with standing up and sitting down 5 times as quickly as possible. The timing commenced with the "GO" signal and concluded when the participant sat back down for the 5th time.[16]

2.4.2. TIMED UP AND GO TEST

The timed up-and-go test was utilized as the main measure to evaluate gait, balance, and mobility. Participants were asked to sit on a chair (46 cm high) equipped with an armrest. Upon receiving the "GO" command from the outcome assessor, they were required to stand, walk 3 m at a comfortable pace, go around a designated point, and return to the chair. The total time taken to complete these tasks was recorded in seconds, starting from the "GO" signal and ending when the participant was seated again.[17]

2.4.3. A 10-M WALK TEST

The 10-m walk test was used to assess walking speed over a short distance. Participants were instructed to walk a 10-m distance at a maximum speed. The walking speed was calculated by dividing the distance by the time taken.[18]

2.5. STATISTICAL ANALYSIS

Data analysis was performed using the IBM Statistical Package for the Social Sciences Statistics version 19 (IBM Corp., United States). Descriptive statistics—including counts, percentages, means, and standard deviations (SD)—were used to summarize the participants' general information. Linear regression analysis examined the relationship between CC and TC and related factors. The statistical significance level was set at $p<0.05$.

Table 1. Characteristics of participants

Characteristics	Value
Sex	
Men, *n* (%)	11 (45.80)
Women, *n* (%)	13 (54.20)
Modified Hoehn and Yahr staging	
Stage 2, *n* (%)	12 (50.00)
Stage 2.5, *n* (%)	6 (25.00)
Stage 3, *n* (%)	6 (25.00)
Age (years)	64.4 (7.22)
Duration of disease (years)	4.0 (1.20)
Levodopa dose (mg/d)	450.58 (299.95)
Body weight (kg)	61.9 (9.66)
Body fat percentage (%)	29.4 (8.05)
Body mass index (kg/m^2)	24.4 (3.52)
Basal metabolic rate (kcal)	1,345.4 (174.81)
Systolic blood pressure (mmHg)	138.9 (13.75)
Diastolic blood pressure (mmHg)	81.0 (8.56)
Pulse pressure (time/min)	77.7 (16.57)
Skeletal muscle mass (%)	25.6 (4.30)
Visceral fat (levels)	10.21 (5.14)
Five times sit-to-stand test (s)	12.5 (1.71)
Timed up and go test (s)	10.7 (1.86)
10-m walking test (m/s)	1.2 (0.25)
Left calf circumference (cm)	33.7 (3.32)
Right calf circumference (cm)	33.4 (3.34)
Left thigh circumference (cm)	45.3 (4.89)
Right thigh circumference (cm)	45.7 (4.90)
Parkinson's Disease Questionnaire 8-item score	
Total score	4.2 (1.22)
Mobility	1.58 (0.78)
Activities of daily living	0.71 (0.55)
Emotional well-being	0.25 (0.53)
Stigma	0.13 (0.34)
Social support	0.17 (0.48)
Cognition	0.79 (0.42)
Communication	0.46 (0.66)
Physical complaints	0.13 (0.34)
Unified Parkinson's Disease Rating Scale score (points)	
Total score	30.0 (10.07)
Part I (mentation, behavior, mood)	1.5 (1.47)
Part II (activities of daily living)	9.8 (4.01)
Part III (motor examination)	17.7 (5.61)
Part IV (complications of therapy)	1.1 (2.52)
Thai Mental State Examination score (points)	
Total score	26.1 (1.78)
Orientation	5.8 (0.38)
Registration	3.0 (0.00)
Attention	3.8 (0.90)
Calculation	2.6 (0.65)
Language	9.6 (0.50)
Memory	1.3 (0.62)

Note: Data is presented as mean (standard deviation) unless stated otherwise.

3. RESULTS

The study involved 24 participants with PD, with a mean age of 64.4 years (SD = 7.22) and a mean disease duration of 4.00 years (SD = 1.12). Based on the CC criteria, eight patients had sarcopenia, representing approximately 33.3%. The mean left and right CC were 33.7 cm and 33.4 cm, respectively, whereas the mean left and right TC were 45.3 cm and 45.7 cm, respectively. Table 1 shows the demographic characteristics and clinical features.

3.1. CC ANALYSIS

The relationships between CC and various factors were examined. Left CC showed a significant negative correlation with UPDRS part II scores with a β coefficient of −0.284 (95% confidence interval [CI]: −0.554 – −0.014, p=0.040), and right CC demonstrated a significant negative correlation with UPDRS part II scores with a β of −0.213 (95% CI: −0.562 – −0.016, p=0.039), indicating that a larger left CC is associated with better ADLs. Additionally, left CC showed a significant negative correlation with the PDQ-8 mobility score (β = −1.940, 95% CI: −3.628 – −0.251, p=0.026). Similarly, the right CC revealed a significant negative correlation with the PDQ-8 mobility score (β = −1.961, 95% CI = −3.657 – −0.265, p=0.025). These results suggest that larger CC is associated with improved mobility as perceived by participants. Data are presented in Table 2, Figures 2 and 3.

3.2. TC ANALYSIS

Left TC was negatively correlated with UPDRS part II scores (β = −0.284, 95% CI: −0.554 – −0.014, p=0.040). Similarly, the right TC negatively correlated with UPDRS part II scores (β = −0.213, 95% CI: −0.562 – −0.016, p=0.039). These results indicate that larger TC is similarly associated with better functional outcomes in ADLs. Data are shown in Table 3 and Figure 4.

4. DISCUSSION

Eight of 24 patients (33.3%) with PD were identified as having sarcopenia based on CC criteria, a prevalence three times higher than that of the healthy population of similar age.[19] The pathogenesis of sarcopenia in PD may involve several interconnected mechanisms. First, degeneration of dopaminergic neurons leads to motor dysfunction and reduced physical activity, contributing to muscle atrophy and weakness.[1] Second, increased pro-inflammatory cytokines in PD cause chronic inflammation, which interferes with muscle protein synthesis and promotes degradation.[20,21] Third, nutritional deficiencies, including

Table 2. The relationship between calf circumference and the factors of interest

Factors	Left calf circumference			Right calf circumference		
	β	95% CI of B	*p*-value	β	95% CI of B	*p*-value
Age	−0.165	−0.355, 0.025	0.085	−0.174	−0.364, 0.016	0.070
Duration of disease	−0.025	−1.252, 1.202	0.966	−0.017	−1.251, 1.217	0.977
Levodopa dose	0.002	−0.003, 0.007	0.406	0.002	−0.003, 0.007	0.400
FTSST	−0.384	−2.301, 0.848	0.347	−0.106	−1.891, 1.483	0.803
TUGT	0.634	−0.510, 2.730	0.168	0.316	−1.172, 2.299	0.506
10MWT	0.444	−3.015, 15.279	0.177	0.323	−5.246, 14.356	0.344
TMSE	0.310	−0.505, 1.125	0.439	0.299	−0.522, 1.119	0.458
UPDRS						
Total score	−0.064	−0.179, 0.051	0.264	−0.072	−0.197, 0.031	0.144
Part I	−0.387	−1.179, 0.405	0.322	−0.296	−1.106, 0.513	0.455
Part II	−0.284	−0.554, −0.014	0.040*	−0.213	−0.562, −0.016	0.039*
Part III	0.018	−0.195, 0.231	0.861	−0.021	−0.237, 0.194	0.839
Part IV	−0.256	−0.717, 0.205	0.261	−0.393	−0.840, 0.054	0.082
PDQ-8						
Total score	−0.790	−1.947, 0.367	0.171	−0.815	−1.976, 0.346	0.159
Mobility	−1.940	−3.628, −0.251	0.026*	−1.961	−3.657, −0.265	0.025*
Activities of daily living	−0.838	−3.483, 1.806	0.518	−0.925	−3.579, 1.729	0.477
Emotional well-being	−0.615	−3.365, 2.134	0.647	−0.635	−3.399, 2.130	0.639
Stigma	1.905	−2.361, 6.170	0.364	1.786	−2.514, 6.086	0.398
Social support	−1.156	−4.163, 1.851	0.434	−1.078	−4.108, 1.952	0.468
Cognition	−0.421	−3.957, 3.115	0.807	−0.332	−3.889, 3.226	0.848
Communication	1.021	−1.165, 3.207	0.343	0.973	−1.230, 3.176	0.370
Physical complaints	0.952	−3.375, 5.280	0.653	1.024	−3.325, 5.372	0.630

Note: *Refers to statistical significance determined at $p<0.05$ using linear regression analysis.
Abbreviations: 10MWT: 10-m walking test; CI: Confidence interval; FTSST: Five times sit-to-stand test; PDQ-8: Parkinson's Disease Questionnaire 8-item; TMSE: Thai Mental State Examination; TUGT: Timed up and go test; UPDRS: Unified Parkinson's Disease Rating Scale.

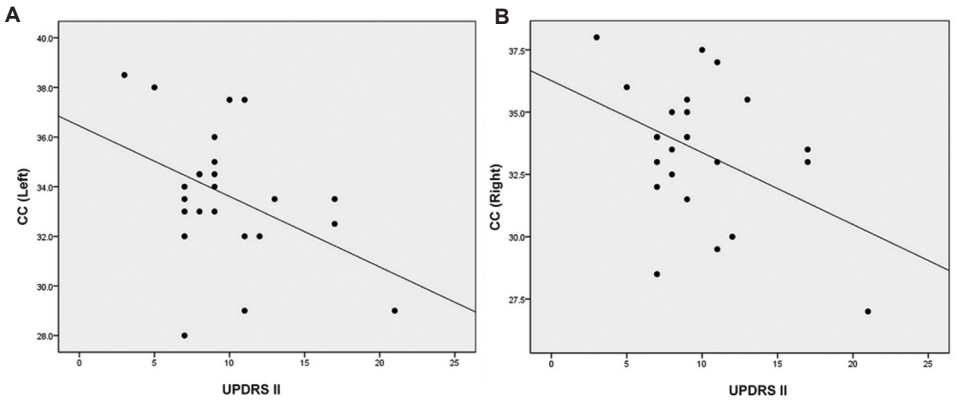

Figure 2. Scatter plot of calf circumference (CC) with Unified Parkinson's Disease Rating Scale (UPDRS) Part II (A) Left CC and (B) Right CC with UPDRS Part II

dysphagia and decreased appetite, are common in PD and can lead to inadequate nutritional intake, which may exacerbate muscle loss.[1] Lastly, psychological factors, such as depression and anxiety, which are common in PD, can diminish motivation for physical activity, further exacerbating muscle loss.[2,22]

Our study also revealed that CC and TC negatively correlated with UPDRS part II scores (ADLs) on both sides. In addition, CC demonstrated a significant negative correlation with the PDQ-8 mobility score on both sides. These negative correlations between lower extremity circumferences and both UPDRS part II and PDQ-8 mobility scores may be explained by different factors. First, increased calf muscle mass contributes to greater muscle strength and power, which are essential for tasks such as walking, climbing stairs, and maintaining body balance.[23] Second, stronger calf muscles improve gait mechanics, facilitating more effective propulsion during walking and providing

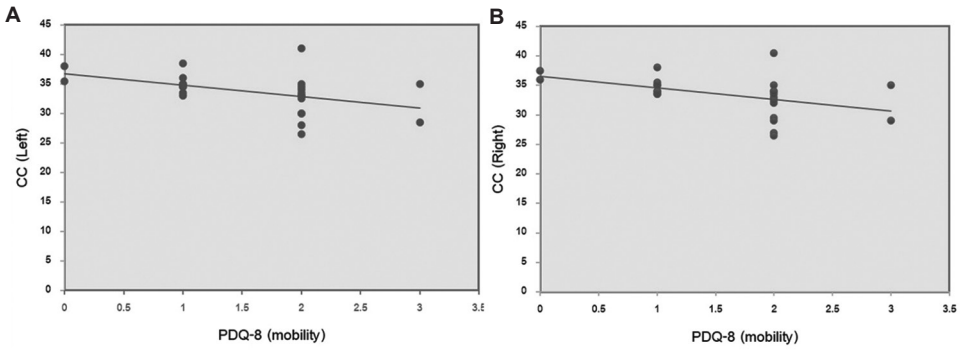

Figure 3. Scatter plot of calf circumference (CC) with Parkinson's Disease Questionnaire 8-item (PDQ-8) mobility score (A) Left CC and (B) Right CC with PDQ-8 mobility

Table 3. The relationship between thigh circumference and the factors of interest

Factors	Left thigh circumference			Right thigh circumference		
	β	95% CI of B	*p*-value	β	95% CI of B	*p*-value
Age	−0.131	−0.425, 0.162	0.364	−0.168	−0.459, 0.122	0.242
Duration disease	0.010	−1.795, 1.815	0.991	−0.266	−2.071, 1.539	0.763
Levodopa dose	0.004	−0.003, 0.011	0.277	0.003	−0.005, 0.010	0.457
FTSST	−0.468	−3.452, 0.986	0.260	−0.407	−3.386, 1.204	0.333
TUGT	0.275	−1.611, 2.953	0.547	0.313	−1.584, 3.137	0.500
10MWT	0.129	−10.407, 15.370	0.692	0.172	−9.973, 16.687	0.605
TMSE	0.551	−0.641, 1.742	0.348	0.445	−0.758, 1.647	0.451
UPDRS						
Total score	−0.157	−0.317, 0.003	0.055	−0.142	−0.313, 0.029	0.099
Part I	−0.260	−1.447, 0.927	0.654	0.024	−1.222, 1.270	0.968
Part II	−0.450	−0.841, −0.026	0.026*	−0.455	−0.867, −0.044	0.032*
Part III	−0.213	−0.512, 0.086	0.153	−0.158	−0.478, 0.162	0.316
Part IV	−0.220	−0.911, 0.472	0.517	−0.342	−1.056, 0.371	0.331
PDQ-8						
Total score	−0.094	−1.925, 1.738	0.916	−0.016	−1.851, 1.820	0.986
Mobility	−1.284	−4.034, 1.465	0.343	−1.252	−4.010, 1.506	0.357
Activities of daily living	−1.246	−5.135, 2.644	0.514	−0.704	−4.628, 3.220	0.714
Emotional well-being	0.538	−3.519, 4.596	0.059	−0.212	−4.283, 3.860	0.915
Stigma	5.714	−0.162, 11.590	0.056	5.452	−0.486, 11.390	0.070
Social support	−1.375	−5.821, 3.071	0.528	−1.297	−5.756, 3.163	0.553
Cognition	−0.211	−5.418, 4.997	0.934	−0.595	−5.807, 4.618	0.815
Communication	1.590	−1.618, 4.798	0.315	1.705	−1.498, 4.908	0.282
Physical complaints	−1.143	−7.519, 5.233	0.714	0.310	−6.098, 6.717	0.921

Note: *Refers to statistical significance determined at $p<0.05$ using linear regression analysis.
Abbreviations: 10MWT: 10-m walking test; CI: Confidence interval; FTSST: Five times sit-to-stand test; PDQ-8: Parkinson's Disease Questionnaire 8-item; TMSE: Thai Mental State Examination; TUGT: Timed up and go test; UPDRS: Unified Parkinson's Disease Rating Scale.

greater ankle stability, thereby reducing the risk of falls.[24] Finally, larger calf muscles may enhance muscular endurance, allowing individuals to engage in daily activities for longer periods without fatigue.[25]

Overall, the connection between larger lower extremity circumferences and improved performance in ADLs and mobility underscores the importance of lower limb strength in maintaining functional independence. Our results highlight CC and TC as potential clinical markers for assessing functional mobility in patients with PD. These findings suggest that interventions aimed at increasing muscle mass, such as resistance training,[26] proven exercises for PD,[27,28] or nutritional support, could enhance the quality of life and functional abilities of individuals with PD. Future research should explore the potential benefits of targeted interventions designed to preserve or increase muscle mass to improve objective and subjective mobility outcomes in this population.

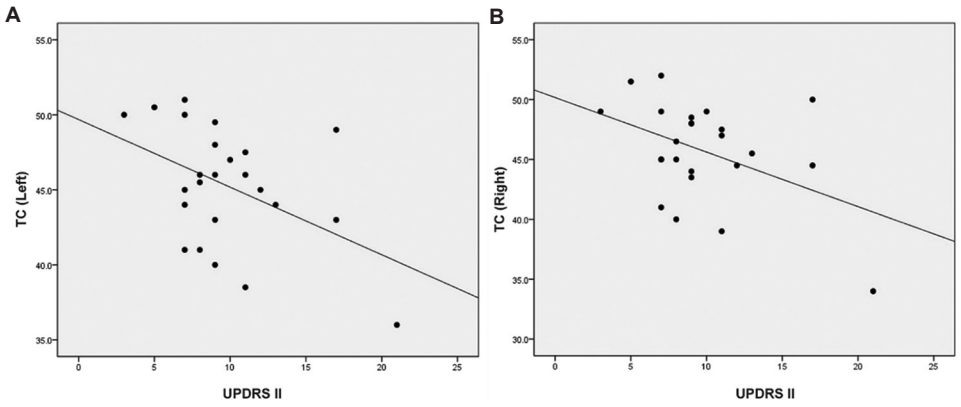

Figure 4. Scatter plot of mid-thigh circumference (TC) with Unified Parkinson's Disease Rating Scale (UPDRS) Part II scale (A) Left TC and (B) Right TC with UPDRS Part II

4.1. LIMITATIONS

This study had a few limitations. The cross-sectional nature of the study limits the ability to infer causality or the directionality of observed relationships. Hence, longitudinal studies are needed to assess how changes in CC and TC over time relate to the progression of motor symptoms and functional decline in PD. Furthermore, the relatively small sample size may limit the generalizability of the findings. Therefore, studies with larger populations are warranted to confirm these results.

5. CONCLUSION

Lower extremity circumferences, particularly calf and thigh measurements, may be promising non-invasive markers of disease severity in PD. They provide a practical, cost-effective approach to tracking functional decline and could support early rehabilitation interventions. Longitudinal studies are necessary to validate these findings and explore the potential of CC and TC as biomarkers for disease progression and therapeutic efficacy.

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CONFLICT OF INTEREST

The authors declared no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Ketsirin Kittipongphakorn, Witid Mitranun
Data curation: Ketsirin Kittipongphakorn, Witid Mitranun, Wisan Teeratantikanon, Soontaraporn Huntula
Methodology: Ketsirin Kittipongphakorn, Witid Mitranun
Resources: Ketsirin Kittipongphakorn, Witid Mitranun, Wisan Teeratantikanon, Soontaraporn Huntula
Writing–original draft: All authors
Writing– review & editing: All authors

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the IRB of Maharat Nakhon Ratchasima Hospital (MNRH IRB: 67052) and the Human Research Ethics Committee of Srinakharinwirot University (SWUEC-661017). The study adhered to the ethical standards outlined in the Declaration of Helsinki, the Belmont Report, the International Conference on Harmonization in Good Clinical Practice, and relevant Thai laws and regulations. All participants provided informed consent.

CONSENT FOR PUBLICATION

Not applicable as the manuscript does not include any identifiable personal data or images requiring consent for publication.

DATA AVAILABILITY STATEMENT

Data will be made available upon reasonable request from the corresponding author.

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