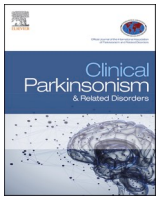
PRDOA 12 (2025) 100309

Contents lists available at ScienceDirect

Clinical Parkinsonism & Related Disorders

journal homepage: www.sciencedirect.com/journal/clinical-parkinsonism-and-related-disorders



Original Articles

The comparison of gait disorders among different motor subtypes in Parkinson's disease patients during the early and middle stages

Jianing Mei [a,1], Yu Wang [a,1], Dongyu Zhu [a], Yang Li [b], Kan Gu [c], Zijun Wei [a], Xueyi Han [a], Qianqian Li [a], Shuyun Jiang [b,*], Yunyun Zhang [a,*]

[a] Department of Neurology, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[b] Department of Gait Analysis, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[c] Department of Acupuncture, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China

ARTICLE INFO

Keywords:
Parkinson's disease
Motor subtypes
Gait disorders
Gait analysis

ABSTRACT

Background and Purpose: There is a scarcity of quantitative research on gait differences among patients with different motor subtypes of Parkinson's disease (PD), especially during the early and middle stages of the condition. The purpose of this study is to describe the gait characteristics of PD with different motor subtypes in the early and middle stages and to identify the most sensitive indicators of gait impairment.
Methods: General information, including age, gender, disease duration, levodopa equivalent daily dose (LEDD), and falls, was collected. Motor and non-motor symptoms of PD were assessed using multiple scales. Patients' walking function and lower limb joint movement ability were analyzed using a 3D gait analysis system.
Results: The study included 64 patients with early and middle-stage PD, of whom 33 were classified as the TD subtype, 24 were classified as the PIGD subtype, and 7 were classified as the Mixed subtype. In addition, 5 healthy subjects were included in the evaluation as healthy controls. The PIGD patients have significantly higher LEDD (431.08 ± 250.90 mg vs. 302.08 ± 164.64 mg, $p = 0.034$) and a higher number of falls (0.29 vs. 0.00, $p = 0.018$) than the TD patients. The overall gait disturbances and motor and non-motor symptoms did not exhibit significant differences between TD and PIGD patients. However, the decrease in GDI ($\beta = -0.730$ vs. $\beta = -0.235$, $p = 0.043$) and hip flexion and extension range ($\beta = -0.533$ vs. $\beta = -0.470$, $p < 0.001$) was more pronounced in PIGD patients compared to TD patients as the MDS-UPDRS III score increased.
Conclusion: There is no significant difference in gait severity between patients with TD and PIGD subtypes during the early and middle stages of PD. However, PIGD patients exhibit a more rapid progression of gait impairment than TD, particularly affecting hip mobility.

1. Introduction

Parkinson's disease (PD) is a highly prevalent neurodegenerative disorder characterized by a spectrum of motor symptoms, including bradykinesia, resting tremor, rigidity, and postural instability. Moreover, it presents diverse non-motor symptoms such as sleep disorders, pain, autonomic dysfunction, cognitive impairment and psychiatric disorders. PD patients are typically classified into three subtypes based on their motor symptoms: tremor-dominant (TD), postural instability and gait difficulty (PIGD), and Mixed subtype. Previous research has demonstrated that PIGD patients exhibit more rapid disease progression, increased motor impairment, poorer treatment response, and a greater negative impact on patients' quality of life [1]. However, the research on the quantitative gait differences between patients with TD and PIGD is limited.

Gait disturbance is a prominent feature of PD. As the disease progresses, gait dysfunction worsens, ultimately resulting in frequent falls, injuries, and even severe fractures [2]. This constitutes the primary cause of disability among patients. Previous studies on gait disorders in PD primarily focus on the symptoms that occur during the middle and

* Corresponding author.
E-mail address: zhangyyshyy@shutcm.edu.cn (Y. Zhang).
[1] Jianing Mei and Yu Wang contributed equally and shared the first authorship.

https://doi.org/10.1016/j.prdoa.2025.100309
Received 14 October 2024; Received in revised form 20 February 2025; Accepted 23 February 2025
Available online 24 February 2025

advanced stages, such as freezing of gait (FOG) [3]. There is a scarcity of research examining the gait characteristics of patients with early and middle-stage PD. Studying gait differences among PD motor subtypes in the early and middle stages is crucial for improving diagnosis, treatment, preventing falls and understanding of the disease. It has significant implications for patient care, therapeutic development, and research, ultimately aiming to enhance the quality of life for individuals living with PD.

The qualitative assessment of gait disorders through visual observation remains the most commonly employed method by clinicians. However, the assessment results of gait scales are susceptible to various factors, including the researcher's familiarity with the scale and patients' compliance, thereby compromising the objectivity of these scales and rendering their assessment outcomes unstable [4]. There is evidence suggesting that subjective clinical assessment scales may lack sensitivity toward the severity and specific characteristics of gait disorders, particularly in detecting early-stage changes in gait [5].

With the advancement of sensor technology, quantitative gait analysis is progressively emerging as a pivotal approach for gait research. It can precisely assess gait patterns and characteristics, thus being regarded as the "gold standard" for evaluating gait [4]. The clinical applicability and validity of gait analysis studies have demonstrated that quantitative gait analysis can enhance diagnostic accuracy, prognostic prediction, and rehabilitation efficacy for various gait disorders in comparison to observation scales for multiple sclerosis, PD, stroke, cerebral palsy, and other diseases [5–7].

The objective of this study was to assess and compare the gait characteristics of TD and PIGD subtypes in the early and middle stages of PD using three-dimensional gait analysis (3DGA) and to provide a basis for further study of gait impairment in these stages.

2. Methods

2.1. Participants

Participants were recruited from patients with PD who presented at the neurology clinic between October 2022 and March 2024. PD was diagnosed clinically according to Movement Disorder Society (MDS) clinical diagnostic criteria. We enrolled patients diagnosed with primary PD, Hoehn & Yahr (H&Y) stage 1 to 3, and aged between 40 and 80. Patients presenting with other conditions that may contribute to abnormal gait, such as lower extremity skeletal disorders or stroke, were excluded. Additionally, individuals exhibiting parkinsonism syndromes like multiple system atrophy or progressive supranuclear palsy were also excluded. Furthermore, patients with severe dementia or mental illness were not included in the study. In addition, healthy age-matched spouses of the patients were included in the evaluation as healthy controls (HC). The protocol underwent review and received approval from the ethics committee of our hospital (IRB 2022–106). All patients were duly informed and provided their signed informed consent before evaluation.

2.2. Clinical assessments

Demographic information, H&Y stage, duration of PD, and levodopa equivalent daily dose (LEDD) were evaluated. Participants were defined as early-stage PD (H&Y stage 1 and 2) and middle-stage PD (H&Y stage 3) according to H&Y stage [8,9]. The LEDD was calculated using the levodopa equivalent dose conversion formula proposed by Tomlinson et al. in 2010 [10]. The Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS-UPDRS) was utilized to comprehensively evaluate the symptoms of PD patients. The motor subtypes were categorized based on the MDS-UPDRS scores. TD was defined as the ratio of the average score of TD items (2.10, 3.15–3.18) to the average score of PIGD items (2.12, 2.13, 3.10–3.12) $\geq$ 1.15, PIGD was defined when the ratio of the average score of TD items to the average score of PIGD items was $\leq$ 0.90, and Mixed subtype was defined as the ratio of the average score of TD items to the average score of PIGD items between 0.90 and 1.15 [11]. The Freezing of Gait Questionnaire (FOG-Q) was used to assess the severity of patients' freezing of gait. The Non-motor Symptom Scale (NMSS) was utilized to evaluate the comprehensive non-motor symptoms of PD. The cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA). The assessment of sleep quality was conducted using the Parkinson's disease sleep scale-2 (PDSS-2). The Epworth Sleeping Scale (ESS) was utilized to evaluate daytime sleepiness. The assessment of constipation was conducted using the Patient Assessment of Constipation Symptom (PAC-SYM). The Patient Health Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) were employed for the evaluation of depression and anxiety. The participants were instructed to abstain from taking PD medication for a minimum of 12 h prior to assessment in order to ensure consistency of results.

2.3. Three-dimensional gait analysis (3DGA)

The 3DGA system was utilized for quantitative gait analysis, employing a range of sophisticated equipment including infrared cameras, A/D converter, HD high-speed cameras, the Cortex 5.5.0 data acquisition software, and the Visual3D biomechanical analysis software.

The subjects' body surface landmarks were marked using 12 mm fluorescent marker balls, and an infrared camera captured their real-time 3D position. This allowed for obtaining the motion angles of the hip, knee, ankle, shoulder, and elbow joints as well as the pelvis and trunk of the lower limbs in the horizontal plane, coronal plane, and sagittal plane. The key anatomical locations of the lower limbs of the subjects were marked with fluorescent markers, including bilateral anterior superior iliac spine, bilateral posterior superior iliac spine, bilateral medial femoral condyle, bilateral lateral femoral condyle, bilateral tibial tuberosity, bilateral lateral malleolus tips, bilateral medial malleolus tips, bilateral second and fifth metatarsal heads, and bilateral calcaneal tuberosity. Long pole fluorescent tags were placed on both thighs and legs 1/3 down from the top. After obtaining static data acquisition, the medial points of both knees and ankles were removed before completing dynamic data acquisition. (Fig. 1).

Professional gait analysts utilized Cortex 5.5.0 data acquisition software for 3D modeling and analysis, while Visual3D analysis software was employed to define, process, and scrutinize the gait cycle. Subsequently, the step length, speed, cadence, percentage of stance phase, and lower limb joint kinematics parameters were computed. Additionally, the Gait Deviation Index (GDI) was determined. The GDI, proposed by Schwartz in 2008 [12], is currently one of the most widely used gait indices. It utilizes three-dimensional gait analysis equipment to measure pelvic coronal, sagittal, and horizontal data, as well as hip coronal, sagittal, and horizontal data, knee flexion and extension data, ankle plantar dorsiflexion data, and step angle data. By calculating these nine parameters, a GDI value $>$ 100 indicates normal gait, while a GDI value $<$ 100 suggests pathological gait, and every less than 10 indicates one standard deviation from normal gait metrics. The research on gait disorders extensively utilizes GDI, which assesses the comprehensive and clinically significant index of gait function in various conditions such as children's muscle atrophy in cerebral palsy, stroke, PD, spinal degenerative diseases, spinal cord injury, and other related ailments.

2.4. Statistical analysis

The Shapiro-Wilk test was employed to assess the normality of measurement data, while the Student's *t*-test or one-way ANOVA was utilized to compare normally distributed data between groups. The Mann-Whitney *U* test was applied to compare differences among measurement data that did not conform to a normal distribution. The X^2 test was employed to compare the count data among different groups. The Pearson correlation analysis was employed to examine the association between gait parameters and the MDS-UPDRS III score. The criterion for

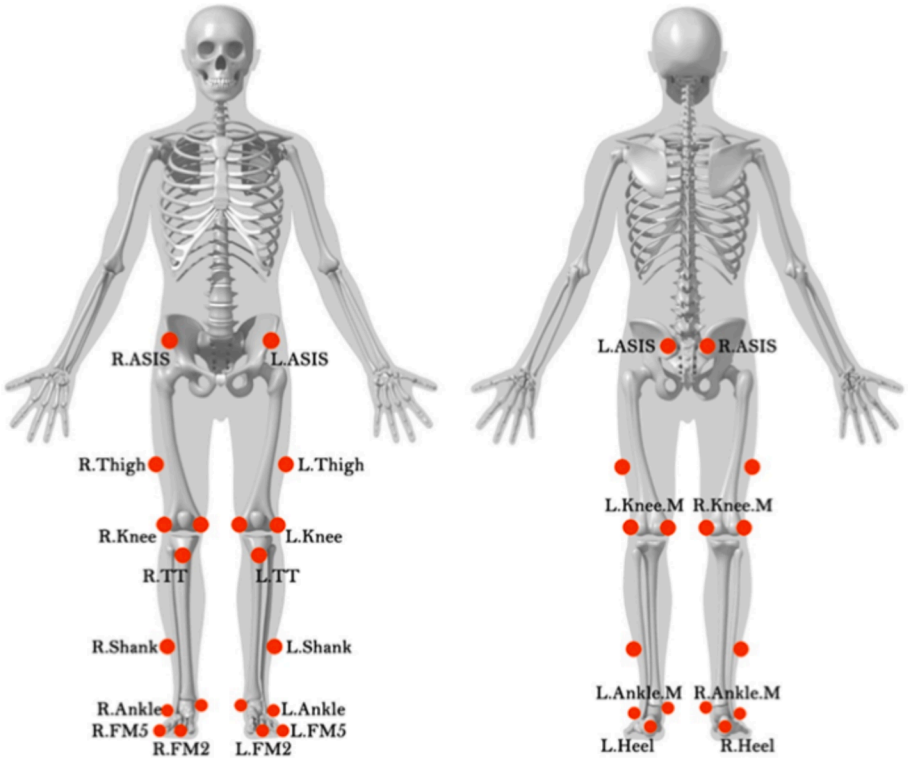


Fig. 1. The location of the fluorescent markers.

statistical significance was set at $p < 0.05$, and all statistical analyses were conducted using SPSS 25.0 software. The linear plot was utilized to visually demonstrate the changing trend of each 3DGA index as PD progressed in its early and middle stages. Then, a linear fitting analysis was conducted, and the regression coefficient was calculated. The difference of regression coefficients between TD and PIGD patients was compared using nonparametric tests. The statistical plots were generated using Origin 2021 software.

3. Results

3.1. Comparison of general characteristics between HC, TD and PIGD with early and middle-stage PD

The study included 64 patients with early and middle-stage PD, of whom 33 were classified as the TD subtype, 24 were classified as the PIGD subtype, and 7 were classified as the Mixed subtype. In addition, 5 healthy spouses of patients were included as HC. The general characteristics of HC, TD and PIGD subtypes of PD in the early and middle stages are listed in Table 1. The gender, age, BMI, disease duration and H&Y stage did not exhibit any significant differences between HC, TD and PIGD patients. The PIGD patients are significantly higher in LEDD (431.08 ± 250.90 mg vs. 302.08 ± 164.64 mg, $p = 0.034$) and number of falls (0.29 vs. 0.00, $p = 0.018$) compared to the TD patients.

Table 1
General characteristics between HC, TD and PIGD with early and middle stages PD.

	HC (n = 5)	TD (n = 33)	PIGD (n = 24)	*p*
Gender (males/ females)	1/4	14/19	13/11	0.290
Age(y)	66.80 ± 4.38	68.06 ± 6.29	66.83 ± 9.58	0.819
BMI	21.72 ± 0.70	23.95 ± 3.16	22.79 ± 3.48	0.210
Duration(y)	/	4.73 ± 3.14	5.06 ± 5.94	0.803
LEDD(mg)	/	302.08 ± 164.64	431.08 ± 250.90	**0.034**
Number of falls (last month)	/	0.00	0.29	**0.018**
H&Y	/	1.97 ± 0.85	2.38 ± 0.92	0.097

3.2. Comparison of clinical features and gait parameters between TD and PIGD with early and middle-stage PD

Comparisons between TD and PIGD with early and middle stages PD for various clinical features, including motor symptoms (MDS-UPDRS III), freezing of gait (FOG-Q), non-motor symptoms (NMSS), cognitive function (MoCA), sleep quality (PDSS-2), daytime sleepiness (ESS), constipation (PAC-SYM), depression (PHQ-9), anxiety (GAD-7) and quality of life (PDQ-39) are listed in Table 2. As expected, tremor scores were significantly higher in the TD group than in the PIGD group (MDS-UPDRS TD 11.21 ± 5.61 vs. 2.08 ± 2.52, $p < 0.001$), while postural instability and gait disturbance scores were significantly higher in the PIGD group than in the TD group (MDS-UPDRS PIGD 6.04 ± 2.69 vs. 4.24 ± 2.25, $p = 0.008$). Freezing of gait occurred in 3 patients (9.1 %)

Table 2
Clinical features between TD and PIGD with early and middle stages PD.

	TD(n = 33)	PIGD(n = 24)	*p*
MDS-UPDRS III	33.58 ± 13.15	33.04 ± 12.24	0.875
MDS-UPDRS TD	11.21 ± 5.61	2.08 ± 2.52	**<0.001**
MDS-UPDRS PIGD	4.24 ± 2.25	6.04 ± 2.69	**0.008**
FOG-Q	0.70 ± 2.30	5.17 ± 5.84	**<0.001**
NMSS	41.31 ± 19.36	53.83 ± 29.03	0.080
MoCA	22.97 ± 3.26	22.58 ± 4.22	0.710
PDSS-2	15.94 ± 7.02	18.67 ± 8.88	0.219
ESS	6.09 ± 4.52	7.71 ± 6.50	0.301
PAC-SYM	9.09 ± 5.98	7.67 ± 6.08	0.384
PHQ-9	6.58 ± 3.33	7.58 ± 3.97	0.317
GAD-7	4.27 ± 4.20	4.21 ± 3.98	0.953
PDQ-39	25.73 ± 11.03	31.96 ± 17.20	0.128

in the TD group and in 12 patients (50.0 %) in the PIGD group. FOG score was significantly higher in PIGD group than in TD group (FOG-Q 5.17 ± 5.84 vs. 0.70 ± 2.30, $p < 0.001$). The overall MDS-UPDRS III score, however, did not exhibit a significant difference between the two groups. The non-motor symptoms and quality of life also did not exhibit any significant differences between TD and PIGD patients.

Comparisons between HC, TD and PIGD with early and middle stages PD for various gait parameters, including GDI, step length, speed, cadence, percentage of stance phase and lower limb joint flexion and extension range are listed in Table 3. The GDI was significantly higher in the HC group than in the TD (98.39 ± 3.46 vs. 87.59 ± 8.64, $p = 0.014$) and PIGD (98.39 ± 3.46 vs. 86.53 ± 9.74, $p = 0.008$) groups. However, the GDI, step length, speed, cadence, percentage of stance phase and lower limb joint flexion and extension range showed no significant differences between TD and PIGD participants in the early and middle stages of PD.

Comparisons of gait parameters between the TD and PIGD with early-stage PD (H&Y 1 and 2) are listed in Table 4. Statistical analysis revealed that no statistically significant differences in gait parameters between TD and PIGD in participants with early PD.

Table 3
Gait parameters between HC, TD and PIGD with early and middle stages PD.

	HC(n = 5)	TD(n = 33)	PIGD(n = 24)	*p*
GDI	98.39 ± 3.46	87.59 ± 8.64	86.53 ± 9.74	**p_1 = 0.014** **p_2 = 0.008** p_3 = 0.659
Step length(cm)	49.77 ± 4.18	46.06 ± 10.25	41.96 ± 8.27	p_1 = 0.405 p_2 = 0.090 p_3 = 0.102
Speed(cm/s)	88.85 ± 6.89	85.56 ± 23.56	76.54 ± 18.49	p_1 = 0.745 p_2 = 0.236 p_3 = 0.113
Cadence(steps/min)	106.67 ± 8.02	108.96 ± 15.51	108.64 ± 12.14	p_1 = 0.732 p_2 = 0.773 p_3 = 0.932
Percentage of stance phase (%)	63.42 ± 0.92	65.05 ± 2.27	65.57 ± 2.76	p_1 = 0.167 p_2 = 0.076 p_3 = 0.425
Ankle range of motion (°)	25.45 ± 4.05	24.49 ± 4.73	22.70 ± 4.26	p_1 = 0.659 p_2 = 0.219 p_3 = 0.144
Knee range of motion (°)	58.98 ± 2.77	54.21 ± 7.63	51.93 ± 7.44	p_1 = 0.179 p_2 = 0.055 p_3 = 0.251
Hip range of motion (°)	38.45 ± 3.11	35.61 ± 6.10	33.46 ± 5.62	p_1 = 0.308 p_2 = 0.083 p_3 = 0.169

p_1: HC vs TD; p_2: HC vs PIGD; p_3: TD vs PIGD.

Table 4
Gait parameters between TD and PIGD with early-stage PD.

	TD(n = 22)	PIGD(n = 8)	*p*
GDI	89.37 ± 8.62	90.01 ± 7.41	0.854
Step length(cm)	50.22 ± 9.19	47.47 ± 5.39	0.325
Speed(cm/s)	93.90 ± 21.96	85.72 ± 13.65	0.238
Cadence(steps/min)	111.13 ± 11.38	108.02 ± 8.49	0.488
Percentage of stance phase (%)	64.33 ± 1.88	64.90 ± 1.67	0.454
Ankle range of motion (°)	25.72 ± 4.59	24.10 ± 2.39	0.350
Knee range of motion (°)	56.90 ± 5.67	54.98 ± 2.94	0.371
Hip range of motion (°)	37.98 ± 4.46	37.56 ± 3.40	0.809

3.3. Tendency of gait parameters of TD and PIGD patients during the early and middle stages of PD as the condition progresses

The correlation analysis revealed significant associations between the MDS-UPDRS III score and gait parameters, including GDI ($r = -0.327$, $p = 0.013$), step length ($r = -0.519$, $p < 0.001$), speed ($r = -0.433$, $p = 0.001$), percentage of stance phase ($r = 0.265$, $p = 0.046$), ankle joint movement ($r = -0.406$, $p = 0.002$), knee joint movement ($r = -0.440$, $p = 0.001$), and hip joint movement ($r = -0.499$, $p < 0.001$). The correlation between cadence and the MDS-UPDRS III score was not found to be statistically significant ($p = 0.653$).

Line plots were generated, linear fitting was conducted, and regression coefficients (β) was calculated to establish the relationship between each gait parameter and the MDS-UPDRS III score. The results demonstrated that with the MDS-UPDRS III score increased, the GDI of PIGD patients exhibited a more pronounced decline compared to TD patients (β = −0.730 vs. β = −0.235, $p = 0.043$) (Table 5, Fig. 2). The step length of PIGD patients exhibited a slower rate of decrease compared to TD patients (β = −0.620 vs. β = −0.891, $p < 0.001$) (Table 5, Fig. 3). The deceleration of gait speed was comparatively more gradual in PIGD patients compared to TD patients (β = −1.392 vs. β = −1.624, $p = 0.003$) (Table 5, Fig. 4). The percentage of stance phase for PIGD and TD exhibited a comparable trend (β = 0.128 vs. β = 0.110, $p = 0.128$) (Table 5, Fig. 5). PIGD patients exhibit a slower decline in ankle range of motion (β = −0.119 vs. β = −0.337, $p = 0.007$), a slower decline in knee range of motion (β = −0.547 vs. β = −0.548, $p = 0.002$), and a faster decline in hip range of motion (β = −0.533 vs. β = −0.470, $p < 0.001$) compared to TD patients (Table 5, Fig. 6).

4. Discussion

The present study employed a 3DGA system to comprehensively compare the gait characteristics of PD patients with TD and PIGD subtypes during the early and middle stages. Our main findings were as follows: Although there was no significant difference in gait impairment between TD patients and PIGD patients of PD in the early and middle stages, the rate of gait deterioration was significantly faster in PIGD patients compared to TD patients, particularly affecting hip range of motion.

To facilitate a standardized scale assessment and gait analysis for

Table 5
Comparison of regression coefficients (β) between TD and PIGD patients.

	MDS-UPDRS III		*p*
	TD patients	PIGD patients	
GDI	β = −0.235	β = −0.730	**0.043**
Step length	β = −0.891	β = −0.620	**<0.001**
Speed	β = −1.624	β = −1.392	**0.003**
Percentage of stance phase	β = 0.110	β = 0.128	0.128
Ankle range of motion	β = −0.337	β = −0.119	**0.007**
Knee range of motion	β = −0.548	β = −0.547	**0.002**
Hip range of motion	β = −0.470	β = −0.533	**<0.001**

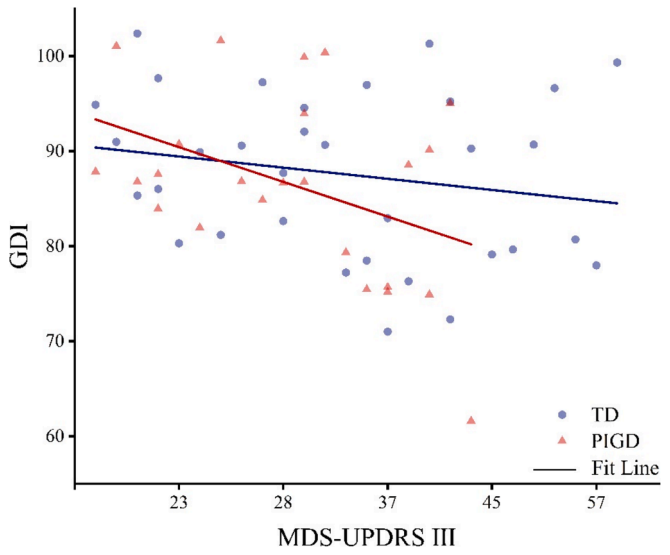


Fig. 2. The linear fit between GDI and MDS-UPDRS III score in TD and PIGD patients.

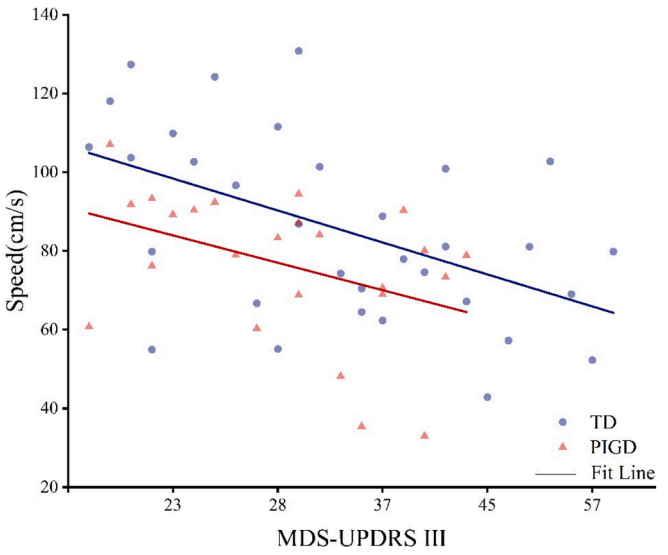


Fig. 4. The linear fit between speed and MDS-UPDRS III score in TD and PIGD patients.

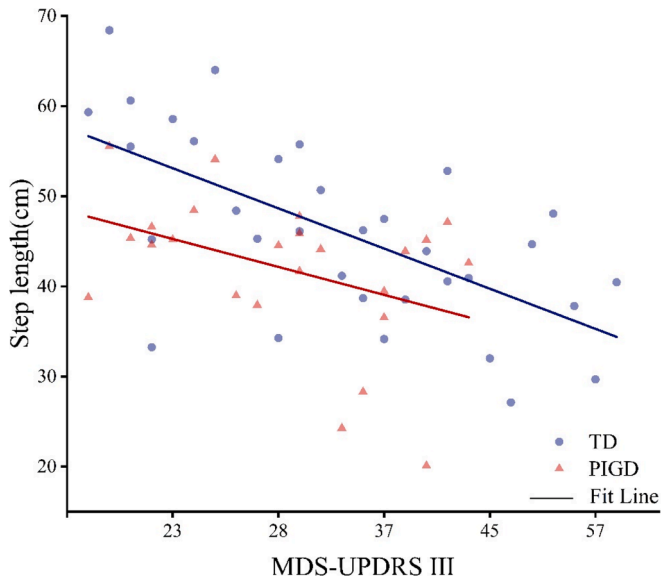


Fig. 3. The linear fit between step length and MDS-UPDRS III score in TD and PIGD patients.

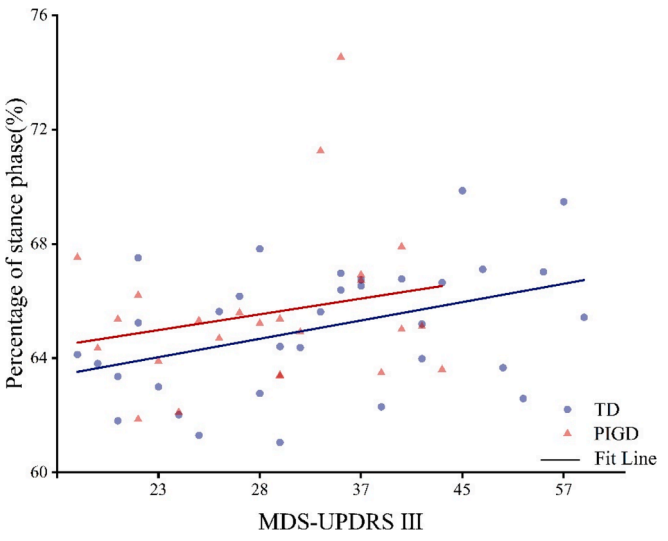


Fig. 5. The linear fit between the percentage of stance phase and MDS-UPDRS III score in TD and PIGD patients.

participants, this study necessitated the cessation of all PD-related medications for a minimum of 12 h (one overnight) before the evaluation procedures. The chosen interval was designed to ensure that all participants were as close to the "OFF" time as possible, without prompting patients to decline assessment out of concern of exacerbated symptoms following medication cessation. While certain PD medications necessitate a more extended period of discontinuation to fully eradicate their effects, for instance, the dopamine receptor agonist pramipexole possesses a protracted half-life and requires approximately 3–5 days for complete systemic elimination. Considering the willingness of the participants and referring to other similar studies, this study determined that stopping medication for 12 h was the most feasible, taking into account the interests of the participants and the consistency of the outcomes.

The present study revealed a notably elevated incidence of LEDD and falls in patients with PIGD compared to those with TD. The obtained result was in line with our initial expectations. Compared to TD patients, PIGD patients exhibit a more accelerated disease progression and more severe movement disorders, including an increased susceptibility to falls, compromised postural control, and a higher likelihood of developing FOG, thereby rendering the treatment of PIGD subtypes considerably more challenging. This study showed that the number and severity of FOG in PIGD patients were significantly higher than those in TD patients, even in patients with PD at early and middle stages. The incidence of FOG in PIGD patients of PD at early and middle stages was as high as 50 %. Previous statistics have shown that FOG can be seen in 50 % of PD patients, and it can reach 80 % in patients with advanced PD [3]. The widespread presence of FOG in early and middle-stage PD patients suggests that early intervention is needed for PD gait disorders to prevent falls in patients, especially in PIGD patients. In this study, there was no significant difference in non-motor symptoms between the two subtypes of PD patients with early and middle stages. Considering that non-motor symptoms such as cognitive function [13] and depression [14] have a significant impact on gait disorders in PD patients, this actually also excluded the interference of non-motor symptoms in the comparison of gait parameters between the two motor subtypes.

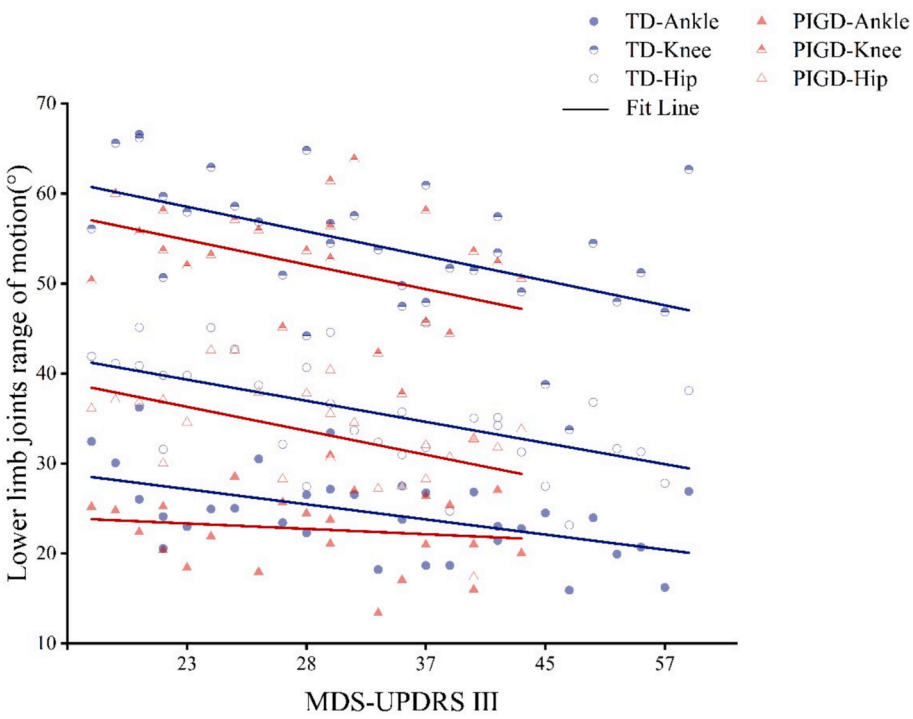


Fig. 6. The linear fit between the lower limb joints range and MDS-UPDRS III score in TD and PIGD patients.

The 3DGA system, which represents quantitative gait analysis, is currently acknowledged as the "gold standard" for gait analysis. It has the capability to detect various gait-related data pertaining to the human body, encompassing spatiotemporal parameters (trajectory, step length, step speed), kinematic parameters (acceleration, angle), dynamic parameters (force, joint torque, joint strength), and more [15]. Previous gait analysis studies have demonstrated that individuals with PD exhibit gait disorders characterized by diminished range of motion and muscle strength in the hip, knee, and ankle joints; the presence of muscle rigidity and postural instability may contribute to reduced propulsion in the lower limbs, consequently impacting spatiotemporal parameters of gait such as speed and step length [16,17].

Our study revealed that the rate of gait deterioration was significantly faster in PIGD patients compared to TD patients in the early and middle stages of PD, particularly affecting the hip range of motion. The hip joint, being the largest articulation in the human body, plays a pivotal role in providing structural support for body weight as well as facilitating ambulation and maintaining equilibrium. Previous studies have demonstrated a reduction in the range of motion for hip flexion and extension during the early stages of PD [18]. The hip joint plays a crucial role in motor function impairment among PD patients. Taniguchi et al. discovered that weakened hip muscle strength and limited range of motion contributed to decreased bed mobility in PD patients [19]. Baudendistel et al.'s study revealed that levodopa treatment improved step length, step speed, and hip flexion and extension range of motion, while no significant improvement was observed in the ankle joint, suggesting that the hip joint has a greater impact on gait abnormalities in PD patients [20]. Currently, there is limited research on the relationship between lower limb joint movement and gait disorders in PD patients; however, some researchers have developed wearable walking devices to control hip and knee joint movements with promising results. These devices have shown potential for improving balance function and reducing the FOG by manipulating these joints' movements [21]. Therefore, further investigation into lower limb joint movement, particularly focusing on the hip joint movement, holds great promise for diagnosing PD and intervening with gait disorders.

Contrary to our expectations, our study revealed no significant differences in gait parameters between TD and PIGD patients in early and middle stages PD. There are also studies that have arrived at a similar conclusion to ours. The gait analysis study by Zhang et al. demonstrated no differences in stride length, speed, and cadence between TD and PIGD patients in early-stage PD, while disparities were observed in parameters related to limb swing [22]. The gait analysis study conducted by Rusz et al. also revealed that there were no significant differences in gait velocity, cadence, and stride length between TD and PIGD patients, whether in single-task or dual-task situations [23]. Herman et al. also demonstrated no significant differences in gait speed, stride length, and variability between the PIGD and TD groups [24]. The findings suggest that certain gait parameters commonly employed may not exhibit significant differences between individuals with TD and PIGD patients. We consider that there are two potential factors contributing to this situation: (1) In the early and middle stages of PD, gait changes such as reduced arm swing, slight shuffling, or mild bradykinesia are common across all subtypes, but they are often subtle and not easily distinguishable, because severe postural instability and marked gait difficulties typically develop later in the disease course. The results of this study indicated that while the gait parameters of PIGD patients were quantitatively inferior to those of TD patients in the early and middle stages PD, there was insufficient statistical evidence to support a significant difference. This suggests that such a possibility cannot be ruled out. (2) In the early and middle stages, patients often develope compensatory mechanisms to manage minor gait disturbances. This compensation can mask the severity of gait issues, making differences between subtypes less apparent. For instance, PIGD patients may require higher levodopa doses owing to more pronounced PD symptoms, this leads to comparable symptom severity between the two motor subtypes. This is substantiated by the markedly higher LEDD observed in PIGD patients compared to TD patients in this study. Furthermore, previous researches have demonstrated that gait disorders in PD patients, particularly FOG, are mitigated when attention is directed or external cues are provided [25]. Gait analysis in this study was conducted in a specialized gait analysis laboratory. The instructions provided by the investigators and the patients' heightened attention in the controlled laboratory environment may have contributed to improved

walking performance among PD patients, which made the difference in gait between the two subtypes insignificant. Besides the aforementioned factors, the classification of TD and PIGD in PD patients is also controversial. Nutt proposed that TD and PIGD are likely to represent different processes in PD [26]. For instance, a patient initially presenting with TD may transition to exhibiting PIGD as PD advances. Therefore, the distinction between TD and PIGD may not be as clear-cut as one might assume, although TD and PIGD are still the most widely used motor subtype classification methods for PD.

The strength of this study is that it comprehensively evaluates both motor and non-motor symptoms in early and middle stages PD patients with gait disorders. The utilization of various scales and extensive coverage, along with incorporating a 3DGA system for quantitative assessment of gait characteristics, enhances the objectivity of the research findings compared to traditional scale evaluations. By comparing the gait parameters between TD and PIGD patients, it was observed that PIGD patients exhibited faster deterioration in their gait, particularly evident in a decrease in hip joint range of motion. There is still potential for further enhancement in this gait analysis study, such as incorporating a larger sample of PD patients and expanding the range of scenarios in gait analysis to include starting, turning, stepping, walking through narrow spaces, and performing dual tasks, and setting a longer withdrawal time for dopamine receptor agonists such as pramipexole before symptom assessment. The incorporation of these additions will enable us to conduct a more comprehensive assessment of gait impairment in PD patients.

5. Conclusion

There is no significant difference in non-motor symptoms and gait severity between patients with TD and PIGD subtypes during the early and middle stages of PD. However, PIGD patients exhibit a more rapid progression of gait impairment than TD, particularly affecting hip mobility. The findings suggest that enhancing hip function during the early and middle stages of PD may benefit patients' gait impairment and mitigate the risk of falls, especially in patients with PIGD. Additionally, the findings of this study also suggest that the gait disparities between individuals with TD and PIGD may be more evident in the longitudinal progression of symptoms rather than the variances observed at a single time point.

CRediT authorship contribution statement

Jianing Mei: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yu Wang:** Writing – review & editing, Project administration, Methodology, Investigation. **Dongyu Zhu:** Software, Resources. **Yang Li:** Software, Resources. **Kan Gu:** Investigation. **Zijun Wei:** Investigation. **Xueyi Han:** Investigation. **Qianqian Li:** Investigation. **Shuyun Jiang:** Supervision, Software, Resources, Project administration. **Yunyun Zhang:** Writing – review & editing, Supervision, Software, Resources, Project administration, Methodology, Investigation.

Declaration of competing interest

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

References

[1] S. Rezvanian, T. Lockhart, C. Frames, R. Soangra, A. Lieberman, Motor Subtypes of Parkinson's Disease Can Be Identified by Frequency Component of Postural Stability, Sensors (basel). 18 (4) (2018 Apr 5) 1102.
[2] A. Mirelman, P. Bonato, R. Camicioli, T.D. Ellis, N. Giladi, J.L. Hamilton, C.J. Hass, J.M. Hausdorff, E. Pelosin, Q.J. Almeida, Gait impairments in Parkinson's disease, Lancet Neurol. 18 (7) (2019 Jul) 697–708.
[3] D.M. Tan, J.L. McGinley, M.E. Danoudis, R. Iansek, M.E. Morris, Freezing of gait and activity limitations in people with Parkinson's disease, Arch. Phys. Med. Rehabil. 92 (7) (2011 Jul) 1159–1165.
[4] A.A. Hulleck, D. Menoth Mohan, N. Abdallah, M. El Rich, K. Khalaf, Present and future of gait assessment in clinical practice: Towards the application of novel trends and technologies, Front. Med. Technol. 16 (4) (2022 Dec) 901331.
[5] P. Dasgupta, J. VanSwearingen, A. Godfrey, M. Redfern, M. Montero-Odasso, E. Sejdic, Acceleration Gait Measures as Proxies for Motor Skill of Walking: A Narrative Review, IEEE Trans. Neural Syst. Rehabil. Eng. 29 (2021) 249–261.
[6] F. Ferrarello, V.A. Bianchi, M. Baccini, G. Rubbieri, E. Mossello, M.C. Cavallini, N. Marchionni, M. Di Bari, Tools for observational gait analysis in patients with stroke: a systematic review, Phys. Ther. 93 (12) (2013 Dec) 1673–1685.
[7] N. Turani, A. Kemiksizoğlu, M. Karataş, R. Ozker, Assessment of hemiplegic gait using the Wisconsin Gait Scale, Scand. J. Caring Sci. 18 (1) (2004 Mar) 103–108.
[8] M.M. Hoehn, M.D. Yahr, Parkinsonism: onset, progression and mortality, Neurology 17 (5) (1967 May) 427–442.
[9] X. Bai, T. Guo, X. Guan, C. Zhou, J. Wu, H. Wu, X. Liu, C. Wu, J. Chen, J. Wen, J. Qin, S. Tan, X. DuanMu, L. Gu, T. Gao, P. Huang, B. Zhang, X. Xu, X. Zheng, M. Zhang, Cortical microstructural alterations in different stages of Parkinson's disease, Brain Imaging Behav. 18 (6) (2024 Dec) 1438–1447.
[10] C.L. Tomlinson, R. Stowe, S. Patel, C. Rick, R. Gray, C.E. Clarke, Systematic review of levodopa dose equivalency reporting in Parkinson's disease, Mov. Disord. 25 (15) (2010 Nov 15) 2649–2653.
[11] G.T. Stebbins, C.G. Goetz, D.J. Burn, J. Jankovic, T.K. Khoo, B.C. Tilley, 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. 28 (5) (2013 May) 668–670.
[12] M.H. Schwartz, A. Rozumalski, The Gait Deviation Index: a new comprehensive index of gait pathology, Gait Posture 28 (3) (2008) 351–357.
[13] L. Arie, T. Herman, S. Shema-Shiratzky, N. Giladi, J.M. Hausdorff, Do cognition and other non-motor symptoms decline similarly among patients with Parkinson's disease motor subtypes? Findings from a 5-year prospective study, J. Neurol. 264 (10) (2017 Oct) 2149–2157.
[14] N.R. Artigas, A.C.L. Dutra, N.M. Soares, G.M. Pereira, V.B. Leotti, J.S. Krimberg, A. S. Pagnussat, C.R.M. Rieder, Depressive symptoms and axial motor disorders in individuals with Parkinson's disease: a cross-sectional study, Arq. Neuropsiquiatr. 80 (11) (2022 Nov) 1126–1133.
[15] E.F. Chehab, T.P. Andriacchi, J. Favre, Speed, age, sex, and body mass index provide a rigorous basis for comparing the kinematic and kinetic profiles of the lower extremity during walking, J. Biomech. 14 (58) (2017 Jun) 11–20.
[16] G. Albani, V. Cimolin, A. Fasano, C. Trotti, M. Galli, A. Mauro, "Masters and servants" in parkinsonian gait: a three-dimensional analysis of biomechanical changes sensitive to disease progression, Funct. Neurol. 29 (2) (2014) 99–105.
[17] M. Pistacchi, M. Gioulis, F. Sanson, E. De Giovannini, G. Filippi, F. Rossetto, M. S. Zambito, Gait analysis and clinical correlations in early Parkinson's disease, Funct. Neurol. 32 (1) (2017) 28–34.
[18] S. Vallabhajosula, T.A. Buckley, M.D. Tillman, C.J. Hass, Age and Parkinson's disease related kinematic alterations during multi-directional gait initiation, Gait Posture 37 (2) (2013) 280–286.
[19] S. Taniguchi, N. D'cruz, M. Nakagoshi, T. Osaki, A. Nieuwboer, Determinants of impaired bed mobility in Parkinson's disease: Impact of hip muscle strength and motor symptoms, NeuroRehabilitation 50 (4) (2022) 445–452.
[20] S.T. Baudendistel, A.C. Schmitt, R.T. Roemmich, I.L. Harrison, C.J. Hass, Levodopa facilitates improvements in gait kinetics at the hip, not the ankle, in individuals with Parkinson's disease, J. Biomech. 121 (2021) 110366.
[21] C. Changcheng, Y.R. Li, C.T. Chen, Assistive Mobility Control of a Robotic Hip-Knee Exoskeleton for Gait Training, Sensors (basel). 22 (13) (2022 Jul 4) 5045.
[22] W. Zhang, Y. Ling, Z. Chen, K. Ren, S. Chen, P. Huang, Y. Tan, Wearable sensor-based quantitative gait analysis in Parkinson's disease patients with different motor subtypes, NPJ Digit Med. 7 (1) (2024 Jun 26) 169.
[23] J. Rusz, R. Krupička, S. Vítečková, T. Tykalová, M. Novotný, J. Novák, P. Dušek, E. Růžička, Speech and gait abnormalities in motor subtypes of de-novo Parkinson's disease, CNS Neurosci. Ther. 29 (8) (2023 Aug) 2101–2110.
[24] T. Herman, A. Weiss, M. Brozgol, N. Giladi, J.M. Hausdorff, Gait and balance in Parkinson's disease subtypes: objective measures and classification considerations, J. Neurol. 261 (12) (2014 Dec) 2401–2410.
[25] J.G. Nutt, B.R. Bloem, N. Giladi, M. Hallett, F.B. Horak, A. Nieuwboer, Freezing of gait: moving forward on a mysterious clinical phenomenon, Lancet Neurol. 10 (8) (2011 Aug) 734–744.
[26] J.G. Nutt, Motor subtype in Parkinson's disease: Different disorders or different stages of disease? Mov. Disord. 31 (7) (2016 Jul) 957–961.