UNIVERSITÀ DEGLI STUDI DI TORINO

DIPARTIMENTO DI NEUROSCIENZE
"Rita Levi Montalcini"

DOTTORATO DI RICERCA IN
NEUROSCIENZE
CICLO XXXIII

"POSTURAL ABNORMALITIES AND GAIT IMPAIRMENTS IN PARKINSON'S DISEASE PATIENTS: AN OBSERVATIONAL MULTICENTER STUDY"

TESI PRESENTATA DA:

Chatkaew Pongmala

TUTOR: Prof. Leonardo Lopiano

COORDINATORE DEL DOTTORATO: Prof. Andrea Calvo

ANNI ACCADEMICI: 2017-2021

SETTORE SCIENTIFICO-DISCIPLINARE DI AFFERENZA: MED/26 – Neurologia

To my beloved family

To me

La dimensione del tuo successo si misura con la forza del tuo desiderio, la grandezza del sogno, e da come gestisci la delusione lungo la strada.

-Robert Kiyosaki-

Content **Page**

Content **Page**

Content **Page**

1. Abstract

Introduction: Gait and Postural abnormalities (PA) such antecollis (AC), Camptocormia (CC), Pisa syndrome (PS) are disabling features of Parkinson's disease (PD). Indirect analyses suggested a higher prevalence of PA among Asian patients compared to Caucasian ones, but no direct comparisons have been performed so far. Furthermore, no study has explored the association between gait impairment and the severity of axial PA.

Objective: To compare prevalence and characteristics of PA between Asian and Caucasian PD patients. To clarify the correlations between axial PA and gait features analyzing data of a large cohort of consecutively recruited PD patients.

Methods: An international multicenter cross-sectional study was performed in 6 European and Asian movement disorders centers. Axial PA, encompassing antecollis (AC), camptocormia (CC), and Pisa syndrome (PS), and appendicular PA (appPA) were systematically searched and analyzed in consecutive patients. Videos and photos were taken in all PD patients with any kind of abnormal posture, defined as an MDS-UPDRS III item 3.13 posture score > 0, to perform a quantitative analysis of gait and posture.

Results: Prevalence of axial PA was 23.6% in Asians and 24.3% in Caucasians (p=0.886), in spite of a longer disease duration among Caucasians, but a longer PA duration among Asians. No differences in prevalence between AC, CC, and PS were found between the two ethnicities. The prevalence of appPA was higher in Asians (p=0.036), but the regression analysis did not confirm a significant difference related to ethnicity. Considering the whole population, male gender, a longer disease duration, and a higher axial score were the factors associated with axial PA. Patients with AC, PS and CC showed a decreased walking velocity, stride length and step length when compared with patients without severe axial PA. The correlation analysis showed that higher degrees of trunk flexion in CC patients were associated with decreased step and stride length. In all patients,

reduced velocity, stride and step length ($p<0.05$) were associated with a more severe disease.

Conclusions: The prevalence of axial PA in PD patients is not influenced by ethnicity. However, Asian PD patients tend to develop PA earlier in the disease course, particularly AC. Furthermore, only the increased degrees of trunk flexion in CC were related to decreased step and stride length.

2. Aims of the study

Postural abnormalities (PA) are frequent and disabling clinical features of Parkinson's disease (PD) (Doherty et al., 2011,). The most recognized type of postural deformities is stooped posture with the rounding of the shoulders combining with the flexion of the hips and knees which was the first postural trunk deviation described by James Parkinson (Parkinson et al., 1817). Recently, a retrospective observational study showed that a third of patients with PD have a deformity of their neck, trunk or limbs (Ashour et al 2006).

Despite stooped posture, there are more severe posture or axial alignment deformities which can affect the quality of life of PD patients. These deformities include camptocormia (CP), antecollis (AC), Pisa syndrome (PS), and scoliosis (Doherty et al., 2011, Srivanitchapoom et al., 2016,). The prevalence of these postural deformities is varied because several diagnostic criteria have been used to characterize each deformity (Ashour et al., 2006, Doherty et al.,2011, Kashihara et al., 2012, Pandey et al., 2016, Cervantes-Arriaga et al., 2016, Yoshii et al., 2016, Ando et al., 2019, Tinazzi et al., 2019). However, some epidemiology studies suggest that the prevalence of camptocormia might be higher in Asian patients (Abe et al., 2010, Doherty et al., 2011). Furthermore, more case reports of antecollis originated from Asian than elsewhere (Yamada et al.,2003, Kashihara et al.,2006, Uzawa et al., 2009)

Many studies on postural deformities showed that postural deformities seem to occur in Asian people more than elsewhere. However, a direct comparison of the prevalence and characteristics of PA between Asian and Caucasian PD patients by using the same clinical criteria has never been performed.

Apart from Postural abnormalities, Gait impairments such as slow in walking, step or stride length shortens (Nonnekes et al., 2018, Mirelman et al., 2019) are also the most common symptoms of Parkinson's disease. Current literature presents study either in gait impairments or postural abnormalities. So far, only few studies evaluated the relationship between postural abnormalities and gait impairments (Geroin et al., 2015, Tramonti et al., 2017, Geroin et al., 2019) To our knowledge, up to date, no study has explored the association between gait impairment and all axial PA (AC, CC, and PS).

Moreover, the severity of axial PA affected to gait has not been yet studied in these PD patients.

Therefore, this international, multicenter, cross-sectional study was designed to systemically analyze PA and gait in a large cohort of consecutive PD patients in Europe and Asia.

The main aim of the study was to compare the prevalence of PA, including AC, CC, and PS among Asian and Caucasian PD patients. Thus, the primary outcome measure was the prevalence of PA.

The Secondary aim was to compare the characteristics of different PA among Asian and Caucasian PD patients, to describe clinical features of PD patients with PA, and evaluate risk factors to PA development. On this line, secondary outcomes were the prevalence of AC, CC, PS in Europe and Asia and related clinical associated variables.

The third aim was to study the correlation and association between gait impairment and the severity of axial PA.

3. Introduction

3.1. The Pathophysiology of Parkinson's disease

Parkinson's disease (PD) is the most common age-related neurodegenerative disease. It was initially described by James Parkinson as the 'Shaking Palsy' in the 1800s. PD is a slowly progressive disease caused by the loss of dopaminergic neurons in the Substantia nigra pars compacta (SNpc) of the midbrain which considered as a disorder of the basal ganglia because the substantia nigra pars compacta (SNpc) is a part of the structure in the basal ganglia. Dopamine is a neurotransmitter and a chemical messenger which is produced from dopaminergic neurons. The death or loss of dopaminergic neurons in Substantia nigra pars compacta causes lesser dopamine. And the consequence of this lesser dopamine causes bradykinesia, rest tremor, rigidity, and stooped posture(figure. 1) (Lewitt et al., 2008, Mazzoni et al., 2012).

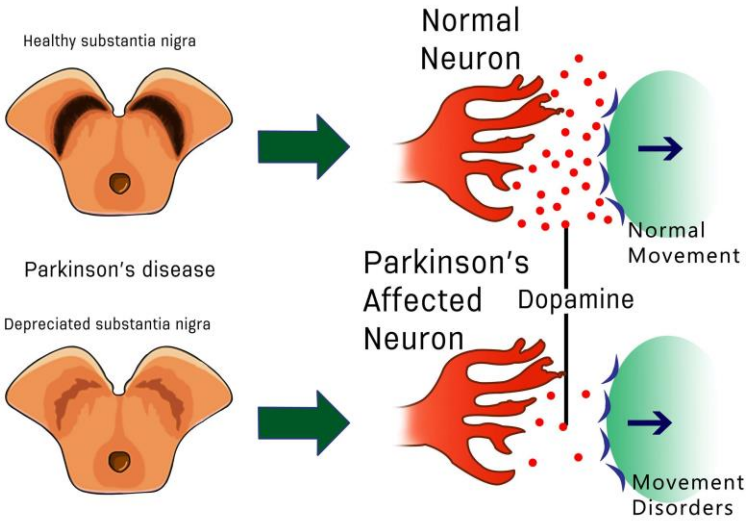


Figure 1. Loss of Dopamine in Substantia nigra can cause movement disorders in a patient with Parkinson's disease

3.2. Postural abnormalities in Parkinson's disease

Because the loss of dopaminergic neurons in basal ganglia lead to the postural changes in PD patients. These postural changes or deformities include stooped posture, dropped head, and a flexed trunk, hips, and knees. In some patients, postural changes progress as more disabling spinal deformities, such as antecollis, camptocormia, and Pisa syndrome (Doherty et al., 2011, Yoshii et al.,2016, Ruttiman et al.,2018). This postural deformity can affect and interfere activity daily living and quality of life of the patients.

The cause of postural deformities remains controversial. Up to date, the evidence suggests that postural deformities have multifactorial pathophysiology such as muscular rigidity, axial dystonia, weakness caused by myopathy, body scheme defects due to centrally impaired proprioception, and structural changes in the spine.

3.3. Postural abnormalities in the Asian and Caucasian population

Doherty et al. compared postural deformities in Parkinson's disease. They found that the prevalence of postural deformities from Asian especially in Japan was higher than elsewhere. In addition, another study from Baik et al also found that the prevalence of postural deformities in Indian patients was higher than American patients. 48.6% of 70 Indian patients with Parkinson's disease were reported to have either striatal or postural deformities. On the contrary, only 33.5% of 164 American patients were found.

Furthermore, there were the study of postural abnormalities in Italian multicenter study from Tinazzi et al. which showed that prevalence of PA in Italian PD patients was 21.5%.

From these studies, it was shown that the prevalence of postural abnormalities in Asian patients with Parkinson's disease seemed to be higher than Caucasian patients.

3.4. Common postural abnormalities in Parkinson's disease

3.4.1. Axial postural abnormalities (axial PA)

3.4.1.1. Sagittal plane abnormalities

3.4.1.1.1. Antecollis

Antecollis is a forward flexion of the head and neck (at least 45°) coupled with increased axial tone (Doherty et al., 2011, Tinazzi et al., 2019). When mild, this might be seen as part of the stooped posture. However, when the deformity progresses, patients with antecollis display markedly reduced the range of motion and eventually develop a fixed deformity. Approximately, 6% of Parkinson's disease patients develop antecollis (Doherty et al., 2011). In recent studies, Kashihara et al studied in 15 patients with Parkinson's disease and found that antecollis was more often found in women and patients whose prominent signs were rigidity and akinesia. Furthermore, Doherty et al found that case reports of antecollis originating in Asian, especially Japan than elsewhere.

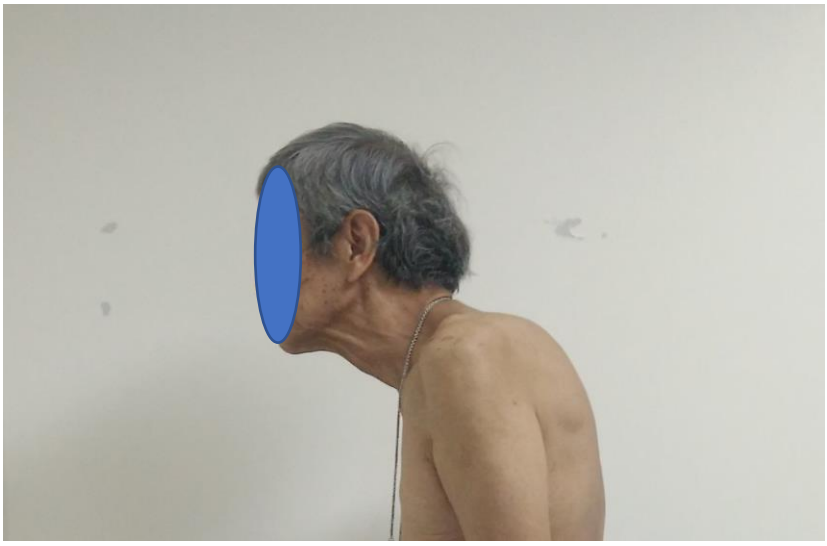


Figure 2. Antecollis (AC)

3.4.1.1.2. Camptocormia

Camptocormia is a forward flexion of the thoracolumbar spine. It is much more manifestation from stooped posture. It is also known as bent spine syndrome. Camptocormia is classified into 2 groups; total camptocormia and upper camptocormia. Total CC is diagnosed in patients with total trunk

flexion ≥ 30 degrees. Upper CC was diagnosed in patients with upper trunk flexion ≥ 45 degrees (Doherty et la., 2011, Fasano et al., 2018, Margraf et al., 2018). Camptocormia often corrects when the patient lies supine. The prevalence of camptocormia in Parkinson's disease patients is between 3 and 17.6%. Ruttiman et al studied that camptocormia typically presents 5–10 years after the onset of Parkinson's disease which affects older patients, and is also associated with the severity of the disease. From epidemiology studies, Doherty et al showed that the prevalence of camptocormia might be higher in Asian patients.

Figure 3. Total camptocormia (TC)

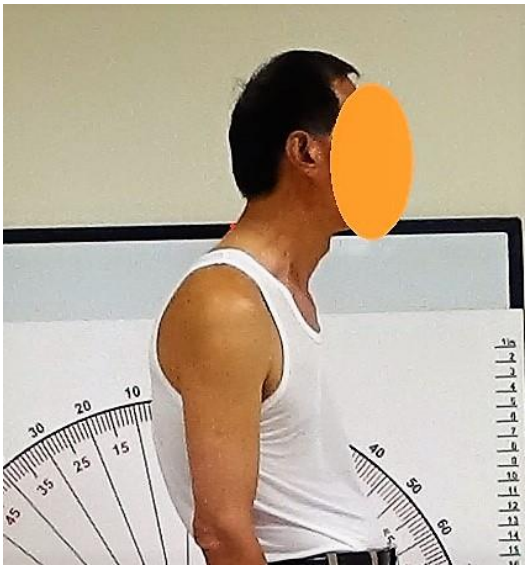


Figure 4. Upper camptocormia (UC)

3.4.1.2. Coronal plane abnormalities

3.4.1.2.1. Pisa syndrome

Pisa syndrome is a lateral flexion of the trunk with at least 10° when sitting or standing, which often resolves when the patient lies supine (Doherty et al., 2011, Tinazzi et al., 2019). Tinazzi et al showed that the prevalence of camptocormia in PD patients was 8-8.8% in Parkinson's disease patients. Pisa syndrome has been described as truncal dystonia and might be possible to be a precursor of development to scoliosis in Parkinson's disease.

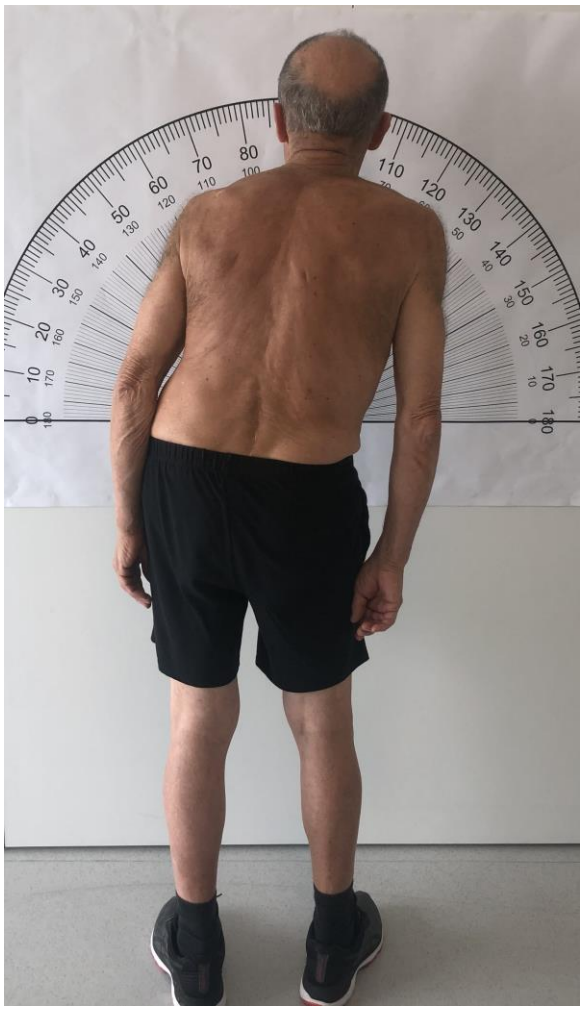


Figure 5. Pisa syndrome (PS)

3.4.1.2.2. Scoliosis

Scoliosis is a lateral flexion of the spine coupled with the rotation of vertebra which does not resolve by passive movement or during the patient lies supine. Scoliosis is measured by Cobb's method as at least 10° of lateral curvature of the spine (Doherty et al., 2011). Doherty et al showed that scoliosis often occurred and more common in Parkinson's disease patients than in the elderly population with the prevalence of 8% to 60%.

3.4.2. Appendicular Postural Abnormalities (appPA) (Ashour et. al., 2006)

3.4.2.1. Striatal hand

Striatal hand is defined as the fixed deformity of the angle at metacarpophalangeal (flexion), proximal interphalangeal (extension), and distal interphalangeal joints (flexion)

3.4.2.2. Striatal foot

Striatal foot is defined as the fixed deformity of the angle of the great toe (flexion or extension) and other toes (plantar flexion)

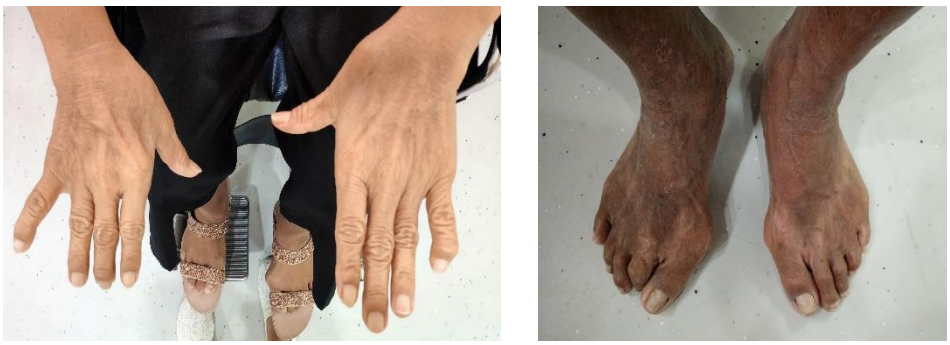


Figure 6. Striatal hand and foot (SH & SF)

3.5. Gait impairments (Mirelman et al., 2019)

Gait impairments are common symptoms of Parkinson's disease. The typical pathological manifestations such as bradykinesia, rigidity, and reduced automaticity and amplitude of movement affect the gait of PD patients (reduced step length, gait velocity, increased axial rigidity, and impaired rhythmicity).

3.5.1. Early stage of PD

In the early stage, symptoms are often unilateral. Changes in posture further affect the magnitude of movement, for example, the reduction of walking speed and step length. Moreover, gait variability is larger than age-matched group too.

3.5.2. Mild to moderate stage of PD

Many of the gait parameters altered in the early stages of the disease progress bilaterally, so that asymmetry might actually decrease, and movement becomes more bradykinetic with disease progression. Increased cadence and short shuffling steps become common in this stage. Postural changes might contribute to the decline in gait by altering gait kinematics.

3.5.3. Advanced stage of PD

Gait is worsened. Freezing of gait become common and frequent, accompanied by reduced postural control and balance and severe risk of falling in this stage.

3.6. The measurement tools to measure the severity and progression of Parkinson's disease

3.6.1. Modified Hoehn and Yahr Scale (Larsen et al., 1983)

The modified Hoehn and Yahr Scale (H&Y) provides a global assessment of severity in Parkinson's Disease based on clinical findings and functional disability. It is a commonly used system for describing how the symptoms of Parkinson's disease progress. This scale is a modified version of the scale which was originally published in 1967 by Hoehn and Yahr.

The modified Hoehn and Yahr scale are as follows:

Stage 0:	No signs of disease
Stage 1.0:	Symptoms are very mild; unilateral involvement only
Stage 1.5:	Unilateral and axial involvement
Stage 2:	Bilateral involvement without impairment of balance
Stage 2.5:	Mild bilateral disease with recovery on pull test
Stage 3:	Mild to moderate bilateral disease; some postural instability; physically independent
Stage 4:	Severe disability; still able to walk or stand unassisted
Stage 5:	Wheelchair bound or bedridden unless aided

3.6.2. The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008)

The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) is a new version of UPDRS that would maintain the overall format of the original UPDRS, but address issues identified in the critique as weaknesses and ambiguities. UPDRS is a rating tool to follow the longitudinal course of Parkinson's Disease. The MDS-UPDRS has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living, Part III (motor examination) and Part IV (motor complications).

3.6.3. Clinical phenotypes of Parkinson's disease (PD phenotype) (Stebbins et al.,2013)

Tremor dominant (TD) and Postural instability/gait difficulty (PIGD) phenotypes of Parkinson's Disease (PD) formulas in this study are used MDS-UPDRS to calculate.

TABLE 1. Items used for tremor dominant and postural instability/gait difficulty calculations[a]

UPDRS	MDS-UPDRS
Tremor score	Tremor score
Part II	Part II
2.16. Tremor	2.10. Tremor
Part III	Part III
3.20. Rest tremor face	3.15. Postural tremor RUE
3.20. Rest tremor RUE	3.15. Postural tremor LUE
3.20. Rest tremor LUE	3.16. Kinetic tremor RUE
3.20. Rest tremor RLE	3.16. Kinetic tremor LUE
3.20. Rest tremor LLE	3.17. Rest tremor RUE
3.21. Action tremor RUE	3.17. Rest tremor LUE
3.21. Action tremor RUE	3.17. Rest tremor RLE
	3.17. Rest tremor LLE
	3.17. Rest tremor lip/jaw
	3.18. Rest constancy
PIGD score	PIGD score
Part II	Part II
2.13. Falling	2.12. Walking and balance
2.14. Freezing	2.13. Freezing
2.15. Walking	
Part III	Part III
3.29. Gait	3.10. Gait
3.30. Postural stability	3.11. Freezing of gait
	3.12. Postural stability

Figure 7. Items used for tremor dominant (TD) and postural instability/gait difficulty (PIGD) calculation

To calculate the MDS-UPDRS TD/PIGD score, the mean of MDS-UPDRS items 2.10, 3.15a, 3.15b, 3.16a, 3.16b, 3.17a, 3.17b, 3.17c, 3.17d, 3.17e, and 3.18 is divided by the mean of MDS-UPDRS items 2.12, 2.13, 3.10, 3.11, and 3.12. (Figure 4.)

If the resultant ratio is ≥1.15, then the patient is classified with Tremor dominant (TD).

If the ratio is ≤0.90, then the patient is classified with Postural instability/gait difficulty (PIGD).

If the ratio is between 0.90 and 1.15, then the patient is classified as indeterminate or mixed type.

3.6.4. PIGD score (Bloem et al., 2016)

The postural instability and gait difficulty score is defined as the sum of MDS-UPDRS items 2.12 walking and balance, 2.13 freezing, 3.10 gait, 3.11 freezing of gait, and 3.12 postural stability. The higher scores reflected greater PIGD. This score is used as a measurement instrument to assess posture, gait, and balance in PD patients.

severity

3.6.5. Axial score (Mei et al., 2019)

Axial score is defined as the sum of MDS-UPDRS item 3.1 speech, 3.2 facial expression, 3.3 neck rigidity, 3.9 arising from chair, 3.10 gait, 3.11 freezing of gait, 3.12 postural stability, 3.13 posture, and 3.14 Global spontaneity of movement. This score is used as a measurement instrument to assess axial impairments and axial symptoms of PD patients.

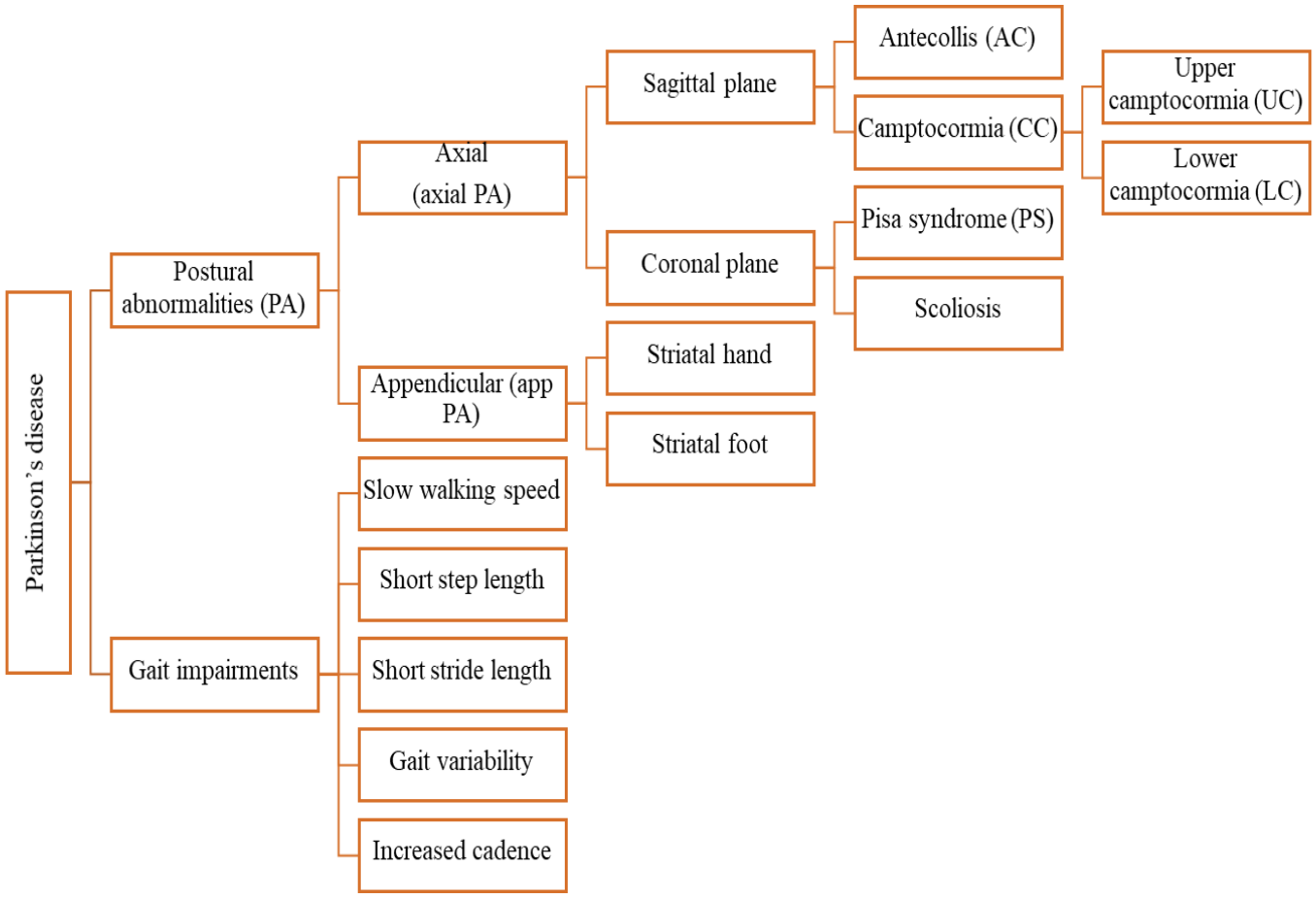
3.6.6. Clinical asymmetry (Fabbri et al., 2016)

Parkinsonism is considered asymmetric when right–left differences in resting tremor, bradykinesia and rigidity were ≥5 points on the MDS-UPDRS items 3.3 neck rigidity, 3.4 right and left finger tapping, 3.6 right and left hand pronation and supination movements , 3.8 right and left leg agility , 3.15 right and left hand postural tremor, 3.16 right and left hand kinetic tremor, and 3.17 rest tremor amplitude (RUE/LUE/RLE/LLE).

3.7. Parkinson’s disease questionnaire–8 (PDQ-8) (Jenkinson et al., 2007)

Parkinson’s disease questionnaire–8 (PDQ-8) is a short-form version which is modified from Parkinson’s disease questionnaire-39. It is a self-administered questionnaire and is used to measure the quality of life in Parkinson’s disease patients.

3.8. Conceptual framework



Flowchart 1. Characteristics and Types of Postural abnormalities and gait impairments in Parkinson's disease.

4. Methods

4.1. Study design and eligibility criteria

For this multicenter, cross-sectional study, consecutive Caucasian and Asian PD outpatients attending 3 tertiary centers for movement disorders in Europe (Italy, Germany, and Portugal) and 3 in Asia (Thailand, South Korea, and Saudi Arabia) were enrolled between May 2019 and May 2021.

4.1.1. Inclusion criteria:

- patients with a diagnosis of Idiopathic PD in agreement with the MDS-criteria (Postuma et al., 2015)
- at least 3 years of disease duration
- age less than 80 years old

4.1.2. Exclusion criteria:

- concomitant neurologic diseases are known to negatively affect posture
- a history of major spinal surgery or muscle and/or skeletal diseases
- treatment with drugs potentially able to induce abnormal postures (typical antipsychotics such as haloperidol, chlorpromazine, zotepine; atypical antipsychotics such as clozapine, sertindole, olanzapine; tricyclic antidepressants; selective serotonin reuptake inhibitors; cholinesterase inhibitors such as donepezil, rivastigmine; antiemetic drugs; lithium carbonate; benzodiazepines; tiapride) (Suzuki et. al., 2002) in the 6 months before enrollment
- clinical features consistent with a diagnosis of atypical parkinsonism (Wenning et. al., 2011).

In each center, all patients were assessed by a systematic evaluation by the same rater identified before study initiation and trained for the postural assessment. Patients were assessed on their usual drug treatment (i.e., daily ON therapeutic status). All evaluations were carried out during a single outpatient visit. A retrospective review of medical records was performed to retrieve demographic, clinical, and genetic relevant data.

All patients with any kind of abnormal posture, defined as an MDS-UPDRS III item 3.13 posture score > 0, underwent through an additional assessment encompassing photographs to analyze the type and degrees of PA. Participants' photos were taken in a standing position in two different planes, frontal (posterior) and sagittal, to account for both anterior and lateral trunk misalignments. Full-body photographs were taken in a standardized manner, in front of a baseline adjustable wall mount goniometer (https://www.ncmedical.com) and the patient standing in front of the wall, 2 meters from the camera set at a height of about 1 meter from the ground. Furthermore, short walking was also recorded. Full body walking was recorded in the sagittal plane. During recording, the distance of the participants and the investigator will be 2-3 meters. Kinovea® software, a freeware program already used for the postural analysis of PD patients (Elwardany et al., 2015, Hisham et al., 2017, Puig-Diví A et al., 2019, Tinazzi et al., 2019) was used to analyze postural angles from the pictures.

4.2. Procedures

In each center, all patients were assessed by a systematic evaluation by the same rater identified before study initiation and trained for the postural assessment. Patients were assessed on their usual drug treatment (i.e., daily ON therapeutic status). All evaluations were carried out during a single outpatient visit. A retrospective review of medical records was performed to retrieve demographic, clinical, and genetic relevant data.

All patients with any kind of abnormal posture, defined as an MDS-UPDRS III item 3.13 posture score > 0, underwent through an additional assessment encompassing photographs and video recording to analyze the type and degrees of PA and gait parameters. Participants' photos were taken in a standing position in two different planes, coronal (posterior) and sagittal planes, to account for both anterior and lateral trunk misalignments. Full-body photographs were taken in a standardized manner, in front of a baseline adjustable wall mount goniometer (https://www.ncmedical.com) and the patient standing in front of the wall, 2 meters from the camera set at a height of about 1 meter from the ground. Full body walking was also recorded in

sagittal plane. Kinovea® software, a freeware program already used for the postural analysis of PD patients (Hisham et al., 2017, Elwardany et al., 2018, Puig-Diví A et al., 2019, Tinazzi et al., 2019) was used to analyze postural angles and gait parameters from the pictures and videos.

All patients underwent an extensive cross-sectional clinical assessment including demographic and clinical data, levodopa equivalent daily dose (LEDD) (Tomlinson et al., 2010), Hoehn Yahr Stage (HY) (Hoehn et al., 1998), MDS-sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part II-III scale (Goetz et al., 2008), the pain NRS scale (Haefeli et al., 2006), and Parkinson's disease questionnaire 8 (PDQ-8) (Jenkinson et al., 2007) for quality of life (QoL). PD phenotype has been defined in agreement with the algorithm of Stebbins and colleagues as tremor dominant (TD) or Postural instability/gait difficulty (PIGD) (Stebbins et al., 2013).

The following clinical and demographic variables were recorded in a paper case report form:

4.2.1. General evaluation for patients with Parkinson's disease

- Sex (male/female);
- Age (years);
- Age at PD onset (years);
- Body mass index (BMI);
- Disease duration (years);
- Total score of modified Hoehn and Yahr (H&Y) scale
- Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Parts II-III scores
- PD phenotype
    - Postural instability/gait difficulty
    - Tremor-dominant
    - Mixed type
- Laterality of motor symptoms at PD onset
    - Right

    - Left
    - Bilateral
- Clinical asymmetry
- Axial score: the sum of MDS-UPDRS item 3.1, 3.2, 3.3, 3.9, 3.10, 3.11, 3.12, 3.13 and 3.14
- Quality of life by means of Parkinson's Disease Questionnaire–8 (PDQ-8)
- Pharmacologic treatment at disease onset and at the latest visit:
    - First and current pharmacological therapy
- L-Dopa monotherapy
- DA monotherapy
- L-Dopa + DA
- Other antiparkinsonian drugs
- Levodopa equivalent daily dose (LEDD) (milligrams)
- Number of falls in the previous month (Kellogg et.al., 1987) and direction
    - Anterior
    - Posterior
    - Right
    - Left
- Comorbidities (heart diseases, malignancies, diabetes, hypertension, mental disorders, obesity, metabolic disorders, cerebrovascular diseases, physical trauma) (Yes/No)
- Associated medical conditions (osteoporosis, arthrosis, rheumatic diseases, otovestibular disorders) (Yes/No)
- Pain (Yes/No)
    - Head: NRS (0-10)
    - Neck: NRS (0-10)
    - Upper limbs: NRS (0-10)
    - Back: NRS (0-10)
    - Lower limbs: NRS (0-10)

4.2.2. Specific evaluation for Parkinson's disease patients with postural abnormalities (Fig. 8)

Neck flexion angle (NF) was defined as the angle between two intersecting lines between a line drawn through anatomical markers at C7 and the tragus of the ear, and vertical line through C7 (Richards et al., 2016, Ailneni et al., 2019, Tinazzi et al., 2019).

Total trunk flexion (TTF) was defined as the angle between the line connecting the C7 with L5 and the line connecting L5 with the Lateral malleolus (Fasano et al., 2018, Margraf et al., 2018).

Upper trunk flexion (UTF) was defined as the outer angle between the two lines between the line connecting L5 with a fulcrum and the line connecting C7 with fulcrum which fulcrum was a line perpendicular to the ground and was the most distant point perpendicular to the L5/C7 line (Fasano et al., 2018, Margraf et al., 2018).

Lateral flexion angle (LF) was defined as the angle between a vertical line and the line connecting the posterior process of the C7 and L5 (Doherty et al., 2011, Tinazzi et al., 2015, Yoshii et al., 2016)**.**

Step length was the distance between the heel contact point of one foot and that of the other foot (Fabbri et al., 2020).

Step variability was defined by using coefficient of variation (CV) of step lengths (Bryant et al., 2011).

$$\% \text{ CV} = (\text{standard deviation} \div \text{mean}) * 100$$

Stride length was defined as the distance between two successive placements of the same foot. (Fabbri et al., 2020)

Velocity was defined by the walking distance divided by walking time (Fabbri et al., 2020).

$$V\ (m/s) = \text{walking distance (m)} / \text{walking time (s)}$$

Cadence was defined as the number of steps during walking in one minute (Fabbri et al., 2020)

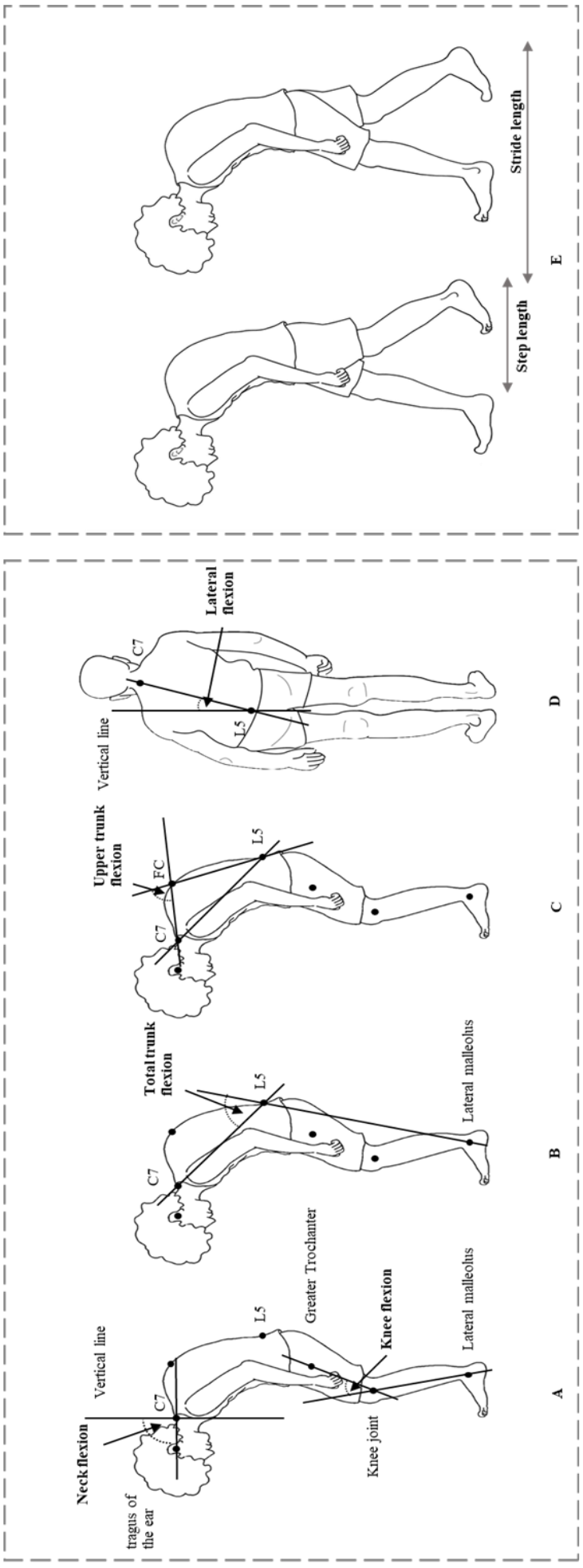


Figure 8. The measurement of body angles and gait. In lateral view was shown neck flexion (NF) (A), knee flexion (KF) (A), total trunk flexion (TTF) (B), and upper trunk flexion (UTF) (C). In back view was shown lateral flexion (LF) (D). Step length (SL) and stride length (ST)(E).

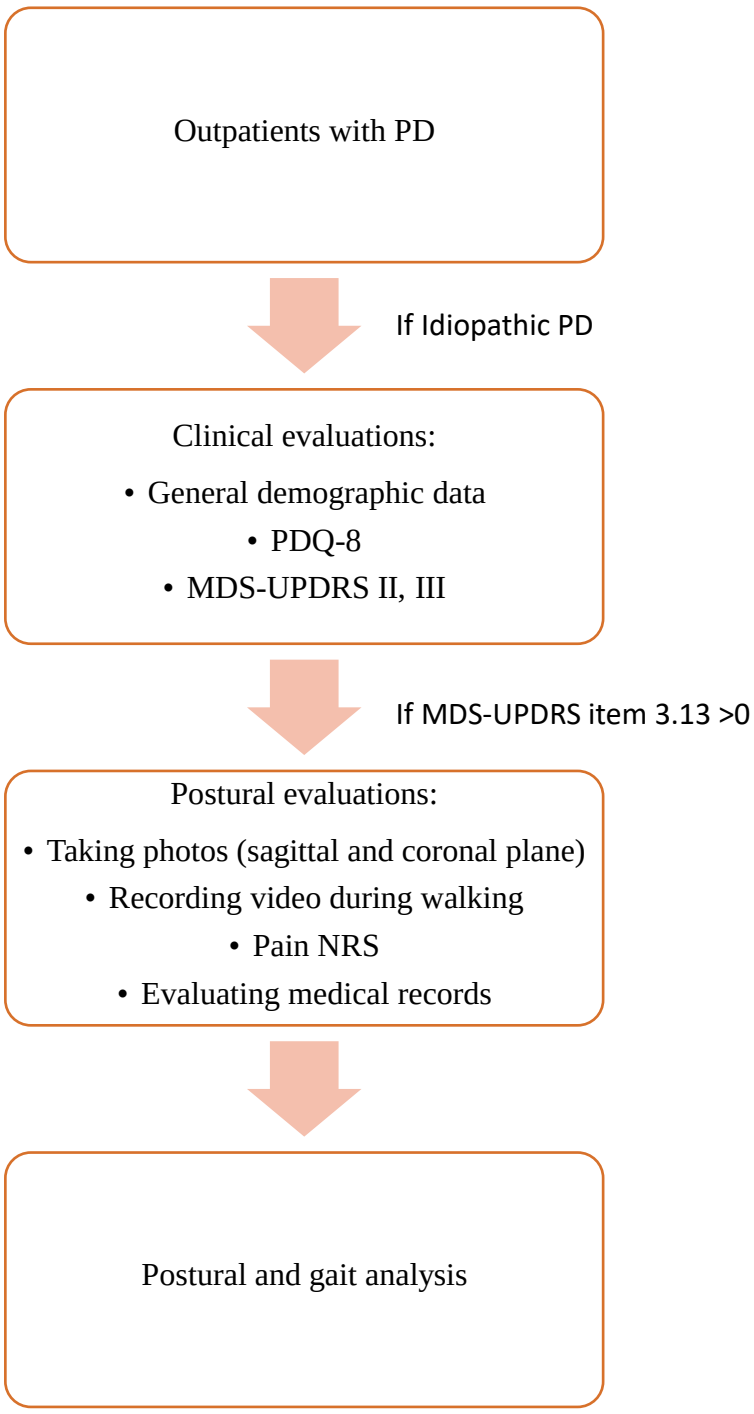
For each postural deformity, the following information were recorded:

- Latency to develop one or more postural deformity after PD onset (months)
- Postural deformity duration (years)
- Postural deformity direction (right/left/anterior);
- In case of Pisa syndrome, the presence of metronome sign (defined as an alternate leaning behavior occurring toward both sides) (Yes/No)
- The pattern of postural deformity onset
    - Acute (<1 month)
    - Subchronic (≥1 month <3 months)
    - Chronic (≥3 months);
- Side of PD symptoms at onset and PS inclination
    - PS ipsilateral PD symptoms onset (number of patients)
    - PS contralateral PD symptoms onset (number of patients)
    - PS with bilateral PD symptoms onset (number of patients)
- Postural deformity after one month of drug modification (Yes/No);
- Postural deformity awareness by the patient (Yes/No)
- Head compensation (in case of PS, CP, AC) (defined as head deviation away from the bending side to preserve a horizontal vision) (Yes/No);

4.2.3. Standard protocol approvals, registrations, and patient consents.

The study protocol was reviewed and approved by the institutional review boards from every center. All patients (or their guardians) were informed about the content of the study and before data collection and written informed consent was obtained by all patients also considering the possibility of taking photographs and walking records for this research.

4.3. Study protocol



Flowchart 2. The diagram is to show the study protocol and the process of this study

4.4. Sample sizes

To ensure an adequate power to address the hypothesis of a different PA prevalence between Asian and Caucasian PD patients, we performed a sample size calculation through the 'n4studies' software.28 (Ngamjarus et al., 2016)

A sample size of 348 PD patients (209 Asian PD patients and 139 Caucasian PD patients) was calculated by using sample size for two independent proportions with an estimation of 49% and 33.5% of the highest prevalence of PA in Asian and Caucasian PD patients (Figure 9.), no dropout rate was considered due to the cross-sectional design of the study. The total number of PD patients to be enrolled were at least 322.

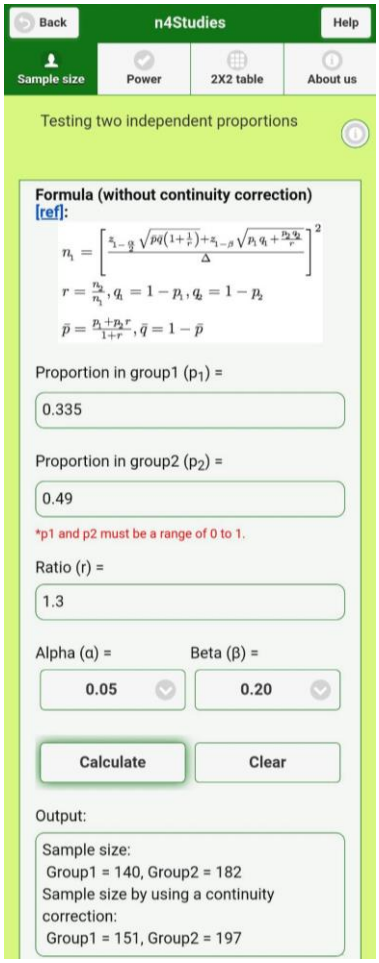


Figure 9. Sample size calculation from n4studies

The proportion in group 1 used the prevalence from “Joint and skeletal deformities in Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy” (Ashour et al., 2016). This proportion were Caucasian representative.

The proportion in group 2 used the prevalence from “Postural & striatal deformities in Parkinson's disease: Are these rare?” (Pandey et al., 2016). This proportion were Asian representative.

The ratio between Asia and Europe were 1.5 because we recruited more patient in Asia than Europe.

Where p1 = 0.335 (Ashour 2016)
p2 = 0.49 (Pandey 2016)
Ratio (n2/n1) = 1.3
Alpha = 0.05, Z(0.975) = 1.959964
Beta = 0.20, Z(0.80) = 0.8416212

Total sample size for Group1(Europe) = **140**, Group2 (Asia) = **182**

4.5. Statistical analyses

Descriptive statistics (mean, standard deviation, and range) were used for continuous variables and frequency for categorical data. The Kolmogorov-Smirnov test was used to test for the normal distribution of data. A Chi-square test was used for categorical data. The values were compared across groups by t-tests for independent variables or nonparametric Mann-Whitney U tests when continuous variables were not normally distributed.

Univariate logistic regression models with PA, Axial PA(APA), AC, CC, PS, Appendicular PA (appPA) as the dependent variable and the sociodemographic and clinical features (ethnicity, sex, age, BMI, age of PD onset, disease duration, H&Y stage, MDS-UPDRS II, III, III right, III left, axial score, PD phenotypes, lateral MS at onset, clinical asymmetry, PDQ-8, LEDD, and fall) as the independent variables were used to calculate unadjusted odds ratio (OR; 95% confidence interval [CI]). Multiple logistic regression models with sociodemographic and clinical features which had $p \leq 0.05$ after performing univariate logistic regression as the independent variables and with PA, APA, AC, CC, PS, appPA as the dependent variable, were used to calculate an adjusted OR (95% CI) for all possible confounding effects.

Furthermore, Pearson's or Spearman's coefficient was used to analyze the correlations between gait (SL, %CV of SL, ST, Velocity, and cadence), axial PA (AC, CC, and PS), degrees of flexion (NF, TTF, UTF, and LF), and clinical features (Age, disease duration, H&Y, MDS-UPDRS II, III, PIGD score, and axial score). Univariate linear regression models with step length, step variability, stride length, velocity, and cadence as the dependent variable and the postural angles and presence of AC, TC, UC, and PS as the independent variables were used to calculate unadjusted odds ratio (OR; 95% confidence interval [CI]). Multiple linear regression models with the postural angles and presence of AC, TC, UC, and PS which had $p \leq 0.05$ after performing univariate linear regression all were used to calculate an adjusted OR (95% CI) for all possible confounding effects. All tests were two-tailed with a P-value < 0.05. Statistical analyses were performed using SPSS (version 27) statistical software.

5. Results

5.1. Postural abnormalities: an observational multicenter study

5.1.1. Postural abnormalities (PA)

5.1.1.1. Prevalence of postural abnormalities (PA)

In this study of Postural abnormalities: an observational multicenter study, we recruited a total of 326 PD patients, 182 Asian (Thailand =76, South Korea =81, and Saudi Arabia =25) and 144 Caucasian ethnicities (Italy =77, Germany =30, and Portugal =37).

Considering all patients, 27% presented (n=88) PA, 23.9% (n=78) axial PA, and 4.9% (n=16) appPA. The most common type of axial PA was antecollis (19.9% of all patients), followed by camptocormia (11.7%), and Pisa syndrome (3.7%) (Flowchart 3 and Table 1).

Flowchart 3. Number of total PD and each type of axial PA in this study

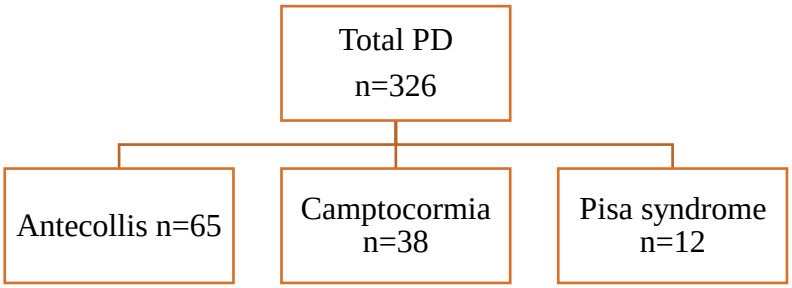


Table 1. Prevalence and clinical features of PD patients with PA

	Total	Asian	Caucasian	P-value
Postural Abnormalities, n (%)	88 (27%)	53 (29.1%)	35 (24.3%)	0.331
Axial PA, n (%)	78 (23.9%)	43 (23.6%)	35 (24.3%)	0.886
Appendicular PA, n (%)	16 (4.9%)	13 (7.1%)	3 (2.1%)	**0.036**
Antecollis, n (%)	65 (19.9%)	32 (17.6%)	33 (22.9%)	0.01
Degrees, mean (SD)	56.47 (10)	53.83 (7.7)	59.02 (11.35)	0.941
Camptocormia, n (%)	38 (11.7%)	21 (11.5%)	17 (11.8%)	
Degrees, mean (SD)				0.876
Lower	36.54 (6.74)	36.11 (6.1)	37.5 (9)	0.973
Upper	49.96 (7.23)	49.5 (5.66)	50.5 (9.1)	
Lower & Upper	57.33 (12.5)		57.33 (12.5)	
	56.67 (2.89)		56.67 (2.89)	0.679
Pisa syndrome, n (%)	12 (3.7%)	6 (3.3%)	6 (4.2%)	0.059
Degrees, mean (SD)	14.67 (6.97)	11.17 (1.33)	18.17 (8.7)	

PA: postural abnormalities; Axial PA: axial postural abnormalities; AC: antecollis; CC: camptocormia; PS: Pisa syndrome; appPA: appendicular postural abnormalities

5.1.1.2. Differences between PD patients without PA and PD patients with PA

PD patients with PA were more often males (p=0.001), older (p=0.002), symmetric in motor symptoms (p=0.012), with a PIGD phenotype (p=0.012), a longer disease duration (p<0.0005), more severe disease (p<0.0005), and a lower QoL (p=0.004) than PD patients without PA; moreover, PD patients with PA showed a higher LEDD (p<0.0005). The average PA duration was 3.21±4.11 years and the onset were 4.49±4.29 years after PD diagnosis (Table 2.).

5.1.1.3. Differences between Asian and Caucasian PD patients with PA

We did not find a significant difference in the prevalence of PA between Asian and Caucasian patients, with 29.1% (n=53/182) and 24.3% (n=35/144) of patients showing PA, respectively (p=0.331).

Caucasian PD patients were older (p=0.011), and had a longer disease duration (p=0.03) than Asian PD patients with PA. However, Asian PD patients had a longer PA duration (p=0.009) than Caucasian PD patients (Table 3).

5.1.1.4. Demographic and clinical features associated with PA

The multiple logistic regression analysis showed that sex (male) (adjusted OR, 2.772; 95% CI, 1.439-5.339; p=0.002), disease duration (adjusted OR, 1.089; 95% CI, 1.015-1.167; p=0.017), and axial score (adjusted OR, 1.236; 95% CI, 1.121-1.362; p<0.0005) were significantly associated with the presence of PA (Table 4).

Table 2. Demographic and clinical features and their differences between PD patients without PA and PD patients with PA

	Total		
	WoPA	**PA**	**P-value**
Patients, n	**238 (73%)**	**88 (27%)**	
Ethnicitiy, n (%)			0.331
Asian	129 (54.2%)	53 (60.2%)	
Caucasian	109 (45.8%)	35 (39.8%)	
Gender, n (%)			**0.001**
Male	120 (50.4%)	63 (71.6%)	
Female	118 (49.6%)	25 (28.4%)	
Age, y, mean (SD)	63.5 (9.4)	67.23 (8.03)	**0.002**
BMI, mean (SD)	24.91 (4.01)	24.7 (4.73)	0.399
Age of PD onset, y, mean (SD)	56.33 (10.39)	58.1 (9.17)	0.19
Disease duration, y, mean (SD)	7.14 (3.96)	9.17 (4.95)	**<0.0005**
H&Y stage, mean (SD)	2.14 (0.69)	2.7 (0.71)	**<0.0005**
MDS-UPDRS score, mean (SD)			
II	10.38 (6.04)	15.77 (9.28)	**<0.0005**
III	26.79 (12.46)	35.83 (14.15)	**<0.0005**
Axial score	7.13 (4.04)	12.55 (5.94)	**<0.0005**
Dominant phenotype, n (%)			**0.012**
PIGD	115 (48.3%)	58 (65.9%)	
Tremor	101 (42.4%)	22 (25%)	
Mixed	22 (9.2%)	8 (9.1%)	
Lateral of PD onset, n (%)			0.356
Right	139 (58.4%)	44 (50%)	
Left	85 (35.7%)	39 (44.3%)	
Bilateral	14 (5.9%)	5 (5.7%)	
Clinical asymmetry, n (%)			**0.012**
Symmetry	134 (56.3%)	63 (71.6%)	
Asymmetry	104 (43.7%)	25 (28.4%)	
PDQ-8, mean (SD)	21.25 (15.8)	27.49 (18.41)	**0.004**
LEDD, mg, mean (SD)	663.45 (422.18)	866.01 (382.59)	**<0.0005**
Fall, n (%)			0.293
No	201 (84.5%)	70 (79.5%)	
Yes	37 (15.5%)	18 (20.5%)	
Latency of PA, y, mean (SD)		4.49 (4.29)	
PA duration, y, mean (SD)		3.21 (4.11)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose

Table 3. Demographic and clinical features and their differences between Asian and Caucasian PD patients with PA

	PA		
	Asian	**Caucasian**	**P-value**
Patients, n	53 (29.1%)	35 (24.3%)	0.331
Gender, n (%)			0.348
Male	36 (67.9%)	27 (77.1%)	
Female	17 (32.1%)	8 (22.9%)	
Age, y, mean (SD)	65.43 (8.22)	69.94 (7)	**0.011**
BMI, mean (SD)	24.28 (4.87)	25.33 (4.51)	0.266
Age of PD onset, y, mean (SD)	57.32 (9.53)	59.29 (8.61)	0.32
Disease duration, y, mean (SD)	8.21 (4.25)	10.63 (5.6)	**0.03**
H&Y stage, mean (SD)	2.64 (0.65)	2.8 (0.8)	0.488
MDS-UPDRS score, mean (SD)			
II	15.49 (9.36)	16.2 (9.27)	0.597
III	33.79 (12.29)	38.91 (16.28)	0.14
Axial score	11.85 (6.81)	13.43 (7.3)	0.412
Dominant phenotype, n (%)			0.648
PIGD	33 (62.3%)	25 (71.4%)	
Tremor	15 (28.3%)	7 (20%)	
Mixed	5 (9.4%)	3 (8.6%)	
Lateral of PD onset, n (%)			0.130
Right	31 (58.5%)	13 (37.1%)	
Left	20 (37.7%)	19 (54.3%)	
Bilateral	2 (3.8%)	3 (8.6%)	
Clinical asymmetry, n (%)			0.610
Symmetry	39 (73.6%)	24 (68.6%)	
Asymmetry	14 (26.4%)	11 (31.4%)	
PDQ-8, mean (SD)	26.89 (12.29)	28.41 (21.45)	0.986
LEDD, mg, mean (SD)	823.99 (343.49)	929.65 (432.63)	0.331
Fall, n (%)			0.125
No	45 (84.9%)	25 (71.4%)	
Yes	8 (15.1%)	10 (28.6%)	
Latency of PA (y)	3.93 (4.13)	5.35 (4.44)	0.18
PA duration (y)	3.6 (3.23)	2.6 (5.15)	**0.009**

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 4. Demographic and clinical features associated with PA*

	WoPA vs PA			WoPA vs PA		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	0.782	0.475-1.285	0.331			
Sex, female VS male	2.478	1.461-4.203	**0.001**	2.772	1.439-5.339	**0.002**
Age	1.049	1.019-1.081	**0.001**	1.032	0.995-1.07	0.093
BMI	0.988	0.932-1.048	0.696			
Age of PD onset	1.018	0.993-1.044	0.161			
Disease duration	1.107	1.047-1.17	**<0.0005**	1.089	1.015-1.167	**0.017**
H&Y stage	3.149	2.12-4.678	**<0.0005**	1.07	0.624-1.835	0.805
MDS-UPDRS score on state						
II	1.104	1.064-1.145	**<0.0005**	1.023	0.964-1.086	0.451
III	1.052	1.031-1.073	**<0.0005**	1.008	0.978-1.038	0.626
Axial score	1.265	1.186-1.35	**<0.0005**	1.236	1.121-1.362	**<0.0005**
Dominant phenotype						
PIGD vs Tremor	0.432	0.247-0.755	**0.003**	0.887	0.445-1.771	0.735
PIGD vs Mixed	0.721	0.302-1.719	0.46	0.661	0.235-1.861	0.433
Lateral MS at onset						
Right vs Left	1.449	0.872-2.41	0.153			
Right vs Bilateral	1.128	0.385-3.309	0.826			
Clinical aymmetry, symmetry vs asymmetry	0.511	0.301-0.868	**0.013**	0.574	0.298-1.104	0.096
PDQ-8	1.022	1.007-1.036	**0.003**	0.979	0.956-1.003	0.084
L-dopa equivalent daily dose	1.001	1.001-1.002	**<0.0005**	1	1-1.001	0.388
Fall, No vs Yes	1.397	0.747-2.611	0.295			

* Variables used to perform in multiple logistic regression were variables $p \leq 0.05$ in univariate logistic regression. In univariate logistic regression, continent had $p > 0.05$ therefore, it was not included in multiple logistic regression.

** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.1.2. Axial postural abnormalities (Axial PA)

5.1.2.1. Prevalence of axial PA

78 from 326 PD patients were found to have postural abnormalities.

Considering all patients, 23.9% presented axial PA. 12.9% presented an isolated axial PA and 9.2% of patients had a combined axial PA (Table 1).

5.1.2.2. Differences between PD patients without axial PA and PD patients with axial PA

PD patients with axial PA were more often males ($p<0.0005$), older ($p<0.0005$), with an older age of PD onset ($p=0.032$), a PIGD phenotype ($p=0.015$), a longer disease duration ($p=0.002$), more severe disease ($p<0.0005$), and a lower QoL ($p=0.007$), and a higher LEDD ($p<0.0005$) than PD patients without axial PA. Axial PA was first noticed on average 4.33±4.25 years after PD onset. The average axial PA duration was 3.38±4.62 years (Table 5).

5.1.2.3. Differences between Asian and Caucasian PD patients with axial PA

We did not find a significant difference in the prevalence of axial PA between Asian and Caucasian patients, with 23.6% (n=43/182) and 24.3% (n=35/144) of patients showing axial PA, respectively ($p=0.886$).

Caucasian PD patients were older ($p=0.042$), and had a longer disease duration ($p=0.009$) than Asian PD patients with PA. However, Asian PD patients had a longer PA duration ($p=0.013$) than Caucasian PD patients (Table 6).

5.1.2.4. Demographic and clinical features associated with axial PA

The multiple logistic regression analysis showed that sex (male) (adjusted OR, 4.036; 95% CI, 1.926-8.456; $p<0.0005$), disease duration (adjusted OR, 2.61; 95% CI, 1.024-6.653; $p=0.044$), and axial score (adjusted OR, 1.242; 95% CI, 1.122-1.375; $p<0.0005$) were significantly associated with the presence of axial PA (Table 7)**.**

Table 5. Demographic and clinical features and their differences between PD patients without axial PA and PD patients with axial PA

	Total		
	Wo Axial PA	**Axial PA**	**P-value**
Patients, n	248 (76.1%)	78 (23.9%)	
Ethnicitiy, n (%)			0.886
Asian	139 (56%)	43 (55.1%)	
Caucasian	109 (44%)	35 (44.9%)	
Gender, n (%)			**<0.0005**
Male	124 (50%)	59 (75.6%)	
Female	124 (50%)	19 (24.4%)	
Age, y, mean (SD)	63.42 (9.41)	67.97 (7.65)	**<0.0005**
BMI, mean (SD)	24.73 (4.05)	25.23 (4.69)	0.579
Age of PD onset, y, mean (SD)	56.11 (10.38)	59.03 (8.82)	**0.032**
Disease duration, y, mean (SD)	7.27 (4.05)	9 (4.96)	**0.002**
H&Y stage, mean (SD)	2.16 (0.69)	2.73 (0.73)	**<0.0005**
MDS-UPDRS score, mean (SD)			
II	10.43 (6.05)	16.29 (9.49)	**<0.0005**
III	26.91 (12.43)	36.62 (14.26)	**<0.0005**
Axial score	7.22 (4.06)	12.96 (6.03)	**<0.0005**
Dominant phenotype, n (%)			**0.015**
PIGD	121 (48.8%)	52 (66.7%)	
Tremor	104 (41.9%)	19 (24.4%)	
Mixed	23 (9.3%)	7 (9%)	
Lateral of PD onset, n (%)			0.362
Right	144 (58.1%)	39 (50%)	
Left	89 (35.9%)	35 (44.9%)	
Bilateral	15 (6%)	4 (5.1%)	
Clinical asymmetry, n (%)			0.068
Symmetry	143 (57.7%)	54 (69.2%)	
Asymmetry	105 (42.3%)	24 (30.8%)	
PDQ-8, mean (SD)	21.36 (15.62)	27.93 (19.19)	**0.007**
LEDD, mg, mean (SD)	671.52 (419.44)	866.42 (393.13)	**<0.0005**
Fall, n (%)			0.093
No	211 (85.1%)	60 (76.9%)	
Yes	37 (14.9%)	18 (23.1%)	
Latency of PA, y, mean (SD)		4.37 (4.17)	
PA duration, y, mean (SD)		3.21 (4.29)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 6. Demographic and clinical features and their differences between Asian and Caucasian PD patients with axial PA

	Axial PA		
	Asian	**Caucasian**	**P-value**
Patients, n	43 (23.6%)	35 (24.3%)	0.365
Gender, n (%)			0.780
Male	32 (74.4%)	27 (77.1%)	
Female	11 (25.6%)	8 (22.9%)	
Age, y, mean (SD)	66.37 (7.85)	69.94 (7)	**0.042**
BMI, mean (SD)	25.14 (4.89)	25.33 (4.51)	0.848
Age of PD onset, y, mean (SD)	58.81 (9.08)	59.29 (8.61)	0.805
Disease duration, y, mean (SD)	7.67 (3.97)	10.63 (5.6)	**0.009**
H&Y stage, mean (SD)	2.67 (0.68)	2.8 (0.8)	0.648
MDS-UPDRS score, mean (SD)			
II	16.37 (9.78)	16.2 (9.27)	0.900
III	34.74 (12.26)	38.91 (16.28)	0.264
Axial score	12.58 (4.83)	13.43 (7.3)	0.766
Dominant phenotype, n (%)			0.697
PIGD	27 (62.8%)	25 (71.4%)	
Tremor	12 (27.9%)	7 (20%)	
Mixed	4 (9.3%)	3 (8.6%)	
Lateral of PD onset, n (%)			0.090
Right	26 (60.5%)	13 (37.1%)	
Left	16 (37.2%)	19 (54.3%)	
Bilateral	1 (2.3%)	3 (8.6%)	
Clinical asymmetry, n (%)			0.909
Symmetry	30 (69.8%)	24 (68.6%)	
Asymmetry	13 (30.2%)	11 (31.4%)	
PDQ-8, mean (SD)	27.54 (17.39)	28.41 (21.45)	0.952
LEDD, mg, mean (SD)	814.95 (354.66)	929.65 (432.63)	0.296
Fall, n (%)			0.299
No	88 (80.7%)	25 (71.4%)	
Yes	21 (19.3%)	10 (28.6%)	
Latency of PA (y)	3.58 (3.81)	5.35 (4.44)	0.115
PA duration (y)	3.71 (3.42)	2.6 (5.15)	**0.013**

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 7. Demographic and clinical features associated with axial PA*

	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	1.038	0.622-1.732	0.887			
Sex, female VS male	3.105	1.749-5.512	**<0.0005**	4.036	1.926-8.456	**<0.0005**
Age, y	1.063	1.029-1.097	**<0.0005**	0.431	0.17-1.093	0.076
BMI	1.028	0.969-1.09	0.367			
Age of PD onset	1.031	1.003-1.059	**0.027**	2.435	0.956-6.202	0.062
Disease duration	1.088	1.029-1.15	**0.003**	2.61	1.024-6.653	**0.044**
H&Y stage	3.186	2.118-4.794	**<0.0005**	1.185	0.676-2.075	0.553
MDS-UPDRS score on state						
II	1.111	1.069-1.154	**<0.0005**	1.021	0.958-1.087	0.521
III	1.055	1.034-1.077	**<0.0005**	1.011	0.98-1.044	0.485
Axial score	1.277	1.194-1.365	**<0.0005**	1.242	1.122-1.375	**<0.0005**
Dominant phenotype						
PIGD vs Tremor	0.425	0.236-0.765	**0.004**	0.912	0.43-1.934	0.81
PIGD vs Mixed	0.708	0.286-1.753	0.456	0.649	0.22-1.912	0.432
Lateral MS at onset						
Right vs Left	1.452	0.857-2.46	0.166			
Right vs Bilateral	0.985	0.309-3.135	0.979			
Clinical asymmetry, symmetry vs asymmetry	0.605	0.352-1.042	0.07			
PDQ-8	1.023	1.008-1.038	**0.003**	0.98	0.956-1.005	0.12
L-dopa equivalent daily dose	1.001	1.000-1.002	**0.001**	1	1.000-1.001	0.347
Fall, No vs Yes	1.711	0.909-3.219	0.096			

* Variables used to perform in multiple logistic regression were variables p≤0.05 in univariate logistic regression. In univariate logistic regression, continent had p>0.05 therefore, it was not included in multiple logistic regression.

** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.1.3. Antecollis (AC)

5.1.3.1. Prevalence of AC

65 from 326 PD patients were found to have antecollis.

Considering all patients, 19.9% presented AC. 9.2% presented an isolated AC and 10.7% of patients had a combined AC (Table 1).

5.1.3.2. Differences between PD patients without AC and PD patients with AC

PD patients with AC were more often males ($p<0.0005$), older ($p<0.0005$), with an older age of PD onset ($p=0.006$), a PIGD phenotype ($p=0.028$), a longer disease duration ($p=0.003$), more severe disease ($p<0.0005$), and a higher LEDD ($p<0.0005$) than PD patients without AC. The average degree of neck flexion was 56.47°±10° (range 45-106.3°). AC was first noticed on average 4.33±4.25 years after PD onset. The average AC duration was 3.38±4.62 years (Table 8).

5.1.3.3. Differences between Asian and Caucasian PD patients with AC

AC prevalence was 17.6% in Asian patients and 22.9% in Caucasian patients ($p= 0.231$). The average degree of neck flexion was 53.83°±7.7° (range 45-74.4°) in Asian patients and 59.02°±11.35° (range 46.2-106.3°) in Caucasian patients ($p=0.01$). AC was first noticed on average 3.18±3.77 years after PD onset in Asian patients and 5.43±4.44 years after PD onset in Caucasian ones ($p= 0.043$). The average AC duration was 4.05±3.8 years in Asian patients and 2.67±5.28 years in Caucasian ones ($p= 0.035$).

AC patients in Caucasians had a longer disease duration ($p=0.015$), had longer latency to develop PA ($p=0.043$), and had more severe neck flexion ($p=0.01$) than Asian patients. While AC patients in Asians had a longer PA duration ($p=0.035$) than Caucasian patients (Table 9).

5.1.3.4. Demographic and clinical features associated with AC

The multiple logistic regression analysis showed that sex (male) (adjusted OR, 3.618; 95% CI, 1.703-7.687; $p=0.001$), and axial score (adjusted OR, 1.230; 95% CI, 1.106-1.367; $p<0.0005$) were significantly associated with the presence of AC (Table 10)**.**

Table 8. Demographic and clinical features and their differences between PD patients without AC and PD patients with AC

	Total		
	WoAC	**AC**	**P-value**
Patients, n	261 (80.1%)	65 (19.9%)	
Ethnicitiy, n (%)			0.231
Asian	150 (57.5%)	32 (49.2%)	
Caucasian	111 (42.5%)	33 (50.8%)	
Gender, n (%)			**<0.0005**
Male	134 (51.3%)	49 (75.4%)	
Female	127 (48.7%)	16 (24.6%)	
Age, y, mean (SD)	63.38 (9.35)	69.06 (7.03)	**<0.0005**
BMI, mean (SD)	24.73 (4.29)	25.33 (3.89)	0.317
Age of PD onset, y, mean (SD)	56.03 (10.36)	59.92 (8.3)	**0.006**
Disease duration, y, mean (SD)	7.32 (4.04)	9.15 (5.16)	**0.003**
H&Y stage, mean (SD)	2.19 (0.71)	2.71 (0.7)	**<0.0005**
MDS-UPDRS score, mean (SD)			
II	10.84 (6.59)	15.85 (9.2)	**<0.0005**
III	27.66 (12.85)	35.54 (14.4)	**<0.0005**
Axial score	7.52 (4.29)	12.91 (6.28)	**<0.0005**
Dominant phenotype, n (%)			**0.028**
PIGD	129 (49.4%)	44 (67.7%)	
Tremor	107 (41%)	16 (24.6%)	
Mixed	25 (9.6%)	5 (7.7%)	
Lateral of PD onset, n (%)			0.293
Right	152 (58.2%)	31 (47.7%)	
Left	94 (36%)	30 (46.2%)	
Bilateral	15 (5.7%)	4 (6.2%)	
Clinical asymmetry, n (%)			0.105
Symmetry	152 (58.2%)	45 (69.2%)	
Asymmetry	109 (41.8%)	20 (30.8%)	
PDQ-8, mean (SD)	21.78 (15.68)	27.56 (19.97)	0.055
LEDD, mg, mean (SD)	681.83 (419.74)	864.17 (396.68)	**<0.0005**
Fall, n (%)			0.062
No	222 (85.1%)	49 (75.4%)	
Yes	39 (14.9%)	16 (24.6%)	
Latency of PA, y, mean (SD)		4.33 (4.25)	
PA duration, y, mean (SD)		3.38 (4.62)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 9. Demographic and clinical features and their differences between Asian and Caucasian PD patients with AC

	AC		
	Asian	**Caucasian**	**P-value**
Patients, n	32 (17.6%)	33 (22.9%)	0.901
Gender, n (%)			0.518
Male	23 (71.9%)	26 (78.8%)	
Female	9 (28.1%)	7 (21.2%)	
Age, y, mean (SD)	67.63 (7.03)	70.45 (6.85)	0.077
BMI, mean (SD)	25.06 (3.33)	25.6 (4.4)	0.864
Age of PD onset, y, mean (SD)	60.09 (8.07)	59.76 (8.64)	0.948
Disease duration, y, mean (SD)	7.59 (3.95)	10.67 (5.76)	**0.015**
H&Y stage, mean (SD)	2.59 (0.56)	2.82 (0.81)	0.328
MDS-UPDRS score, mean (SD)			
II	15.28 (9.15)	16.39 (9.36)	0.524
III	32.03 (10.77)	38.94 (16.68)	0.067
Axial score	12.16 (4.83)	13.64 (7.43)	0.422
Dominant phenotype, n (%)			0.461
PIGD	20 (62.5%)	24 (72.7%)	
Tremor	10 (31.3%)	6 (18.2%)	
Mixed	2 (6.3%)	3 (9.1%)	
Lateral of PD onset, n (%)			0.152
Right	19 (59.4%)	12 (36.4%)	
Left	12 (37.5%)	18 (54.5%)	
Bilateral	1 (3.1%)	3 (9.1%)	
Clinical asymmetry, n (%)			0.934
Symmetry	22 (68.8%)	23 (69.7%)	
Asymmetry	10 (31.3%)	10 (30.3%)	
PDQ-8, mean (SD)	26.66 (17.84)	28.42 (22.09)	0.89
LEDD, mg, mean (SD)	771.67 (337.93)	953.87 (432.69)	0.089
Fall, n (%)			0.28
No	26 (81.3%)	23 (69.7%)	
Yes	6 (18.8%)	10 (30.3%)	
Latency of PA (y)	3.18 (3.77)	5.43 (4.44)	**0.043**
PA duration (y)	4.05 (3.8)	2.73 (5.28)	**0.035**

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 10. Demographic and clinical features associated with AC*

	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	1.394	0.808-2.403	0.232			
Sex, female VS male	2.903	1.57-5.365	**0.001**	3.618	1.703-7.687	**0.001**
Age, y	1.084	1.045-1.124	**<0.0005**	0.737	0.335-1.622	0.448
BMI	1.034	0.971-1.1	0.302			
Age of PD onset	1.043	1.012-1.074	**0.006**	1.456	0.66-3.213	0.352
Disease duration	1.09	1.029-1.155	**0.003**	1.569	0.71-3.468	0.265
H&Y stage	2.705	1.797-4.072	**<0.0005**	1.033	0.582-1.834	0.911
MDS-UPDRS score on state						
II	1.087	1.048-1.127	**<0.0005**	1.002	0.938-1.07	0.956
III	1.042	1.022-1.064	**<0.0005**	0.995	0.962-1.03	0.788
Axial score	1.228	1.153-1.307	**<0.0005**	1.230	1.106-1.367	**<0.0005**
Dominant phenotype						
PIGD vs Tremor	0.438	0.234-0.821	0.01	0.808	0.371-1.761	0.592
PIGD vs Mixed	0.586	0.212-1.625	0.305	0.581	0.18-1.882	0.366
Lateral MS at onset						
Right vs Left	1.565	0.89-2.75	0.12			
Right vs Bilateral	1.308	0.406-4.207	0.653			
Clinical asymmetry, symmetry vs asymmetry	0.62	0.347-1.108	0.107			
PDQ-8	1.02	1.004-1.035	**0.014**	0.984	0.959-1.01	0.222
L-dopa equivalent daily dose	1.001	1.000-1.002	**0.003**	1.000	1.000-1.001	0.335
Fall, No vs Yes	1.859	0.962-3.593	0.065			

* Variables used to perform in multiple logistic regression were variables $p \leq 0.05$ in univariate logistic regression. In univariate logistic regression, continent had $p > 0.05$ therefore, it was not included in multiple logistic regression.

** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.1.4. Camptocormia

5.1.4.1. Prevalence of CC

38 from 326 PD patients were found to have camptocormia.

Considering all patients, 11.7% presented CC. 3.4% presented an isolated CC and 8.3% of patients had a combined CC (Table 1).

5.1.4.2. Differences between PD patients without CC and PD patients with CC

PD patients with CC were more often males (p=0.008), older (p=0.016), a longer disease duration (p=0.008), more severe disease (p<0.005), and a higher LEDD (p=0.001) than PD patients without CC. The average degree of total trunk flexion was 36.54°±6.74° (range 30-49°). The average degree of upper trunk flexion was 49.96°±7.23° (range 45-75°). CC was first noticed on average 4.44±4.4 years after PD onset. The average CC duration was 2.81±2.7 years (Table 11).

5.1.4.3. Differences between Asian and Caucasian PD patients with CC

CC prevalence was 11.5% in Asian patients and 11.8% in Caucasian patients (p= 0.941) (Table S2). The average degree of total trunk flexion was 36.11°±6.1° (range 30-49°) in Asian patients and 37.5°±9° (range 30-38°) in Caucasian patients (p=0.876). The average degree of upper back flexion was 49.5°±5.66° (range 45-63°) in Asian patients and 50.5°±9.1° (range 42-75°) in Caucasian patients (p=0.973) (Table 2). CC was first noticed on average 3.67±3.96 years after PD onset in Asian patients and 5.4±4.84 years after PD onset in Caucasian ones (p= 0.043). The average CC duration was 3±2.39 years in Asian patients and 2.57±3.11 years in Caucasian ones (p= 0.385) (Table 12).

5.1.4.4. Demographic and clinical features associated with CC

The multiple logistic regression analysis showed that sex (male) (adjusted OR, 2.552; 95% CI, 1.086-5.997; p=0.032), and axial score (adjusted OR, 1.121; 95% CI, 1.011-1.244; p=0.031) were significantly associated with the presence of CC (Table 13).

Table 11. Demographic and clinical features and their differences between PD patients without CC and PD patients with CC

	Total		
	WoCC	**CC**	**P-value**
Patients, n	288 (88.3%)	38 (11.7%)	
Ethnicitiy, n (%)			0.941
Asian	161 (55.9%)	21 (55.3%)	
Caucasian	127 (44.1%)	17 (44.7%)	
Gender, n (%)			**0.008**
Male	154 (53.5%)	29 (76.3%)	
Female	134 (46.5%)	9 (23.7%)	
Age, y, mean (SD)	64.04 (9.28)	68.08 (7.97)	**0.016**
BMI, mean (SD)	24.85 (3.98)	24.87 (5.78)	0.463
Age of PD onset, y, mean (SD)	56.52 (10.17)	58.97 (9.37)	0.162
Disease duration, y, mean (SD)	7.49 (4.3)	9.16 (4.43)	**0.008**
H&Y stage, mean (SD)	2.23 (0.72)	2.76 (0.75)	**<0.0005**
MDS-UPDRS score, mean (SD)			
II	11.24 (6.98)	16.32 (9.23)	**0.001**
III	28.21 (13.27)	36.95 (13.1)	**<0.0005**
Axial score	8.02 (4.99)	12.92 (4.87)	**<0.0005**
Dominant phenotype, n (%)			0.237
PIGD	148 (51.4%)	25 (65.8%)	
Tremor	113 (39.2%)	10 (26.3%)	
Mixed	27 (9.4%)	3 (7.9%)	
Lateral of PD onset, n (%)			0.974
Right	162 (56.3%)	21 (55.3%)	
Left	109 (37.8%)	15 (39.5%)	
Bilateral	17 (5.9%)	2 (5.3%)	
Clinical asymmetry, n (%)			0.075
Symmetry	169 (58.7%)	28 (73.7%)	
Asymmetry	119 (41.3%)	10 (26.3%)	
PDQ-8, mean (SD)	22.42 (16.71)	26.82 (16.76)	0.079
LEDD, mg, mean (SD)	691.79 (413.8)	918.49 (426.67)	**0.001**
Fall, n (%)			0.098
No	243 (84.4%)	28 (73.7%)	
Yes	45 (15.6%)	10 (26.3%)	
Latency of PA, y, mean (SD)		4.44 (4.4)	
PA duration, y, mean (SD)		2.81 (2.7)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 12. Demographic and clinical features and their differences between Asian and Caucasian PD patients with CC

	CC		
	Asian	**Caucasian**	**P-value**
Patients, n	21 (11.5%)	17 (11.8%)	0.516
Gender, n (%)			0.455
Male	17 (81%)	12 (70.6%)	
Female	4 (19%)	5 (29.4%)	
Age, y, mean (SD)	67.1 (8.57)	69.29 (7.24)	0.419
BMI, mean (SD)	25.38 (6.31)	24.24 (5.17)	0.452
Age of PD onset, y, mean (SD)	59.43 (10.37)	58.41 (8.25)	0.597
Disease duration, y, mean (SD)	7.81 (3.8)	10.82 (4.68)	0.052
H&Y stage, mean (SD)	2.71 (0.78)	2.82 (0.73)	0.726
MDS-UPDRS score, mean (SD)			
II	16.9 (10.55)	15.59 (7.55)	0.872
III	38.43 (13.48)	35.12 (12.8)	0.509
Axial score	12.48 (4.2)	13.47 (5.68)	0.757
Dominant phenotype, n (%)			0.456
PIGD	12 (57.1%)	13 (76.5%)	
Tremor	7 (33.3%)	3 (17.6%)	
Mixed	2 (9.5%)	1 (5.9%)	
Lateral of PD onset, n (%)			0.134
Right	14 (66.7%)	7 (41.2%)	
Left	7 (33.3%)	8 (47.1%)	
Bilateral	0 (0%)	2 (11.8%)	
Clinical asymmetry, n (%)			0.697
Symmetry	16 (76.2%)	12 (70.6%)	
Asymmetry	5 (23.8%)	5 (29.4%)	
PDQ-8, mean (SD)	26.64 (16.67)	27.05 (17.38)	0.941
LEDD, mg, mean (SD)	826.74 (389.1)	1031.82 (455.01)	0.186
Fall, n (%)			0.258
No	17 (81%)	11 (64.7%)	
Yes	4 (19%)	6 (35.3%)	
Latency of PA (y)	3.67 (3.96)	5.4 (4.84)	0.324
PA duration (y)	3 (2.39)	2.57 (3.11)	0.385

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 13. Demographic and clinical features associated with CC*

	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	1.026	0.52-2.027	0.941			
Sex, female VS male	2.804	1.282-6.134	**0.01**	2.552	1.086-5.997	**0.032**
Age, y	1.056	1.012-1.101	**0.012**	1.038	0.99-1.088	0.121
BMI	1.001	0.924-1.085	0.978			
Age of PD onset	1.026	0.99-1.063	0.161			
Disease duration	1.077	1.007-1.152	**0.03**	1.033	0.949-1.124	0.452
H&Y stage	2.635	1.635-4.248	**<0.0005**	1.255	0.658-2.392	0.491
MDS-UPDRS score on state						
II	1.079	1.036-1.123	**<0.0005**	0.988	0.929-1.05	0.689
III	1.044	1.02-1.07	**<0.0005**	1.007	0.972-1.043	0.702
Axial score	1.168	1.097-1.244	**<0.0005**	1.121	1.011-1.244	**0.031**
Dominant phenotype						
PIGD vs Tremor	0.524	0.242-1.135	0.101			
PIGD vs Mixed	0.658	0.185-2.333	0.517			
Lateral MS at onset						
Right vs Left	1.062	0.524-2.15	0.868			
Right vs Bilateral	0.908	0.196-4.208	0.901			
Clinical asymmetry, symmetry vs asymmetry	0.507	0.237-1.084	0.08			
PDQ-8	1.015	0.996-1.034	0.13			
L-dopa equivalent daily dose	1.001	1.000-1.002	**0.004**	1.001	1.000-1.001	0.217
Fall, No vs Yes	1.929	0.876-4.245	0.103			

* Variables used to perform in multiple logistic regression were variables p≤0.05 in univariate logistic regression. In univariate logistic regression, continent had p>0.05 therefore, it was not included in multiple logistic regression.

** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.1.5. Pisa syndrome (PS)

5.1.5.1. Prevalence of PS

12 from 326 PD patients were found to have Pisa syndrome.

Considering all patients, 3.7% presented PS. 0.3% presented an isolated PS and 3.4% of patients had a combined PS (Table 1).

5.1.5.2. Differences between PD patients without PS and PA patients with PS

PD patients with PS were older (p=0.01), a longer disease duration (p=0.005), more severe disease (p<0.05), a lower QoL (p=0.031), and a higher LEDD (p=0.009) than PD patients without PS. The average degree of lateral flexion was 14.67±6.97 ° (range 30-49°). PS was first noticed on average 6.03±4.35 years after PD onset. The average PS duration was 2.83±2.29 years (Table 14).

5.1.5.3. Differences between Asian and Caucasian PD patients with PS

PS prevalence was 3.3% in Asian patients and 4.2% in Caucasian patients (p= 0.679). The average degree of flexion was 11.17°±1.33° (range 10-13°) in Asian patients and 18.17°±8.7° (range 10-33°) in Caucasian patients (p=0.059). PS was first noticed on average 6±4.58 years and 6±6.06 years after PD onset in Asian and Caucasian patients, respectively (p= 0.872). The average PS duration was 3.97±2.47 years in Asian patients and 1.7±1.51 years in Caucasian ones (p= 0.64).PS patients in Caucasians took more LEDD than in Asian patients (p=0.03) (Table 15).

5.1.5.4. Demographic and clinical features associated with PS

The multiple logistic regression analysis showed that disease duration (adjusted OR, 1.200; 95% CI, 1.03-1.399; p=0.02), MDS-UPDRS II (adjusted OR, 1.137; 95% CI, 1.001-1.29; p=0.048), and axial score (adjusted OR, 1.232; 95% CI, 1.015-1.494; p=0.035) were significantly associated with the presence of PS (Table 16).

Table 14. Demographic and clinical features and their differences between PD patients without PS and PD patients with PS

	Total		
	WoPS	**PS**	**P-value**
Patients, n	314 (96.3%)	12 (3.7%)	
Ethnicitiy, n (%)			0.679
Asian	176 (56.1%)	6 (50%)	
Caucasian	138 (43.9%)	6 (50%)	
Gender, n (%)			0.454
Male	175 (55.7%)	8 (66.7%)	
Female	139 (44.3%)	4 (33.3%)	
Age, y, mean (SD)	64.26 (9.17)	70.92 (8.34)	**0.01**
BMI, mean (SD)	24.9 (4.25)	23.67 (2.96)	0.319
Age of PD onset, y, mean (SD)	56.74 (10.14)	58.75 (9.14)	0.573
Disease duration, y, mean (SD)	7.52 (4.17)	12.17 (6.29)	**0.005**
H&Y stage, mean (SD)	2.27 (0.73)	3 (0.74)	**0.001**
MDS-UPDRS score, mean (SD)			
II	11.42 (6.92)	22.75 (11.81)	**0.001**
III	28.81 (13.1)	40.17 (19.58)	**0.04**
Axial score	8.27 (4.75)	17.17 (8.82)	**<0.0005**
Dominant phenotype, n (%)			0.265
PIGD	165 (52.5%)	8 (66.7%)	
Tremor	121 (38.5%)	2 (16.7%)	
Mixed	28 (8.9%)	2 (16.7%)	
Lateral of PD onset, n (%)			0.878
Right	177 (56.4%)	6 (50%)	
Left	119 (37.9%)	5 (41.7%)	
Bilateral	18 (5.7%)	1 (8.3%)	
Clinical asymmetry, n (%)			0.098
Symmetry	187 (59.6%)	10 (83.3%)	
Asymmetry	127 (40.4%)	2 (16.7%)	
PDQ-8, mean (SD)	22.45 (16.36)	35.42 (22.27)	**0.031**
LEDD, mg, mean (SD)	706.71 (416.16)	1020.58 (452.89)	**0.009**
Fall, n (%)			0.121
No	263 (83.8%)	8 (66.7%)	
Yes	51 (16.2%)	4 (33.3%)	
Latency of PA, y, mean (SD)		6.03 (4.35)	
PA duration, y, mean (SD)		2.83 (2.29)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 15. Demographic and clinical features and their differences between Asian and Caucasian PD patients with CC

	PS		
	Asian	**Caucasian**	**P-value**
Patients, n	6 (3.3%)	6 (4.2%)	1.000
Gender, n (%)			0.221
Male	3 (50%)	5 (83.3%)	
Female	3 (50%)	1 (16.7%)	
Age, y, mean (SD)	68.5 (10.52)	73.33 (5.32)	0.573
BMI, mean (SD)	24.83 (2.48)	22.5 (3.15)	0.17
Age of PD onset, y, mean (SD)	58.67 (12.29)	58.83 (5.71)	0.936
Disease duration, y, mean (SD)	9.83 (5.12)	14.5 (6.92)	0.167
H&Y stage, mean (SD)	2.83 (0.41)	3.17 (0.98)	0.434
MDS-UPDRS score, mean (SD)			
II	24.33 (11.29)	21.17 (13.17)	0.748
III	37 (11.52)	43.33 (26.2)	1.000
Axial score	17 (4.24)	17.33 (12.37)	0.936
Dominant phenotype, n (%)			0.287
PIGD	3 (50%)	5 (83.3%)	
Tremor	2 (33.3%)		
Mixed	1 (16.7%)	1 (16.7%)	
Lateral of PD onset, n (%)			0.549
Right	3 (50%)	3 (50%)	
Left	3 (50%)	2 (33.3%)	
Bilateral		1 (16.7%)	
Clinical asymmetry, n (%)			1.000
Symmetry	5 (83.3%)	5 (83.3%)	
Asymmetry	1 (16.7%)	1 (16.7%)	
PDQ-8, mean (SD)	38.02 (17.94)	32.81 (27.44)	0.629
LEDD, mg, mean (SD)	774.17 (327.15)	1267 (445.53)	**0.03**
Fall, n (%)			0.221
No	5 (83.3%)	3 (50%)	
Yes	1 (16.7%)	3 (50%)	
Latency of PA (y)	6 (4.58)	6.06 (4.55)	0.872
PA duration (y)	3.97 (2.47)	1.7 (1.51)	0.064

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 16. Demographic and clinical features associated with PS*

	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	1.275	0.402-4.041	0.679			
Sex, female VS male	1.589	0.469-5.385	0.457			
Age, y	1.106	1.019-1.201	**0.016**	1.088	0.985-1.203	0.097
BMI	0.926	0.796-1.076	0.315			
Age of PD onset	1.021	0.961-1.085	0.498			
Disease duration	1.168	1.065-1.282	**0.001**	1.200	1.03-1.399	**0.02**
H&Y stage	3.393	1.62-7.109	**0.001**	0.705	0.199-2.498	0.588
MDS-UPDRS score on state						
II	1.139	1.074-1.207	**<0.0005**	1.137	1.001-1.29	**0.048**
III	1.052	1.015-1.091	**0.006**	0.967	0.903-1.035	0.337
Axial score	1.256	1.136-1.389	**<0.0005**	1.232	1.015-1.494	**0.035**
Dominant phenotype						
PIGD vs Tremor	0.341	0.071-1.634	0.178			
PIGD vs Mixed	1.473	0.297-7.3	0.635			
Lateral MS at onset						
Right vs Left	1.239	0.37-4.154	0.728			
Right vs Bilateral	1.639	0.187-14.38	0.656			
Clinical asymmetry, symmetry vs asymmetry	0.294	0.063-1.367	0.118			
PDQ-8	1.038	1.008-1.069	**0.012**	0.96	0.904-1.019	0.179
L-dopa equivalent daily dose	1.001	1.000-1.002	**0.017**	1.000	0.999-1.002	0.724
Fall, No vs Yes	2.578	0.748-8.884	0.133			

* Variables used to perform in multiple logistic regression were variables p≤0.05 in univariate logistic regression. In univariate logistic regression, continent had p>0.05 therefore, it was not included in multiple logistic regression.

** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.1.6. Appendicular postural abnormalities (app PA)

5.1.6.1. Prevalence of app PA

16 from 326 PD patients were found to have appendicular PA.

Considering all patients, 4.9% presented app PA. 2.4% presented an isolated app PA and 2.4% of patients had a combined app PA (Table 1).

5.1.6.2. Differences between PD patients without app PA patients and PD patients with app PA

PD patients with app PA were Asian (p=0.036), a lower BMI (p<0.0005), a longer disease duration (p=0.002), a higher H&Y stage (p=0.018), a higher axial score (p=0.046), and a higher LEDD (p=0.045) than PD patients without app PA (Table 17).

5.1.6.3. Differences between PD patients with app PA and PD patients with axial PA

Patients with appPA had a lower BMI (p=0.001), with a younger age(p=0.041) and earlier age at PD onset (p=0.013) than patients with axial PA (Table 18).

5.1.6.4. Differences between Asian and Caucasian PD patients with app PA

AppPA showed a prevalence of 7.1% (n=13) in Asian patients and 2.1% (n=3) in Caucasian patients, that was statistically different (p=0.036, Table 2). AppPA was first noticed on average 5.31±5.58 years and 4±5.29 years after PD onset for Asia and Caucasian patients, respectively (p= 0.945). The average appPA duration was 3.42±2.91 years in Asian patients and 10.33±16.17 years in Caucasian ones (p= 0.946). AppPA patients in Asian were younger than Caucasian patients (p=0.043) (Table 19)

5.1.6.5. Demographic and clinical features associated with PS

The multiple logistic regression analysis showed that lower BMI (adjusted OR, 0.835, 95% CI, 0.714-0.977; p=0.024), and a longer disease duration (adjusted OR, 1.140, 95% CI, 1.036-1.254; p=0.007) were variables significantly associated with its presence (Table 20).

Table 17. Demographic and clinical features and their differences between PD patients without app PA and PD patients with app PA

	Total		
	Wo app PA	**app PA**	**P-value**
Patients, n	310 (95.1%)	16 (4.9%)	
Ethnicitiy, n (%)			**0.036**
Asian	169 (54.5%)	13 (81.3%)	
Caucasian	141 (45.5%)	3 (18.8%)	
Gender, n (%)			0.306
Male	176 (56.8%)	7 (43.8%)	
Female	134 (43.2%)	9 (56.3%)	
Age, y, mean (SD)	64.48 (9.22)	65.06 (9.31)	0.814
BMI, mean (SD)	25.03 (4.2)	21.31 (2.55)	**<0.0005**
Age of PD onset, y, mean (SD)	56.98 (10.05)	53.56 (10.73)	0.212
Disease duration, y, mean (SD)	7.49 (4.12)	11.5 (6.42)	**0.002**
H&Y stage, mean (SD)	2.27 (0.73)	2.75 (0.78)	**0.018**
MDS-UPDRS score, mean (SD)			
II	11.65 (7.18)	15.44 (11.14)	0.183
III	28.91 (13.33)	35.44 (16.06)	0.106
Axial score	8.45 (5.12)	11.44 (6.22)	**0.046**
Dominant phenotype, n (%)			0.193
PIGD	161 (51.9%)	12 (75%)	
Tremor	120 (38.7%)	3 (18.8%)	
Mixed	29 (9.4%)	1 (6.3%)	
Lateral of PD onset, n (%)			0.228
Right	177 (57.1%)	6 (37.5%)	
Left	116 (37.4%)	8 (50%)	
Bilateral	17 (5.5%)	2 (12.5%)	
Clinical asymmetry, n (%)			**0.023**
Symmetry	183 (59%)	14 (87.5%)	
Asymmetry	127 (41%)	2 (12.5%)	
PDQ-8, mean (SD)	22.59 (16.67)	29.49 (17.38)	0.094
LEDD, mg, mean (SD)	709.58 (422.21)	886.75 (369.58)	**0.045**
Fall, n (%)			0.065
No	255 (82.3%)	16 (100%)	
Yes	55 (17.7%)	0 (0%)	
Latency of PA, y, mean (SD)		5.06 (5.38)	
PA duration, y, mean (SD)		4.72 (7.03)	

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 18. Demographic and clinical features and their differences between PD patients with app PA and PD patients with axial PA

	Total		
	Axial PA	**app PA**	**P-value**
Patients, n	78 (23.9%)	16 (4.9%)	
Ethnicitiy, n (%)			**0.023**
Asian	43 (55.1%)	13 (81.3%)	
Caucasian	35 (44.9%)	3 (18.8%)	
Gender, n (%)			**0.022**
Male	59 (75.6%)	7 (43.8%)	
Female	19 (24.4%)	9 (56.3%)	
Age, y, mean (SD)	67.97 (7.65)	65.06 (9.31)	**0.041**
BMI, mean (SD)	25.23 (4.69)	21.31 (2.55)	**0.001**
Age of PD onset, y, mean (SD)	59.03 (8.82)	53.56 (10.73)	**0.013**
Disease duration, y, mean (SD)	9 (4.96)	11.5 (6.42)	0.197
H&Y stage, mean (SD)	2.73 (0.73)	2.75 (0.78)	0.436
MDS-UPDRS score, mean (SD)			
II	16.29 (9.49)	15.44 (11.14)	0.197
III	36.62 (14.26)	35.44 (16.06)	0.21
Axial score	12.96 (6.03)	11.44 (6.22)	**0.039**
Dominant phenotype, n (%)			0.494
PIGD	52 (66.7%)	12 (75%)	
Tremor	19 (24.4%)	3 (18.8%)	
Mixed	7 (9%)	1 (6.3%)	
Lateral of PD onset, n (%)			0.395
Right	39 (50%)	6 (37.5%)	
Left	35 (44.9%)	8 (50%)	
Bilateral	4 (5.1%)	2 (12.5%)	
Clinical asymmetry, n (%)			0.284
Symmetry	54 (69.2%)	14 (87.5%)	
Asymmetry	24 (30.8%)	2 (12.5%)	
PDQ-8, mean (SD)	27.93 (19.19)	29.49 (17.38)	0.837
LEDD, mg, mean (SD)	866.42 (393.13)	886.75 (369.58)	0.921
Fall, n (%)			0.081
No	60 (76.9%)	16 (100%)	
Yes	18 (23.1%)	0 (0%)	
Latency of PA, y, mean (SD)	4.37 (4.17)	5.06 (5.38)	0.695
PA duration, y, mean (SD)	3.21 (4.29)	4.72 (7.03)	0.455

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 19. Demographic and clinical features and their differences between Asian and Caucasian PD patients with app PA

	App PA		
	Asian	**Caucasian**	**P-value**
Patients, n	13 (7.1%)	3 (2.1%)	**0.036**
Gender, n (%)			0.375
Male	5 (38.5%)	2 (66.7%)	
Female	8 (61.5%)	1 (33.3%)	
Age, y, mean (SD)	62.85 (8.69)	74.67 (5.13)	**0.043**
BMI, mean (SD)	21.39 (2.75)	21 (1.73)	0.631
Age of PD onset, y, mean (SD)	52.62 (9.97)	57.67 (15.37)	0.381
Disease duration, y, mean (SD)	10.23 (4.92)	17 (10.39)	0.118
H&Y stage, mean (SD)	2.62 (0.51)	3.33 (1.53)	0.444
MDS-UPDRS score, mean (SD)			
II	13.85 (8.73)	22.33 (19.66)	0.590
III	10.69 (5.33)32.46 (13.2)	48.33 (24.13)	0.2
Axial score	10.69 (5.33)	14.67 (10.02)	0.542
Dominant phenotype, n (%)			0.540
PIGD	9 (69.2%)	3 (100%)	
Tremor	3 (23.1%)	0	
Mixed	1 (7.7%)	0	
Lateral of PD onset, n (%)			0.710
Right	5 (38.5%)	1 (33.3%)	
Left	6 (46.2%)	2 (66.7%)	
Bilateral	2 (15.4%)	0	
Clinical asymmetry, n (%)			0.226
Symmetry	12 (92.3%)	2 (66.7%)	
Asymmetry	1 (7.7%)	1 (33.3%)	
PDQ-8, mean (SD)	26.44 (14.36)	42.71 (26.58)	0.28
LEDD, mg, mean (SD)	869.27 (321.36)	962.5 (627.87)	0.946
Fall, n (%)			
No	13 (100%)	3 (100%)	
Yes	0	0	
Latency of PA (y)	5.31 (5.58)	4 (5.29)	0.945
PA duration (y)	3.42 (2.91)	10.33 (16.17)	0.946

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 20. Demographic and clinical features associated with app PA*

	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Ethnicity, Asian vs Caucasian*	0.277	0.077-0.99	**0.048**	0.278	0.067-1.158	0.079
Sex, female VS male	0.592	0.215-1.631	0.311			
Age, y	1.007	0.953-1.065	0.805			
BMI	0.765	0.66-0.887	**<0.0005**	0.835	0.714-0.977	**0.024**
Age of PD onset	0.969	0.925-1.016	0.189			
Disease duration	1.153	1.06-1.255	**0.001**	1.140	1.036-1.254	**0.007**
H&Y stage	2.28	1.196-4.347	**0.012**	1.524	0.563-4.126	0.407
MDS-UPDRS score on state						
II	1.056	1.000-1.115	0.051			
III	1.032	0.998-1.067	0.062			
Axial score	1.092	1.009-1.181	**0.029**	1.027	0.91-1.159	0.669
Dominant phenotype						
PIGD vs Tremor	0.335	0.093-1.215	0.096			
PIGD vs Mixed	0.463	0.058-3.696	0.467			
Lateral MS at onset						
Right vs Left	2.034	0.688-6.015	0.199			
Right vs Bilateral	3.471	0.649-18.545	0.146			
Clinical asymmetry, symmetry vs asymmetry	0.206	0.046-0.921	**0.039**	0.414	0.079-2.179	0.298
PDQ-8	1.022	0.995-1.049	0.112			
L-dopa equivalent daily dose	1.001	1.000-1.002	0.106			
Fall, No vs Yes	0	0	0.997			

* Variables used to perform in multiple logistic regression were variables $p \leq 0.05$ in univariate logistic regression. In univariate logistic regression, continent had $p > 0.05$ therefore, it was not included in multiple logistic regression.

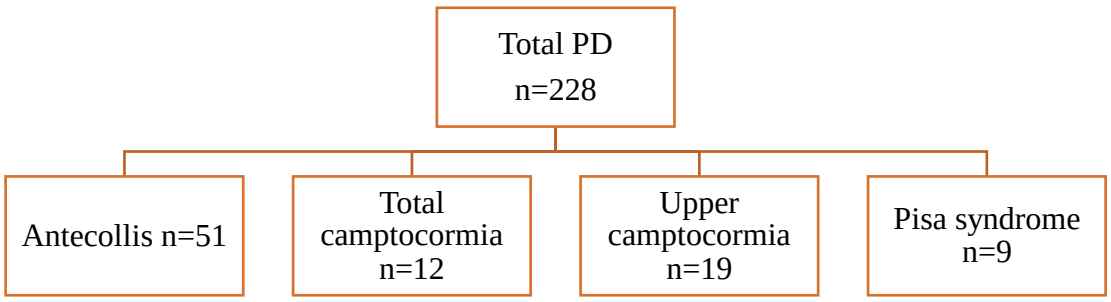
** Demographic and clinical features associated with PD patients with PA compared with PD patients without PA.

PA: postural abnormalities; BMI: Body Mass Index; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8.

5.2. Gait and Axial Postural Abnormalities correlations in Parkinson's disease

In this study of gait and axial Postural Abnormalities correlations in Parkinson's disease, we recruited 228 PD who had a clinically defined PA, i.e., MDS-UPDRS III item 3.13 posture score > 0. 51 patients antecollis (22.4%), followed by total camptocormia (n=12; 5.8%), upper camptocormia (n=19; 8.9%), and Pisa syndrome (n=9; 3.9%)(Flowchart 4).

Flowchart 4. Number of total PD and each type of axial PA in this study



PD patients with axial PA were more often male (p=0.001), older (p<0.0005), a higher age at PD onset (p=0.039), with a PIGD phenotype (p=0.017), a longer disease duration (p=0.014), more severe disease (p<0.0005), and a higher LEDD (p<0.0005) than PD patients without axial PA.

Overall, PD patients with axial PA had a shorter step length (p<0.0005), a shorter stride length (p<0.0005), and a slower walking speed (p<0.0005) than PD patients without axial PA.

5.2.1. The Association between each axial PA and gait

5.2.1.1. Antecollis (AC)

51 patients with AC and an average 55.97°±8.27° (range 45-79.9°) degree of neck flexion was included. AC was first noticed on average 4.32±4.25 years after PD onset. The average AC duration was 3.95±4.98 years.

AC patients had an average step length of 43.35±12.77 cm, a step length variability (%CV) of 11.15±18.86 %, stride length of 86.8±24.77 cm, gait velocity of 0.76 ±0.24 m/s and a cadence 107.18±19.35 steps/min (Table 21).

AC patients were more often male (p=0.02), older (p<0.0005), had a higher age at PD onset (p=0.01), more severe disease (p<0.001), a longer disease duration (p=0.012), and a higher LEDD (p=0.004), than PD patients without AC (Table 21). Moreover, AC patients had a shorter step length (p<0.0005), a shorter stride length (p<0.0005), and a slower walking speed (p<0.0005) than PD patients without AC (Table 21).

The correlation analysis showed that higher HY stage, MDS-UPDRS II, III, PIGD score, and axial score were related to decreased step length, stride length, and velocity (p<0.05). Moreover, higher MDS-UPDRS II, PIGD score, and higher Axial score were also related to increased step variability (p<0.05). In addition, a higher age and a higher age at PD onset in AC patients were also related to decreased step variability (p<0.05) (Table 22).

Furthermore, a higher HY stage, MDS-UPDRS II, and III were related to increased neck flexion (p<0.05). However, an increased neck flexion was related to decreased cadence (Table 22).

The multiple linear regression analysis showed that male sex (adjusted OR, -7.138; 95% CI, (-10.723) – (-3.553); p<0.0005), MDS-UPDRS III (adjusted OR, -0.155; 95% CI, (-0.307) – (-0.004); p=0.045) and PIGD score (adjusted OR, -1.534; 95% CI, (-2.571) - (-0.498); p=0.004) were significantly associated with the step length (Table 23).

The multiple linear regression analysis showed that axial score (adjusted OR, 1.053; 95% CI, 0.140 – 1.967; p=0.024) were significantly associated with the step variability (Table 24).

The multiple linear regression analysis showed that male sex (adjusted OR, -13.914; 95% CI, (-20.770) – (-7.058); p<0.0005), and PIGD score (adjusted OR, -3.161; 95% CI, (-5.143) - (-1.179); p=0.002) were significantly associated with the stride length (Table 25).

The multiple linear regression analysis showed that PIGD score (adjusted OR, -0.033; 95% CI, (-0.055) – (-0.01); p=0.005) were significantly associated with the velocity (Table 26).

No association were found between clinical features and cadence (Table 27).

Table 21. Demographic and clinical features of PD patients without AC and PD patients with AC

	Total		
	WoAC	**AC**	**P-value**
Patients, n	177 (77.7%)	51 (22.3%)	**<0.0005**
Gender, n (%)			**0.02**
Male	89 (50.3%)	35 (68.6%)	
Female	88 (49.7%)	16 (31.4%)	
Age, y, mean (SD)	63.02 (9.02)	68.9 (6.69)	**<0.0005**
Age of PD onset, y, mean (SD)	55.46 (10.39)	59.71 (8.5)	**0.01**
Disease duration, y, mean (SD)	7.54 (4.16)	9.22 (5.01)	**0.012**
H&Y stage, mean (SD)	2.25 (0.78)	2.75 (0.66)	**<0.0005**
MDS-UPDRS score, mean (SD)			
II	11.43 (6.92)	15.22 (8.98)	**0.005**
III	27.65 (12.97)	33.33 (13.31)	**0.007**
PIGD	3.89 (2.86)	6.14 (4.28)	**0.003**
Axial	8.42 (4.02)	12.18 (5.52)	**<0.0005**
Dominant phenotype, n (%)			0.083
PIGD	80 (45.2%)	32 (62.7%)	
Tremor	80 (45.2%)	15 (29.4%)	
Mixed	17 (9.6%)	4 (7.8%)	
Lateral of PD onset, n (%)			0.557
Right	104 (58.8%)	26 (51%)	
Left	65 (36.7%)	23 (45.1%)	
Bilateral	8 (4.5%)	2 (3.9%)	
Clinical asymmetry, n (%)			0.195
Symmetry	111 (62.7%)	37 (72.5%)	
Asymmetry	66 (37.3%)	14 (27.5%)	
PDQ-8, mean (SD)	22.21 (15.6)	25.92 (17.63)	0.249
LEDD, mg, mean (SD)	693.66 (438.08)	856.31 (385.97)	**0.004**
Step length (CM)	50.15 (10.4)	43.35 (12.77)	**<0.0005**
Step variability (%CV)	6.44 (4.45)	11.15 (18.86)	0.17
Stride length (cm)	100.34 (20.65)	86.8 (24.77)	**<0.0005**
Velocity (m/s)	0.93 (0.23)	0.76 (0.24)	**<0.0005**
Cadence (steps/min)	110.49 (14.06)	107.18 (19.35)	0.099

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 22. Correlation between clinical features, degrees of flexion, and gait parameters

AC	Neck flexion	Step length	Step variability	Stride length	Velocity	Cadence
Neck flexion		-0.054	0.070	-0.063	-0.230	**-.320***
Age	0.060	0.039	**-.370****	0.016	0.214	0.157
Age of PD onset	0.009	0.012	**-.302***	-0.013	0.099	0.011
Disease duration	0.057	0.038	0.016	0.052	0.117	0.181
H&Y stage	**.470****	**-.311***	0.248	**-.319***	**-.435****	**-.330***
MDS-UPDRS score						
II	**.406****	**-.362****	**.428****	**-.358****	**-.397****	-0.132
III	**.285***	**-.421****	0.226	**-.389****	**-.496****	-0.228
PIGD	0.178	**-.574****	**.501****	**-.609****	**-.608****	-0.097
Axial	0.197	**-.459****	**.490****	**-.478****	**-.475****	-0.101

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty**.**

Table 23. Demographic, clinical features, neck flexion, and presence of AC associated with step length

	Step length					
	Unadjusted			Adjusted		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Presence of AC, No vs Yes	-6.800	-10.235 - (-3.364)	**<0.0005**	-5.017	-11.858 - 1.824	0.149
Neck Flexion	-0.233	-0.377 - (-0.090)	**0.002**	0.103	-0.174 - 0.380	0.461
Sex, Female vs Male	-5.753	-8.625 - (-2.881)	**<0.0005**	-7.138	-10.723 - (-3.553)	**<0.0005**
Age	-0.350	-0.511 - (-0.190)	**<0.0005**	0.144	-0.268 - 0.557	0.490
Age of PD onset	-0.251	-0.394 - (-0.109)	**0.001**			
Disease duration	-0.115	-0.451 - 0.221	0.502	-0.215	-0.573 - 0.142	0.235
H&Y stage	-3.471	-5.313 - (-1.629)	**<0.0005**	-0.030	-3.383 - 3.324	0.986
MDS-UPDRS score						
II	-0.512	-0.696 - (-0.328)	**<0.0005**	-0.016	-0.311 - 0.278	0.912
III	-0.241	-0.349 - (-0.134)	**<0.0005**	-0.155	-0.307 - (-0.004)	0.045
PIGD	-1.978	-2.467 - (-1.489)	**<0.0005**	-1.534	-2.571 - (-0.498)	**0.004**
Axial	-1.134	-1.416 - (-0.852)	**<0.0005**	-0.212	-1.011 - 0.586	**0.600**
LEDD	-0.004	-0.007 - (-0.000)	**0.029**	-0.002	-0.006 - 0.002	0.253

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate logistic regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with AC compared with PD patients without AC.

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 24. Demographic, clinical features, neck flexion, and presence of AC associated with step variability

	Step variability					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of AC, No vs Yes	4.706	1.668 - 7.744	**0.003**	3.099	-8.066 - 19.989	0.429
Neck Flexion	0.184	0.057 - 0.312	**0.01**	-0.097	-4.624 - 10.823	0.544
Sex, Female vs Male	0.483	-2.109 - 3.076	0.71			
Age	-0.034	-0.179 - 0.112	0.65			
Age of PD onset	-0.057	-0.185 - 0.07	0.38			
Disease duration	0.161	-0.132 - 0.454	0.28			
H&Y stage	2.502	0.878 - 4.127	**0.003**	-2.451	-0.413 - 0.219	0.211
MDS-UPDRS score						
II	0.417	0.256 - 0.579	**<0.0005**	0.176	-6309 - 1.406	0.290
III	0.165	0.069 - 0.260	**0.001**	-0.064	-0.237 - 0.108	0.460
PIGD	1.409	0.886 - 1.931	**<0.0005**	0.312	-0.877 - 1.501	0.604
Axial	0.890	0.637 - 1.142	**<0.0005**	1.053	0.140 - 1.967	**0.024**
LEDD	0.002	-0.001 - 0.005	0.12			

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with AC compared with PD patients without AC.

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 25. Demographic, clinical features, neck flexion, and presence of AC associated with stride length

	Stride length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of AC, No vs Yes	-13.535	-20.309 - (-6.761)	**<0.0005**	-10.171	-23.254 - 2.912	0.126
Neck Flexion	-0.450	-0.732 - (-0.168)	**0.002**	0.247	-0.283 - 0.776	0.359
Sex, Female vs Male	-11.428	-17.092 - (-5.764)	**<0.0005**	-13.914	-20.770 - (-7.058)	**<0.0005**
Age	-0.723	-1.038 - (-0.408)	**<0.0005**	0.235	-0.554 - 1.024	0.556
Age of PD onset	-0.518	-0.798 - (-0.238)	**<0.0005**	-0.398	-1.081 - 0.286	0.252
Disease duration	-0.247	-0.909 - 0.416	0.464			
H&Y stage	-6.844	-10.479 - (-3.210)	**<0.0005**	0.779	-5.634 - 7.193	0.810
MDS-UPDRS score						
II	-1.007	-1.370 - (-0.645)	**<0.0005**	-0.016	-0.579 - 0.546	0.955
III	-0.452	-0.664 - (-0.239)	**<0.0005**	-0.235	-0.526 - 0.055	0.111
PIGD	-4.005	-4.951 - (-3.059)	**<0.0005**	-3.161	-5.143 - (-1.179)	**0.002**
Axial	-2.287	-2.839 - (-1.735)	**<0.0005**	-0.562	-2.089 - 0.965	0.468
LEDD	-0.007	-0.014 - (-0.001)	**0.032**	-0.004	-0.012 - 0.003	0.275

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with AC compared with PD patients without AC.

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 26. Demographic, clinical features, neck flexion, and presence of AC associated with velocity

	Velocity					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of AC, No vs Yes	-0.170	-0.243 - (-0.097)	**<0.0005**	-0.118	-0.269 - (0.032)	0.123
Neck Flexion	-0.006	-0.009 - (-0.003)	**<0.0005**	0.002	-0.004 - 0.008	0.578
Sex, Female vs Male	-0.058	-0.121 - 0.006	0.074			
Age	-0.005	-0.009 - (-0.002)	**0.003**	0.005	-0.004 - 0.015	0.235
Age of PD onset	-0.004	-0.007 - (-0.001)	**0.015**	-0.006	-0.014 - 0.002	0.135
Disease duration	-0.002	-0.009 - 0.005	0.637			
H&Y stage	-0.070	-0.110 - (-0.031)	**0.001**	0.023	-0.051 - 0.097	0.539
MDS-UPDRS score						
II	-0.011	-0.015 - (-0.007)	**<0.0005**	-0.001	-0.007 - 0.006	0.778
III	-0.006	-0.008 - (-0.003)	**<0.0005**	-0.002	-0.006 - 0.001	0.146
PIGD	-0.041	-0.052 - (-0.03)	**<0.0005**	-0.033	-0.055 - (-0.01)	**0.005**
Axial	-0.023	-0.029 - (-0.017)	**<0.0005**	-0.006	-0.023 - 0.012	0.525
LEDD	-0.0001	-0.0002 - (-0.00003)	**0.008**	-0.0001	-0.0002 - 0.00003	0.160

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with AC compared with PD patients without AC.

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 27. Demographic, clinical features, neck flexion, and presence of AC associated with cadence

	Cadence					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of AC, No vs Yes	-3.306	-8.155 - 1.543	0.181			
Neck Flexion	-0.244	-0.442 - (-0.045)	**0.016**	-0.092	-0.347 - 0.164	0.479
Sex, Female vs Male	4.955	0.958 - 8.951	**0.015**	3.309	-2.391 - 9.009	0.253
Age	0.106	-0.122 - 0.333	0.361			
Age of PD onset	0.041	-0.158 - 0.240	0.686			
Disease duration	0.228	-0.229 - 0.685	0.327			
H&Y stage	-1.958	-4.532 - 0.616	0.135			
MDS-UPDRS score						
II	-0.281	-0.546 - (-0.016)	**0.038**	-0.263	-0.716 - 0.189	0.252
III	-0.225	-0.375 - (-0.076)	**0.003**	-0.126	-0.353 - 0.101	0.273
PIGD	-0.768	-1.519 - (-0.017)	**0.045**	-0.411	-1.409 - 0.587	0.417
Axial	-0.351	-0.783 - 0.081	0.111			
LEDD	-0.003	-0.008 - 0.001	0.166			

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with AC compared with PD patients without AC.

AC: Antecollis; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

5.2.1.2. Total Camptocormia (TC)

12 patients with TC and an average 35.42°±5.63° (range 30-49.9°) degree of total trunk flexion was included. TC was first noticed on 5.11±5.55 years after PD onset. The average TC duration was 4.01±2.34 years.

TC patients had an average step length of 40.16±8.02 cm, a step length variability (%CV) of 6.66±5.34 %, stride length of 78.96 ±13.9 cm, gait velocity of 0.77 ±0.19 m/s and a cadence 117±19.8 steps/min (Table 28).

TC patients were older (p=0.032), had a higher MDS-UPDRS II (p=0.048), PIGD score (p=0.009), and axial score (p<0.0005) than PD patients without TC (Table 28).

Moreover, TC patients had a shorter step length (p=0.002), a shorter stride length (p=0.001), and a slower walking speed (p=0.026), than PD patients without TC (Table 28).

The correlation analysis showed that a higher degrees of total trunk flexion was related to decreased step and stride length. A higher age and a higher age at PD onset in TC patients were also related to increased total trunk flexion, decreased step and stride length (p<0.05). A higher HY stage, and Axial score were related to increased step variability (p<0.05). However, a longer disease duration was related to decreased step variability (p<0.005) (Table 29).

The multiple linear regression analysis showed that male sex (adjusted OR, -5.792; 95% CI, (-9.450) – (-2.134); p=0.002) were significantly associated with the step length (Table 30).

The multiple linear regression analysis showed that axial score (adjusted OR, 1.056; 95% CI,0.232 – 1.881; p=0.012) were significantly associated with the step variability (Table 31).

The multiple linear regression analysis showed that male sex (adjusted OR, -11.679; 95% CI, (-18.664) – (-4.694); p=0.001), and PIGD score (adjusted OR, -2.003; 95% CI, (-3.928) - (-0.079); p=0.041) were significantly associated with the stride length (Table 32).

The multiple linear regression analysis showed that total trunk flexion (adjusted OR, -0.011; 95% CI, (-0.018) – (-0.003); p=0.007) was significantly associated with the velocity (Table 33).

The multiple linear regression analysis showed that male sex (adjusted OR, 4.295; 95% CI,0.079 – 8.511; p=0.046) were significantly associated with the cadence (Table 34).

Table 28. Demographic and clinical features of PD patients without TC and PD patients with TC

	Total		
	WoTC	**TC**	**P-value**
Patients, n	195 (94.2%)	12 (5.8%)	**<0.0005**
Gender, n (%)			0.611
Male	99 (50.8%)	7 (58.3%)	
Female	96 (49.2%)	5 (41.7%)	
Age, y, mean (SD)	63.72 (8.94)	69.83 (7.64)	**0.032**
Age of PD onset, y, mean (SD)	55.98 (10.19)	60.58 (10.72)	0.115
Disease duration, y, mean (SD)	7.72 (4.38)	9.33 (5)	0.157
H&Y stage, mean (SD)	2.29 (0.77)	2.58 (0.67)	0.233
MDS-UPDRS score, mean (SD)			
II	11.6 (7.1)	15.75 (7.91)	**0.048**
III	27.62 (12.73)	32 (10.94)	0.106
PIGD	4.12 (3.2)	8.17 (4.75)	**0.009**
Axial	8.74 (4.41)	14.92 (4.3)	**<0.0005**
Dominant phenotype, n (%)			0.139
PIGD	91 (46.7%)	9 (75%)	
Tremor	86 (44.1%)	3 (25%)	
Mixed	18 (9.2%)	0 (0%)	
Lateral of PD onset, n (%)			0.652
Right	110 (56.4%)	8 (66.7%)	
Left	76 (39%)	4 (33.3%)	
Bilateral	9 (4.6%)	0 (0%)	
Clinical asymmetry, n (%)			0.802
Symmetry	123 (63.1%)	8 (66.7%)	
Asymmetry	72 (36.9%)	4 (33.3%)	
PDQ-8, mean (SD)	22.64 (16.15)	26.56 (18.2)	0.442
LEDD, mg , mean (SD)	699.73 (430.92)	783.38 (431.15)	0.44
Step length (CM)	49.48 (11.12)	40.16 (8.02)	**0.002**
Step variability (%CV)	7.57 (10.45)	6.66 (5.34)	0.706
Stride length (cm)	99.12 (21.9)	78.96 (13.9)	**0.001**
Velocity (m/s)	0.91 (0.24)	0.77 (0.19)	**0.026**
Cadence (steps/min)	110.16 (14.98)	117 (19.8)	0.547

WoCC: Without camptocormia; TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 29. Correlation between clinical features, degrees of flexion, and gait parameters

TC	Total trunk flexion	Step length	Step variability	Stride length	Velocity	Cadence
Total Trunk Flexion		**-.717****	-0.129	**-.725****	-0.390	0.312
Age	**.703***	**-.613***	0.045	**-.696***	-0.452	0.123
Age of PD onset	**.586***	**-.590***	0.285	**-.675***	-0.467	0.075
Disease duration	-0.232	0.384	**-.579***	0.450	0.375	0.038
H&Y stage	-0.384	-0.074	**.698***	-0.152	-0.350	-0.391
MDS-UPDRS score						
II	-0.332	0.135	0.274	0.099	0.083	-0.021
III	-0.127	-0.351	0.082	-0.182	-0.254	-0.259
PIGD	-0.524	0.351	0.722	-0.043	-0.015	0.042
Axial	-0.401	0.235	**.620***	0.070	-0.167	-0.383

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty.

Table 30. Demographic, clinical features, neck flexion, and presence of TC associated with step length

	Step length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of TC, No vs Yes	-9.323	-15.761 - (-2.886)	**0.005**	5.946	-4.38 - 16.271	0.256
Total Trunk Flexion	-0.628	-0.813 - (-0.443)	**<0.0005**	-0.250	-0.593 - 0.093	0.151
Sex, Female vs Male	-5.770	-8.734 - (-2.805)	**<0.0005**	-5.792	-9.450 - (-2.134)	**0.002**
Age	-0.338	-0.503 - (-0.173)	**<0.0005**	0.071	-0.344 - 0.486	0.735
Age of PD onset	-0.245	-0.391 - (-0.098)	**0.001**	-0.121	-0.474 - 0.233	0.501
Disease duration	-0.105	-0.453 - 0.242	0.550			
H&Y stage	-3.081	-5.032 - (-1.13)	**0.002**	1.384	-2.200 - 4.969	0.446
MDS-UPDRS score						
II	-0.551	-0.751 - (-0.351)	**<0.0005**	-0.075	-0.414 - 0.263	0.660
III	-0.210	-0.328 - (-0.092)	**0.001**	-0.070	-0.233 - 0.093	0.399
PIGD	-1.934	-2.467 - (-1.402)	**<0.0005**	-0.928	-1.937 - 0.081	0.071
Axial	-1.160	-1.451 - (-0.868)	**<0.0005**	-0.633	-1.422 - 0.156	0.115
LEDD	-0.003	-0.007 - 0.000	0.086			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with TC compared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 31. Demographic, clinical features, neck flexion, and presence of TC associated with step variability

	Step variability					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of TC, No vs Yes	-0.913	-6.916 - 5.090	0.765			
Total Trunk Flexion	0.083	-0.106 - 0.272	0.386			
Sex, Female vs Male	0.384	-2.422 - 3.191	0.787			
Age	-0.033	-0.190 - 0.124	0.680			
Age of PD onset	-0.060	-0.197 - 0.077	0.386			
Disease duration	0.186	-0.131 - 0.503	0.248			
H&Y stage	2.534	0.741 - 4.326	**0.006**	-2.996	-6.965 - 0.972	0.138
MDS-UPDRS score						
II	0.487	0.303 - 0.671	**<0.0005**	0.279	-0.084 - 0.642	0.130
III	0.168	0.059 - 0.277	**0.003**	-0.102	-0.282 - 0.078	0.264
PIGD	1.535	0.946 - 2.125	**<0.0005**	0.315	-0.804 - 1.434	0.578
Axial	0.960	0.686 - 1.233	**<0.0005**	1.056	0.232 - 1.881	**0.012**
LEDD	0.002	-0.001 - 0.006	0.159			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with TC compared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 32. Demographic, clinical features, neck flexion, and presence of TC associated with stride length

	Stride length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of TC, No vs Yes	-20.162	-32.799 - (-7.526)	**0.002**	8.802	-10.892 - 28.496	0.378
Total Trunk Flexion	-1.255	-1.617 - (-0.894)	**<0.0005**	-0.436	-1.090 - 0.218	0.189
Sex, Female vs Male	-11.492	-17.330 - (-5.654)	**<0.0005**	-11.679	-18.664 - (-4.694)	**0.001**
Age	-0.505	-0.793 - (-0.218)	**0.001**	-0.123	-0.528 - 0.283	0.550
Age of PD onset	-0.227	-0.912 - 0.458	0.514			
Disease duration	-6.027	-9.873 - (-2.180)	**0.002**	0.211	-0.480 - 0.901	0.547
H&Y stage	-1.083	-1.477 - (-0.689)	**<0.0005**	3.796	-3.041 - 10.633	0.274
MDS-UPDRS score						
II	-1.083	-1.477 - (-0.689)	**<0.0005**	-0.127	-0.773 - 0.518	0.697
III	-0.382	-0.616 - (-0.148)	**0.001**	-0.064	-0.376 - 0.247	0.683
PIGD	-3.933	-4.960 - (-2.906)	**<0.0005**	-2.003	-3.928 - (-0.079)	**0.041**
Axial	-2.343	-2.913 - (-1.772)	**<0.0005**	-1.354	-2.858 - 0.151	0.077
LEDD	-0.006	-0.013 - 0.001	0.097			

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with TC compared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 33. Demographic, clinical features, neck flexion, and presence of TC associated with velocity

	Velocity					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of TC, No vs Yes	-0.140	-0.278 - (-0.001)	**0.048**	0.228	-0.002 - 0.457	0.052
Total Trunk Flexion	-0.012	-0.016 - (-0.008)	**<0.0005**	-0.011	-0.018 - (-0.003)	**0.007**
Sex, Female vs Male	-0.059	-0.124 - 0.007	0.078			
Age	-0.005	-0.009 - (-0.001)	**0.006**	0.004	-0.006 - 0.013	0.419
Age of PD onset	-0.004	-0.007 - 0.000	**0.024**	-0.004	-0.012 - 0.004	0.370
Disease duration	-0.002	-0.009 - 0.006	0.677			
H&Y stage	-0.058	-0.100 - (-0.016)	**0.007**	0.058	-0.023 - 0.138	0.158
MDS-UPDRS score						
II	-0.011	-0.015 - (-0.007)	**<0.0005**	0.001	-0.007 - 0.008	0.886
III	-0.005	-0.007 - (-0.002)	**<0.0005**	-0.001	-0.004 - 0.003	0.694
PIGD	-0.040	-0.052 - (-0.028)	**<0.0005**	-0.018	-0.04 - 0.005	0.120
Axial	-0.024	-0.030 - (-0.017)	**<0.0005**	-0.017	-0.034 - 0.001	0.061
LEDD	-0.0001	-0.0002 - (-0.00001)	**0.035**	-0.0001	-0.0002 - (-0.000004)	0.060

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with TCcompared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 34. Demographic, clinical features, neck flexion, and presence of TC associated with cadence

	Cadence					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of TC, No vs Yes	6.840	-2.122 - 15.802	0.134			
Total Trunk Flexion	-0.022	-0.307 - 0.263	0.880			
Sex, Female vs Male	4.985	0.819 - 9.151	**0.019**	4.295	0.079 - 8.511	**0.046**
Age	0.124	-0.112 - 0.359	0.301			
Age of PD onset	0.053	-0.154 - 0.259	0.616			
Disease duration	0.244	-0.233 - 0.720	0.314			
H&Y stage	-1.168	-3.909 - 1.573	0.402			
MDS-UPDRS score						
II	-0.168	-0.461 - 0.126	0.261			
III	-0.180	-0.345 - (-0.015)	**0.033**	-0.149	-0.315 - 0.018	0.080
PIGD	-0.752	-1.580 - 0.077	0.075			
Axial	-0.343	-0.798 - 0.112	0.139			
LEDD	-0.002	-0.007 - 0.003	0.373			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with TC compared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

5.2.1.3. Upper Camptocormia (UC)

19 patients with UC and an average 50.42°±7.68° (range 45-75°) degree of upper trunk flexion was included. UC was first noticed on 4.93±4.08 years after PD onset. The average UC duration was 2.84±2.96 years.

UC patients had an average step length of 47.01±12.2 cm, a step length variability (%CV) of 6.9±5.22 %, stride length of 93.84 ±24.19 cm, gait velocity of 0.82 ±0.25 m/s and a cadence 103.63±12.03 steps/min (Table 35).

UC patients were more often males ($p<0.0005$), with higher H&Y ($p=0.002$), MDS-UPDRS III ($p=0.028$), III ($p=0.003$), and axial score; ($p=0.001$), symmetric in motor symptoms ($p=0.021$), and a higher LEDD ($p<0.0005$) than PD patients without UC (Table 35).

Moreover, UC patients had less cadence ($p=0.002$) than PD patients without UC (Table 35).

The correlation analysis showed that a higher degrees of upper trunk flexion were related to decreased velocity and cadence ($p<0.05$). A higher MDS-UPDRS III, PIGD score, and Axial score were related to decreased step length, stride length, but increased step variability ($p<0.005$). In addition, A higher PIGD score and axial score were related to decreased velocity (Table 36).

The multiple linear regression analysis showed that male sex (adjusted OR, -6.094; 95% CI, (-9.630) – (-2.559); $p=0.001$), and PIGD score (adjusted OR, -1.289; 95% CI, (-2.251) - (-0.327); $p=0.009$) were significantly associated with the step length (Table 37).

The multiple linear regression analysis showed that H&Y stage (adjusted OR, -3.713; 95% CI, (-7.415) – (-0.010); $p=0.049$), and PIGD score (adjusted OR, 1.279; 95% CI, 0.457 – 2.101; $p=0.003$) were significantly associated with the step variability (Table 38).

The multiple linear regression analysis showed that male sex (adjusted OR, -12.011; 95% CI, (-18.923) – (-5.099); $p=0.001$), PIGD score (adjusted OR, -2.483; 95% CI, (-4.364) - (-0.602); $p=0.01$), and axial score (adjusted OR, -1.517; 95% CI, (-3.013) - (-0.021); $p=0.047$) were significantly associated with the stride length (Table 39).

The multiple linear regression analysis showed that PIGD score (adjusted OR, -0.023; 95% CI, (-0.045) - (-0.001); $p=0.041$), and axial score (adjusted OR, -0.020;

95% CI, (-0.038) - (-0.003); p=0.024) were significantly associated with the velocity (Table 40).

No association were found between clinical features and cadence (Table 41).

Table 35. Demographic and clinical features of PD patients without UC and PD patients with UC

	Total		
	WoCC	**UC**	**P-value**
Patients, n	195 (91.1%)	19 (8.9%)	**<0.0005**
Gender, n (%)			**<0.0005**
Male	99 (50.8%)	18 (94.7%)	
Female	96 (49.2%)	1 (5.3%)	
Age, y, mean (SD)	63.72 (8.94)	65.95 (7.44)	0.338
Age of PD onset, y, mean (SD)	55.98 (10.19)	57 (8.89)	0.765
Disease duration, y, mean (SD)	7.72 (4.38)	9 (4.4)	0.13
H&Y stage, mean (SD)	2.29 (0.77)	2.84 (0.69)	**0.002**
MDS-UPDRS score, mean (SD)			
II	11.6 (7.1)	16.42 (10.16)	**0.028**
III	27.62 (12.73)	38.42 (14.9)	**0.003**
PIGD	4.12 (3.2)	5.65 (3.55)	0.05
Axial	8.74 (4.41)	11.53 (4.44)	**0.006**
Dominant phenotype, n (%)			0.467
PIGD	91 (46.7%)	10 (52.6%)	
Tremor	86 (44.1%)	6 (31.6%)	
Mixed	18 (9.2%)	3 (15.8%)	
Lateral of PD onset, n (%)			0.629
Right	110 (56.4%)	11 (57.9%)	
Left	76 (39%)	8 (42.1%)	
Bilateral	9 (4.6%)	0 (0%)	
Clinical asymmetry, n (%)			**0.021**
Symmetry	123 (63.1%)	17 (89.5%)	
Asymmetry	72 (36.9%)	2 (10.5%)	
PDQ-8, mean (SD)	22.64 (16.15)	24.67 (15.31)	0.446
LEDD, mg , mean (SD)	699.73 (430.92)	1007.89 (372.08)	**<0.0005**
Step length (CM)	49.48 (11.12)	47.01 (12.2)	0.511
Step variability (%CV)	7.57 (10.45)	6.9 (5.22)	0.933
Stride length (cm)	99.12 (21.9)	93.84 (24.19)	0.46
Velocity (m/s)	0.91 (0.24)	0.82 (0.25)	0.152
Cadence (steps/min)	110.16 (14.98)	103.63 (12.03)	**0.012**

WoCC: Without camptocormia; UC: Upper Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 36. Correlation between clinical features, degrees of flexion, and gait parameters

UC	Upper trunk flexion	Step length	Step variability	Stride length	Velocity	Cadence
Upper Trunk Flexion		-0.382	0.138	-0.380	**-.532***	**-.602****
Age	0.006	-0.150	-0.118	-0.154	-0.031	0.318
Age of PD onset	-0.041	-0.089	-0.115	-0.090	-0.013	0.221
Disease duration	0.082	-0.041	0.014	-0.045	0.011	0.105
H&Y stage	-0.113	-0.382	0.344	-0.387	-0.320	0.046
MDS-UPDRS score						
II	0.183	-0.179	0.164	-0.175	-0.277	-0.364
III	-0.023	**-.490***	**.608****	**-.486***	-0.453	-0.164
PIGD	0.270	**-.637****	**.543***	**-.631****	**-.580***	-0.135
Axial	0.230	**-.580****	**.515***	**-.575****	**-.553***	-0.191

UC: Upper Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty.

Table 37. Demographic, clinical features, neck flexion, and presence of UC associated with step length

	Step length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of UC, No vs Yes	-2.47	-7.786 - 2.843	0.360			
Upper Trunk Flexion	0.04	-0.136 - 0.209	0.674			
Sex, Female vs Male	-5.96	-8.896 - (-3.029)	**<0.0005**	-6.094	-9.630 - (-2.559)	**0.001**
Age	-0.29	-0.462 - (-0.127)	**0.001**	0.051	-0.350 - 0.452	0.801
Age of PD onset	-0.21	-0.355 - (-0.059)	**0.006**	-0.139	-0.704	0.435
Disease duration	-0.13	-0.472 - 0.219	0.472			
H&Y stage	-3.25	-5.141 - (-1.357)	**0.001**	1.258	-2.117 - 4.633	0.462
MDS-UPDRS score						
II	-0.51	-0.700 - (-0.321)	**<0.0005**	0.049	-0.238 - 0.336	0.735
III	-0.22	-0.329 - (-0.108)	**<0.0005**	-0.075	-0.235 - 0.085	0.355
PIGD	-2.19	-2.708 - (-1.680)	**<0.0005**	-1.289	-2.251 - (-0.327)	**0.009**
Axial	-1.23	-1.524 - (-0.932)	**<0.0005**	-0.711	-1.476 - 0.054	0.068
LEDD	0.00	-0.008 - (-0.001)	**0.019**	-0.003	-0.007 - 0.001	0.133

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with UC compared with PD patients without UC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose.

Table 38. Demographic, clinical features, neck flexion, and presence of UC associated with step variability

	Step variability					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of UC, No vs Yes	-0.673	-5.462 - 4.116	0.782			
Upper Trunk Flexion	-0.012	-0.169 - 0.145	0.884			
Sex, Female vs Male	0.646	-2.089 - 3.381	0.642			
Age	-0.037	-0.191 - 0.118	0.640			
Age of PD onset	-0.072	-0.207 - 0.064	0.298			
Disease duration	0.226	-0.083 - 0.536	0.151			
H&Y stage	2.314	0.595 - 4.033	**0.009**	-3.713	-7.415 - (-0.010)	**0.049**
MDS-UPDRS score						
II	0.433	0.261 - 0.605	**<0.0005**	0.124	-0.183 - 0.431	0.427
III	0.167	0.067 - 0.268	**0.001**	-0.127	-0.298 - 0.044	0.143
PIGD	1.515	0.952 - 2.079	**<0.0005**	0.392	-0.654 - 1.439	0.460
Axial	1.013	0.741 - 1.286	**<0.0005**	1.279	0.457 - 2.102	**0.003**
LEDD	0.00	-0.001 - 0.006	0.117			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with UC compared with PD patients without UC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 39. Demographic, clinical features, neck flexion, and presence of UC associated with stride length

	Stride length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of UC, No vs Yes	-5.279	-15.752 - 5.194	0.322			
Upper Trunk Flexion	0.063	-0.275 - 0.401	0.713			
Sex, Female vs Male	-11.980	-17.755 - (-6.206)	**<0.0005**	-12.011	-18.923 - (-5.099)	**0.001**
Age	-0.607	-0.936 - (-0.278)	**<0.0005**	0.067	-0.717 - 0.851	0.865
Age of PD onset	-0.427	-0.719 - (-0.136)	**0.004**	-0.268	-0.956 - 0.420	0.442
Disease duration	-0.266	-0.948 - 0.415	0.442			
H&Y stage	-6.310	-10.043 - (-2.577)	**0.001**	2.796	-3.803 - 9.394	0.403
MDS-UPDRS score						
II	-0.992	-1.367 - (-0.618)	**<0.0005**	0.111	-0.451 - 0.672	0.697
III	-0.412	-0.631 - (-0.194)	**<0.0005**	-0.114	-0.426 - 0.199	0.474
PIGD	-4.312	-5.319 - (-3.304)	**<0.0005**	-2.483	-4.364 - (-0.602)	**0.010**
Axial	-2.424	-3.007 - (-1.841)	**<0.0005**	-1.517	-3.013 - (-0.021)	**0.047**
LEDD	-0.008	-0.015 - (-0.001)	**0.022**	-0.006	-0.013 - 0.002	0.140

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with UC compared with PD patients without UC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 40. Demographic, clinical features, neck flexion, and presence of UC associated with velocity

	Velocity					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of UC, No vs Yes	-0.093	-0.207 - 0.020	0.107			
Upper Trunk Flexion	-0.001	-0.005 - 0.003	0.631			
Sex, Female vs Male	-0.064	-0.129 - 0.0004	0.051			
Age	-0.004	-0.008 - (-0.001)	**0.022**	-0.001	-0.005 - 0.004	0.686
Age of PD onset	-0.003	-0.006 - 0.0003	0.073			
Disease duration	-0.002	-0.010 - 0.005	0.536			
H&Y stage	-0.062	-0.103 - (-0.021)	**0.003**	0.058	-0.021 - 0.136	0.148
MDS-UPDRS score						
II	-0.011	-0.015 - (-0.007)	**<0.0005**	0.001	-0.006 - 0.007	0.868
III	-0.005	-0.008 - (-0.003)	**<0.0005**	-0.001	-0.005 - 0.003	0.578
PIGD	-0.044	-0.056 - (-0.033)	**<0.0005**	-0.023	-0.045 - (-0.001)	**0.041**
Axial	-0.025	-0.032 - (-0.019)	**<0.0005**	-0.020	-0.038 - (-0.003)	**0.024**
LEDD	-0.0001	-0.0002 - (-00003)	**0.005**	-0.0001	-0.0002 - 0.00001	0.100

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with UC compared with PD patients without TC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 41. Demographic, clinical features, neck flexion, and presence of UC associated with cadence

	Cadence					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of UC, No vs Yes	-6.528	-13.519 - 0.463	0.067			
Upper Trunk Flexion	-0.211	-0.440 - 0.018	0.071			
Sex, Female vs Male	4.600	0.615 - 8.584	**0.024**	2.817	-2.843 - 8.477	0.327
Age	0.099	-0.129 - 0.327	0.393			
Age of PD onset	0.043	-0.157 - 0.243	0.673			
Disease duration	0.188	-0.270 - 0.645	0.420			
H&Y stage	-1.262	-3.830 - 1.307	0.334			
MDS-UPDRS score						
II	-0.284	-0.550 - (-0.019)	**0.036**	-0.213	-0.670 - 0.245	0.360
III	-0.197	-0.346 - (-0.048)	**0.010**	-0.086	-0.340 - 0.169	0.506
PIGD	-0.833	-1.648 - (-0.018)	**0.045**	0.296	-1.235 - 1.826	0.703
Axial	-0.499	-0.945 - (-0.054)	**0.028**	-0.597	-1.773 - 0.580	0.318
LEDD	-0.003	-0.008 - 0.001	0.176			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with UC compared with PD patients without UC.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

5.2.1.4. Pisa syndrome (PS)

9 patients with PS and an average 13.44°±4.42° (range 10-24°) degree of lateral flexion was included. PS was first noticed on 6.7±4.33 years after PD onset. The average PS duration was 3.5±2.25 years.

PS patients had an average step length of 38.53±14.61 cm, a step length variability (%CV) of 20.57±35.99 %, stride length of 78.72±25.42 cm, gait velocity of 0.72 ±0.35 m/s and a cadence 111.56±27.53 steps/min (Table 42).

PS patients had a higher MDS-UPDRS II (p=0.002), a higher PIGD score (p=0.048), and a higher axial score (p=0.004) than PD patients without PS (Table 42).

Moreover, PS patients had a shorter step length (p=0.015), and a shorter stride length (p=0.016) than PD patients without PS (Table 42).

The correlation analysis showed that a higher lateral flexion was related to decreased axial score. A higher MDS-UPDRS III, and PIGD score were related to decreased step length, stride length, and velocity. A higher PIGD score was also related to increased step variability (Table 43).

The multiple linear regression analysis showed that male sex (adjusted OR, -6.554; 95% CI, (-1.149) – (-3.110); p<0.0005), and PIGD score (adjusted OR, -1.074; 95% CI, (-2.006) - (-0.142); p=0.024) were significantly associated with the step length (Table 44).

The multiple linear regression analysis showed that presence of PS (adjusted OR, 20.794; 95% CI,8.619 – 32.968; p=0.001), and axial score (adjusted OR, 0.897; 95% CI, 0.138 – 1.656; p=0.021) were significantly associated with the step variability (Table 45).

The multiple linear regression analysis showed that male sex (adjusted OR, -12.600; 95% CI, (-19.267) – (-5.934); p<0.0005), and PIGD score (adjusted OR, -2.173; 95% CI, (-3.977) - (-0.369); p=0.019) were significantly associated with the stride length (Table 46).

The multiple linear regression analysis showed that axial score (adjusted OR, -0.018; 95% CI, (-0.035) – (-0.001); p=0.035) were significantly associated with the velocity (Table 47).

No association were found between clinical features and cadence (Table 48).

Table 42. Demographic and clinical features of PD patients without PS and PD patients with PS

	Total		
	WoPS	**PS**	**P-value**
Patients, n	219 (96.1%)	9 (3.9%)	**<0.0005**
Gender, n (%)			0.943
Male	119 (54.3%)	5 (55.6%)	
Female	100 (45.7%)	4 (44.4%)	
Age, y, mean (SD)	64.13 (8.84)	69.44 (8.76)	0.059
Age of PD onset, y, mean (SD)	56.31 (10.15)	58.89 (10.28)	0.519
Disease duration, y, mean (SD)	7.81 (4.34)	10.56 (5.53)	0.105
H&Y stage, mean (SD)	2.34 (0.78)	2.89 (0.6)	**0.029**
MDS-UPDRS score, mean (SD)			
II	11.85 (7.17)	22.56 (10.27)	**0.002**
III	28.62 (13.18)	36.33 (13.11)	0.082
PIGD	4.35 (3.33)	7.6 (4.56)	**0.048**
Axial	9.05 (4.5)	14.33 (5.79)	**0.004**
Dominant phenotype, n (%)			0.266
PIGD	107 (48.9%)	5 (55.6%)	
Tremor	93 (42.5%)	2 (22.2%)	
Mixed	19 (8.7%)	2 (22.2%)	
Lateral of PD onset, n (%)			0.52
Right	126 (57.5%)	4 (44.4%)	
Left	84 (38.4%)	4 (44.4%)	
Bilateral	9 (4.1%)	1 (11.1%)	
Clinical asymmetry, n (%)			0.409
Symmetry	141 (64.4%)	7 (77.8%)	
Asymmetry	78 (35.6%)	2 (22.2%)	
PDQ-8, mean (SD)	22.63 (15.99)	32.99 (16.84)	0.065
LEDD, mg , mean (SD)	723.03 (433.56)	900.78 (357.37)	0.096
Step length (CM)	49.04 (11)	38.53 (14.61)	**0.031**
Step variability (%CV)	6.96 (6.83)	20.57 (35.99)	0.09
Stride length (cm)	98.07 (21.9)	78.72 (25.42)	**0.031**
Velocity (m/s)	0.9 (0.24)	0.72 (0.35)	0.163
Cadence (steps/min)	109.68 (14.79)	111.56 (27.53)	0.492

WoPS: Without Pisa syndrome; PS: Pisa syndrome; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; PDQ-8: Parkinson's Disease Questionnaire-8; LEDD: L-dopa equivalent daily dose.

Table 43. Correlation between clinical features, degrees of flexion, and gait parameters

PS	Lateral flexion	Step length	Step variability	Stride length	Velocity	Cadence
Lateral flexion		-0.133	-0.218	-0.210	-0.335	-0.642
Age	0.327	0.132	-0.380	0.073	0.045	-0.188
Age of PD onset	0.326	0.237	-0.452	0.173	0.025	-0.400
Disease duration	-0.088	-0.231	0.239	-0.206	0.024	0.446
H&Y stage	0.445	-0.143	0.168	-0.151	-0.035	0.034
MDS-UPDRS score						
II	-0.083	-0.557	0.515	-0.543	-0.500	0.012
III	0.364	**-.918****	0.649	**-.939****	**-.892****	-0.313
PIGD	-0.120	**-.969****	**.893***	**-.977****	**-.961****	-0.044
Axial	**-.774***	-0.409	0.575	-0.348	-0.223	0.436

PS: Pisa syndrome; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty**.**

Table 44. Demographic, clinical features, neck flexion, and presence of PS associated with step length

	Step length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of PS, No vs Yes	-10.518	-17.987 - (-3.048)	**0.006**	1.846	-9.764 - 13.456	0.754
Lateral Flexion	-0.828	-1.334 - (-0.323)	**0.001**	-0.322	-1.149 - 0.505	0.443
Sex, Female vs Male	-5.753	-8.625 - (-2.881)	**<0.0005**	-6.554	-9.998 - (-3.110)	**<0.0005**
Age	-0.350	-0.511 - (-0.190_	**<0.0005**	0.051	-0.346 - 0.448	0.800
Age of PD onset	-0.251	-0.394 - (-0.109)	**0.001**	-0.147	-0.692	0.403
Disease duration	-0.115	-0.451 - 0.221	0.502			
H&Y stage	-3.471	-5.313 - (-1.629)	**<0.0005**	0.628	-2.674 - 3.930	0.707
MDS-UPDRS score						
II	-0.512	-0.696 - (-0.328)	**<0.0005**	0.021	-0.267 - 0.308	0.888
III	-0.241	-0.349 - (-0.134)	**<0.0005**	-0.133	-0.287 - 0.021	0.091
PIGD	-1.978	-2.467 - (-1.489)	**<0.0005**	-1.074	-2.006 - (-0.142)	**0.024**
Axial	-1.134	-1.416 - (-0.852)	**<0.0005**	-0.581	-1.318 - 0.155	0.121
LEDD	-0.004	-0.007 - (-0.000)	**0.029**	-0.003	-0.007 - 0.001	0.111

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with PS compared with PD patients without PS.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 45. Demographic, clinical features, neck flexion, and presence of PS associated with step variability

	Step variability					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of PS, No vs Yes	13.61	7.225 - 20.003	**<0.0005**	20.794	8.619 - 32.968	**0.001**
Lateral Flexion	0.56	0.110 - 1.001	**0.015**	-0.550	-1.420 - 0.320	0.213
Sex, Female vs Male	0.483	-2.109 - 3.076	0.714			
Age	-0.034	-0.179 - 0.112	0.649			
Age of PD onset	-0.057	-0.185 - 0.07	0.378			
Disease duration	0.161	-0.132 - 0.454	0.281			
H&Y stage	2.502	0.878 - 4.127	**0.003**	-2.251	-5.721 - 1.218	0.202
MDS-UPDRS score						
II	0.417	0.256 - 0.579	**<0.0005**	0.077	-0.218 - 0.373	0.605
III	0.165	0.069 - 0.260	**0.001**	-0.044	-0.203 - 0.115	0.587
PIGD	1.409	0.886 - 1.931	**<0.0005**	0.379	-0.595 - 1.352	0.443
Axial	0.890	0.637 - 1.142	**<0.0005**	0.897	0.138 - 1.656	**0.021**
LEDD	0.002	-0.001 - 0.005	0.122			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with PS compared with PD patients without PS.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 46. Demographic, clinical features, neck flexion, and presence of PS associated with stride length

	Stride length					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of PS, No vs Yes	-19.359	-34.128 - (-4.590)	**0.010**	7.202	-15.272 - 29.675	0.527
Lateral Flexion	-1.588	-2.586 - (-0.589)	**0.002**	-0.570	-2.171 - 1.031	0.482
Sex, Female vs Male	-11.428	-17.092 - (-5.764)	**<0.0005**	-12.600	-19.267 - (-5.934)	**<0.0005**
Age	-0.723	-1.038 - (-0.408)	**<0.0005**	0.060	-0.708 - 0.828	0.877
Age of PD onset	-0.518	-0.798 - (-0.238)	**<0.0005**	-0.270	-0.940 - 0.399	0.426
Disease duration	-0.247	-0.909 - 0.416	0.464			
H&Y stage	-6.844	-10.479 - (-3.210)	**<0.0005**	1.972	-4.420 - 8.363	0.543
MDS-UPDRS score						
II	-1.007	-1.370 - (-0.645)	**<0.0005**	0.055	-0.505 - 0.612	0.846
III	-0.452	-0.664 - (-0.239)	**<0.0005**	-0.183	-0.481 - 0.155	0.227
PIGD	-4.005	-4.951 - (-3.059)	**<0.0005**	-2.173	-3.977 - (-0.369)	**0.019**
Axial	-2.287	-2.839 - (-1.735)	**<0.0005**	-1.375	-2.801 - 0.051	0.059
LEDD	-0.007	-0.014 - (-0.001)	**0.032**	-0.006	-0.014 - 0.001	0.109

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with PS compared with PD patients without PS.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 47. Demographic, clinical features, neck flexion, and presence of PS associated with velocity

	Velocity					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of PS, No vs Yes	-0.178	-0.339 - (-0.016)	**0.031**	0.128	-0.137 - 0.392	0.341
Lateral Flexion	-0.018	-0.029 - (-0.007)	**0.001**	-0.009	-0.027 - 0.010	0.369
Sex, Female vs Male	-0.058	-0.121 - 0.006	0.074			
Age	-0.005	-0.009 - (-0.002)	**0.003**	0.002	-0.007 - 0.011	0.708
Age of PD onset	-0.004	-0.007 - (-0.001)	**0.015**	-0.003	-0.011 - 0.005	0.495
Disease duration	-0.002	-0.009 - 0.005	0.637			
H&Y stage	-0.070	-0.110 - (-0.031)	**0.001**	0.048	-0.028 - 0.124	0.216
MDS-UPDRS score						
II	-0.011	-0.015 - (-0.007)	**<0.0005**	0.000	-0.007 - 0.006	0.930
III	-0.006	-0.008 - (-0.003)	**<0.0005**	-0.002	-0.005 - 0.002	0.339
PIGD	-0.041	-0.052 - (-0.03)	**<0.0005**	-0.019	-0.041 - 0.002	0.071
Axial	-0.023	-0.029 - (-0.017)	**<0.0005**	-0.018	-0.035 - (-0.001)	**0.035**
LEDD	-0.0001	-0.0002 - (-0.00003	**0.008**	-0.0001	-0.0002 - 0.00001	0.068

* Variables used to perform in multiple linear regression were variables p≤0.05 in univariate linear regression. In univariate linear regression, continent had p>0.05 therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with PS compared with PD patients without PS.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

Table 48. Demographic, clinical features, neck flexion, and presence of PS associated with cadence

	Cadence					
	Unadjusted			Adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Presence of PS, No vs Yes	1.872	-8.465 - 12.209	0.722			
Laterak Flexion	-0.487	-1.188 - 0.214	0.173			
Sex, Female vs Male	4.955	0.958 - 8.951	**0.015**	2.957	-2.421 - 8.335	0.279
Age	0.106	-0.122 - 0.333	0.361			
Age of PD onset	0.041	-0.158 - 0.240	0.686			
Disease duration	0.228	-0.229 - 0.685	0.327			
H&Y stage	-1.958	-4.532 - 0.616	0.135			
MDS-UPDRS score						
II	-0.281	-0.546 - (-0.016)	**0.038**	-0.262	-0.702 - 0.177	0.240
III	-0.225	-0.375 - (-0.076)	**0.003**	-0.128	-0.350 - 0.095	0.257
PIGD	-0.768	-1.519 - (-0.017)	**0.045**	-0.243	-1.171 - 0.684	0.605
Axial	-0.351	-0.783 - 0.081	0.111			
LEDD	-0.003	-0.008 - 0.001	0.166			

* Variables used to perform in multiple linear regression were variables $p \leq 0.05$ in univariate linear regression. In univariate linear regression, continent had $p > 0.05$ therefore, it was not included in multiple linear regression.

** Demographic and clinical features associated with PD patients with PS compared with PD patients without PS.

TC: Total Camptocormia; H&Y: Hoehn and Yahr scale; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PIGD: Postural instability/gait difficulty; LEDD: L-dopa equivalent daily dose

6. Discussion

6.1. Postural abnormalities: an observational multicenter study

We performed a multicenter, cross-sectional study evaluating 326 PD outpatients attending tertiary movement disorder centers in Europe and Asia, with the aim to compare PA prevalence and features between Caucasian and Asian PD populations.

We found a global axial PA prevalence of 23.9% without statistically significant differences between Asian and Caucasian patients (23.6% vs. 24.3%; p= 0.36). Specifically, no differences between CC, PS, AC and combined axial PA prevalence were found between the two ethnicities. The overall prevalence of appPA was 4.9%, with Asian patients being more affected from striatal hand or foot than Caucasian ones (p=0.036).

This is the first study directly comparing the PA prevalence, including an extensive clinical assessment of PD patients belonging to different ethnicities, by using the same systematic approach.

A few previous data suggested that the PA prevalence in Asian PD population was higher when compared to PD patients of other ethnicities (Doherty et al., 2011, Baik et al., 2016). However, no comparisons were performed and differences were postulated by the comparison of prevalence from different studies employing heterogeneous diagnostic criteria and measurement tools for PA definition.

Our findings, did not confirm the hypothesis of a higher rate of axial PA in Asian patients if compared to the Caucasian ones. Moreover, we did not find any difference also considering the single forms of axial PA prevalence (namely, CC, PS, and AC) and both univariate and multiple logistic regression, adjusted for sex and disease duration, confirming the absence of an association between axial PA and ethnicity. Interestingly, while acknowledging a longer disease duration for Caucasian AC patients vs. Asian ones, we observed that AC had a significantly earlier onset in Asian patients but was more severe in Caucasian ones.

In our study, the prevalence of CC was 11.5% in Asian and 11.8% in Caucasian patients. These data are similar to the ones recently published in a multicenter Italian study on PA (11.2%) (Tinazzi et al., 2019).

PS prevalence was 3.3% in Asian and 4.2% in Caucasian populations. The low prevalence of PS in our study is similar to the one reported by one German, one Chinese, and one Japanese study (1%, 3.6%, and 4.65%, respectively) (Ando et al., 2019, Liu et al., 2019, Schlenstedt et al., 2019). At the same time, the general

prevalence of PS seems to be lower in our study than previously reported from Italian studies (8-8.8%) (Tinazzi et al., 2015, Artusi et al., 2019 Tinazzi et al., 2019). This difference may be due to differences in diagnostic criteria, measuring methods, and sample sizes among different studies. Nevertheless, if we extract the prevalence of PS among our Italian patients, we found a percentage of 6.5% (data not shown), which is quite similar to the ones reported by previous Italian studies (Tinazzi et al., 2015, Tinazzi et al., 2019). PS higher prevalence has been associated to an older age, a lower BMI, a longer disease duration, higher HY, and to a combination of levodopa plus dopamine-agonist (Tinazzi et al., 2015, Tinazzi et al., 2019).

Furthermore, no statistically difference was pointed out for AC prevalence (17.6% in Asian vs 22.9% in Caucasian patients). AC seems overrepresented in our population when compared with previous studies from an Italian multicenter study reporting (6.5%) (Tinazzi et al., 2019). We explained this finding by the accuracy of the method we used for AC diagnosis, which considered a C7- tragus angle ≥ 45° by means of photo analysis, independently from the presence of other postural deformities, such as a thoracic anterior flexion.

Concerning appPA, we found that 7.1% of Asian and 2.1% of Caucasian PD patients can suffer from an isolated or combined form of striatal hand or foot. These prevalence are lower than those reported in previous studies from Asia, US, and Mexico (9.9%-28.6%)(Ashour et al., 2006, Cervantes-Arriaga et al., 2016 Pandey et al., 2016).At the same time, the clinical features associated with appPA, encompassing a lower BMI, a younger age at PD onset, higher clinical symmetry, and less number of falls than patients with axial PA, are partly consistent with and partly add more information to the few previous studies, reporting that appPA often occurs in patients with a younger age at PD onset (Pandey et al., 2016). Shared diagnostic criteria for the identification of striatal hands and feet are missing. his aspect should be considered when interpreting the differences, we observed in the prevalence of appPA. Moreover, according to our study design, we performed an initial more comprehensive evaluation of patients based on MDS-UPDRS 3.13 item ≥ 1, and mild app striatal deformities, in the absence of axial postural abnormalities, could have been overlooked.

In general, patients with axial PA were more often male, older, with longer disease duration, more severe motor symptoms, more advanced disease stage, and a higher load of dopaminergic therapy. PA patients also showed more commonly a PIGD

phenotype with clinical symmetry and had poorer QoL. This result confirmed that PA had an impact on patients' life. The multivariate logistic regression confirmed that male gender, longer disease duration, and higher axial score were associated with the presence of PA which was similarly to data reported in previous studies (Tiple et al., 2009, Seki et al., 2011, Kashihara et al., 2012, Oeda et al., 2013, Tinazzi et al., 2019). However, the multivariate logistic regression did not confirm the association between PA and a higher LEDD. Once we stratified this analysis for ethnicity, different variables appeared to be significant, being male gender and a higher axial score significant in both groups but a longer disease duration was significant only for Caucasian patients. This finding highlighted the role of disease duration for axial PA development among Caucasian patients, while this was not confirmed for Asian ones.

When considering the entire cohort (independently from the presence of PA), it must be considered that both Caucasian and Asian patients shared similar sex distribution, age, age at PD onset, disease duration, HY stage, MDS-UPDRS II and III, lateralization of PD onset and QoL. Conversely, Caucasian patients had a higher weight ($p<0.0005$), and slightly higher falling rate ($p=0.046$) than Asian patients. However, Asian patients had a more severe axial score than Caucasian ones ($p=0.001$), suggesting that Asian patients could develop more severe axial symptoms. In addition, they seem to tend to develop PA earlier than Caucasian ones, even if PA latency did not reach the statistical difference (3.9 vs. 5.3 yrs.).

In spite of no difference in age between the whole Asian and Caucasian populations enrolled, Caucasian patients with PA were older than Asian patients with PA ($p=0.011$), and had a longer disease duration ($p=0.03$). According to the time to PA onset, this finding might be further in favor of a later development of PA in Caucasian vs. Asian patients, especially concerning AC. It would be interesting to analyze in future prospective studies whether not only the LEDD, which seems similar in our study with the only exception for the PS group, but also the combination and sequences of introduction of different antiparkinsonian treatments, which is presumably different among Asia and Europe (levodopa vs. dopamine-agonist-vs. amantadine) may have an effect in delaying the onset of PA or if this finding is merely related to phenotypic or ethnicity differences.

Finally, among the three main axial PA, we found that both in Asian and Caucasian PD patients, PS may develop in more advanced disease phases and after a longer

disease duration than CC and AC, endorsing the hypothesis of a different pathophysiology between the three PA (Doherty et al., 2011, Tinazzi et la., 2019).
The interpretation of results should consider our study shortcomings. First, the cross-sectional design and the collection of information such as PA appearance/duration was based on patients' interview. Second, several Asian PD patients did not allow us to take pictures with clothes off, as per a cultural aspect, thus making the exact calculation of angles slightly less precise. Third, lack of consensus for AC and PS measurement and diagnostic criteria should be considered in the comparison of our findings with those of previous studies. Although it was consistent in our cohort of patients, thus it did not hamper the internal comparison between Asian and Caucasian PD patients.

6.2. Gait and Axial Postural Abnormalities correlations in Parkinson's disease

In this multicenter study on 228 PD patients objectively evaluated for the presence and degree of PA and by a video-assisted gait analysis, we found that severe axial PA, were associated with specific gait impairment, if compared to PD patients with milder PA, i.e. with MDS-UPDRS III item 3.13 posture score > 0 but whose PA do not have the criteria for AC, UC, TC or PS.
In particular, step length and stride length were significantly shorter in patients with AC, TC and PS, gait velocity was lower in patients with AC and TC, and gait variability was more pronounced in patients with PS, if compared to patients with milder PA.
Similar findings were observed in other studies with TC and PS patients having a slower walking speed, a shorter step length, and a shorter stride length than PD patients without TC, and PS (Tramonti et al., 2017, Geroin et al., 2019)However, when we performed a multiple regression analysis accounting for many demographic and clinical factors, only the correlations between gait velocity and the severity of TC and between gait variability and the presence of PS survived, indicating that severe forms of anterior and lateral trunk flexion can have a specific impact on specific gait features, independently from other PD features, further characterizing patients with severe axial PA.
A previous pilot study has compared stabilometric and gait assessment of PD patients with and without PS, showing as PS patients had a greater body sway velocity for the anteroposterior and medial lateral directions to maintain postural

uprightness, despite being able to maintain their ability to walk thanks to compensatory strategies (Geroin et al., 2015). However, gait variability, which is likely to be associated to altered stabilometric measures, was not considered in this study on PS patients. At the same time, it has been suggested that the impairment of gait variability may be independent from PA, and particularly from TC as it is probably more related to basal ganglia dysfunction and disease severity itself (Geroin et al., 2019). We have to acknowledge that the low number of our PS patients do not allow firm conclusion. To our knowledge, this is the first study that explored the association between quantitative gait analysis and the presence and severity of the full range of severe axial PA in a large group of PD patients, including AC, TC, UC, and PS. Previous studies showed that patients with severe PA have a higher degree of motor symptoms, and impairment in daily life activities and quality of life. Nonetheless, it has been postulated that patients with PA may represent a phenotypic group with a higher burden of axial symptoms and more disabling phenotype (Geroin et al., 2020), and the net impact of PA on patients remains to be clarified.

In this study, the multiple linear regression analysis told us that male sex and a higher PIGD score were associated with the decreased stride length, and a higher axial motor score was associated with an increased step variability in AC, TC, UC, and PS. The association between the severity of trunk flexion and gait impairment was observed for TC and PS, with the higher degrees of anterior trunk flexion the lower the gait velocity, and the presence of PS (i.e. >10° of lateral trunk bending) significantly correlated with an higher gait variability, independently from other clinical and demographic characteristics.

The main strengths of this study are the high sample size and the quantitative assessment with the same, standardized methodology in a multicenter study, including PD patients from different countries and ethnicities. However, some limitations should be considered. First, we featured gait by a video software, which is not as accurate as the gold standard represented by infrared cameras in spite of having been already used for gait analysis in PD. Second, we did not have a control group of PD patients with MDS-UPDRS item 3.13 Posture <1 . However, the fact that we have enrolled only patients with a clinical diagnosis of PA (i.e., MDS-UPDRS posture item 3.13 ≥ 1) allowed us to analyze the impact of PA on gait in a group of patients with different severity of PA (severe axial PA and mild forms of PA) likely emphasizing the finding related to the impact of TC and PS on gait.

Third, we have found only small number of PS patients. However, the fact of having found a significant effect of PS severity on gait variability even in a small sample of patients, highlight the significant of this finding.

Our results highlight the impact of severe axial PA on PD patients' gait, with a specific detrimental effect on gait velocity and variability. These findings contribute to a better comprehension of the disability provided by severe axial PA and underline the importance of finding adequate therapeutic and prevention strategies for these disabling PD symptoms. Personalized rehabilitation strategies should be elaborated based on the different feature of axial PA, aiming to target not only postural but also possible associated gait pattern alterations.

7. Conclusion

Our study does not confirm the role of ethnicity as a risk factor for axial PA development in PD. However, it is possible that Asian patients tend to develop PA earlier. The prevalence of app PA could be higher in Asians but studies including more cases of app PA should be performed. We confirm that the most relevant demographic/clinical features associated with PA in both ethnicities are male sex (ratio 2.3:1), with disease duration being a risk factor only for Caucasian patients.

In addition, our study does not confirm the association between the severity of PA and gait impairments, with the exception of slower gait speed related to the severity of CC. Generally, the most relevant demographic/clinical features associated with gait impairments in PD patients with PA are male sex with older age, longer disease duration, and more severe disease.

Nowadays, having a global perspective, by means of multicenter global studies, on parkinsonian symptoms whose treatment remains challenging, may be useful to understand the pathophysiology and reach better management of those symptoms.

8. Acknowledgement

This project is the result from an international collaboration from many institutions. Thanks to my university, Department of Neuroscience, University of Turin, Italy. Thanks to Division of Neurology, Department of Medicine, Siriraj Hospital, Mahidol University, Thailand. Thanks to Department of Neurology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Neuroscience Center, Samsung Medical Center, Republic of Korea, Thanks to National Neuroscience Institute, King Fahad Medical City, Saudi Arabia. Thanks to Department of Neurology, University Hospital Schleswig-Holstein, Campus Kiel, Germany. Thanks to CNS—Campus Neurológico, Portugal. This project would not be accomplished without their collaboration.

First of all, I would like to thank to Professor Leonardo Lopiano, my tutor. Thank you for accepting me and being my tutor and allowing me to conduct this international project. I am very grateful for his hospitality and his helpfulness during the time I was in Italy. I know I am not a good student. I might make you headache sometimes. However, thank you for being patience with me.

I would like to thank to Dr.Maurizio Zibetti. Thank you for listening and giving many useful suggestions for me. He was the bridge between me and my tutor. Sometimes, I could not explain or communicate well with my tutor because of my inadequate language. He was always the one to understand and often acted as the one to explain my need to my tutor. I am very grateful for his help.

I am very indebted to Dr.Margherita Fabbri and Dr.Carlo Alberto Artusi, they are the most contributors in this project. I am very grateful and indebted for their help. Without them this project would not be accomplished. They spent and sacrificed their time to help me doing this project. They helped and gave me lots of useful suggestions and advises. This project would not be occurred and succeeded without their help and effort. Thank you so much!! I could not explain as a word how grateful I am to them.

To all colleagues and all PD patients from Italy for their help in collecting all data.

To Dr.Yuvadee Pitakpatapee, Dr. Takarn Wangthumrong, Dr.Tanita Sangpeamsook, Dr. Jindapa Srikajon, Dr. Apichart Pisarnpong, Dr. Meitee Vichutavate, Ms.Montira Engchuan, Dr. Prachaya Srivanitchapoomfrom, all PD patients from Thailand for their help in collecting all data and their hospitality during the time I was there.

To Dr.Jinyoung Youn, Dr. Jin Whan Cho, and Dr. Minkyeong Kim, and all PD patients from South Korea for their help in collecting all data.

To Dr. Heba M. Zamil Shinawi, Dr. Mona Talib Obaid, and all PD patients from Saudi Arabia for their help in collecting all data and their hospitality during the time I was there.

To Dr.Alexander Baumann, Dr Nils G. Margraf, and all PD patients from Germany for their help in collecting all data.

To Filipa Pona-Ferreira, Mariana Leitão, Teresa Lobo, Verónica Caniça, Madalena F. Costa, Susana Soares Dias, Raquel Nunes, Inês Lousada and João Belo, and Professor Joaquim J Ferreira and all PD patients from Portugal for their help in collecting all data.

Thanks to everyone I mentioned above for their contributions and their suggestion and advices for this project. Without them, this project could not be occurred and accomplished.

Lastly, thanks to my beloved family, my biggest encouragement. Without them, I could not survive during these hard times. They always keep pushing and encouraging me to get through every difficulty. I love you all.

Thanks to the person who were apart.

Thanks to all difficulties moments during these years which shaped me into the person I am today.

9. References

- Abe K, Uchida Y, Notani M. Camptocormia in Parkinson's disease. Parkinsons Dis 2010; published online June 30.DOI:10.4061/2010/267640.
- Ailneni RC, Syamala KR, Kim IS, Hwang J. Influence of the wearable posture correction sensor on head and neck posture: Sitting and standing workstations. Work. 2019 Jan 1;62(1):27-35.
- Ando Y, Fujimoto KI, Ikeda K, Utsumi H, Okuma Y, Oka H, Kamei S, Kurita A, Takahashi K, Nogawa S, Hattori N. Postural Abnormality in Parkinson's Disease: A Large Comparative Study With General Population. Movement Disorders Clinical Practice. 2019 Mar;6(3):213-21.
- Artusi CA, Montanaro E, Tuttobene S, Romagnolo A, Zibetti M, Lopiano L. Pisa syndrome in parkinson's disease is associated with specific cognitive alterations. Frontiers in neurology. 2019 May 31; 10:577.
- Ashour R, Jankovic J. Joint and skeletal deformities in Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy. Mov Disord. 2006 Nov;21(11):1856-63.
- Baik JS. Understanding of skeletal deformities in Parkinson's disease. The Indian journal of medical research. 2016 Nov;144(5):650.
- Cervantes-Arriaga A, Rodríguez-Violante M, Morales-Briceño H, Neri-Nani G, Millán-Cepeda R, Velázquez-Osuna S. Frequency and clinical correlates of postural and striatal deformities in Parkinson's disease. Clinical neurology and neurosurgery. 2016 Mar 1;142:140-4.
- Doherty KM, van de Warrenburg BP, Peralta MC, Silveira-Moriyama L, Azulay JP, Gershanik OS, Bloem BR. Postural deformities in Parkinson's disease. Lancet Neurol. 2011 Jun;10(6):538-49. doi: 10.1016/S1474-4422(11)70067-9.
- Elwardany SH, Eleiny KE, Arabia S. Reliability of Kinovea computer program in measuring cervical range of motion in sagittal plane. Open Access Library Journal. 2015;2(09):1.
- Fabbri M, Coelho M, Abreu D, Guedes LC, Rosa MM, Costa N, Antonini A, Ferreira JJ. Do patients with late-stage Parkinson's disease still respond to levodopa?. Parkinsonism & related disorders. 2016 May 1;26:10-6.

- Fabbri M, Pongmala C, Artusi CA, Imbalzano G, Romagnolo A, Lopiano L, Zibetti M. Video analysis of long-term effects of levodopa-carbidopa intestinal gel on gait and posture in advanced Parkinson's disease. Neurological Sciences. 2020 Jul 1;41(7).
- Fasano A, Geroin C, Berardelli A, Bloem BR, Espay AJ, Hallett M, Lang AE, Tinazzi M. Diagnostic criteria for camptocormia in Parkinson's disease: a consensus-based proposal. Parkinsonism & related disorders. 2018 Aug 1;53:53-7.
- Geroin C, Smania N, Schena F, Dimitrova E, Verzini E, Bombieri F, Nardello F, Tinazzi M, Gandolfi M. Does the Pisa syndrome affect postural control, balance, and gait in patients with Parkinson's disease? An observational cross-sectional study. Parkinsonism & Related Disorders. 2015 Jul 1;21(7):736-41.
- Geroin C, Gandolfi M, Maddalena I, Smania N, Tinazzi M. Do Upper and Lower Camptocormias Affect Gait and Postural Control in Patients with Parkinson’s Disease? An Observational Cross-Sectional Study. Parkinson’s Disease. 2019 Jul 24;2019.
- Geroin C, Artusi CA, Gandolfi M, Zanolin E, Ceravolo R, Capecci M, Andrenelli E, Ceravolo MG, Bonanni L, Onofrj M, Telese R. Does the Degree of Trunk Bending Predict Patient Disability, Motor Impairment, Falls, and Back Pain in Parkinson's Disease?. Frontiers in neurology. 2020 Mar 31;11:207.
- Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stern MB, Dodel R, Dubois B. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Movement disorders: official journal of the Movement Disorder Society. 2008 Nov 15;23(15):2129-70.
- Haefeli M, Elfering A. Pain assessment. European Spine Journal. 2006 Jan;15(1):S17-24.
- Hisham NA, Nazri AF, Madete J, Herawati L, Mahmud J. Measuring ankle angle and analysis of walking gait using kinovea. 2017: 247-250.
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967 May;17(5):427-42.

- Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N. The Parkinson's Disease Questionnaire (PDQ-39): development and validation of a Parkinson's disease summary index score. Age Ageing. 1997 Sep;26(5):353-7.
- Karcioglu O, Topacoglu H, Dikme O, Dikme O. A systematic review of the pain scales in adults: Which to use?. The American journal of emergency medicine. 2018 Jan 6.
- Kashihara K, Ohno M, Tomita S. Dropped head syndrome in Parkinson's disease. Mov Disord 2006; 21: 1213–16.
- Kashihara K, Imamura T. Clinical correlates of anterior and lateral flexion of the thoracolumbar spine and dropped head in patients with Parkinson's disease. Parkinsonism & related disorders. 2012 Mar 1;18(3):290-3.8.
- Kashihara K. Postural disorders in Parkinson's disease: clinical characteristics, frequency, pathophysiology and management. Neurodegenerative Disease Management. 2012 Dec;2(6):577-88.
- Larsen TA, LeWitt PA, Calne DB. Theoretical and practical issues in assessment of deficits and therapy in parkinsonism. Lisuride and other dopamine agonists. 1983:363-73.
- LeWitt PA, Taylor DC. Protection against Parkinson's disease progression: clinical experience. Neurotherapeutics. 2008 Apr 1;5(2):210-25.
- Liu K, Ou R, Wei Q, Cao B, Chen Y, Song W, Wu Y, Shang H. Pisa Syndrome in Chinese Patients with Parkinson's Disease. Frontiers in neurology. 2019 Jun 20; 10:651.
- Margraf NG, Wolke R, Granert O, Berardelli A, Bloem BR, Djaldetti R, Espay AJ, Fasano A, Furusawa Y, Giladi N, Hallett M. Consensus for the measurement of the camptocormia angle in the standing patient. Parkinsonism & related disorders. 2018 Jun 8.
- Mazzoni P, Shabbott B, Cortés JC. Motor control abnormalities in Parkinson's disease. Cold Spring Harbor perspectives in medicine. 2012 Jun 1;2(6):a009282.
- Mirelman A, Bonato P, Camicioli R, Ellis TD, Giladi N, Hamilton JL, Hass CJ, Hausdorff JM, Pelosin E, Almeida QJ. Gait impairments in Parkinson's disease. The Lancet Neurology. 2019 Jul 1;18(7):697-708.
- Ngamjarus C, Chongsuvivatwong V.n4Studies: Sample size and power calculations for android. The Royal Golden Jubilee Ph.D. Program - The Thailand Research Fund&Prince of Songkla University. 2014.

- Nonnekes J, Goselink RJ, Růžička E, Fasano A, Nutt JG, Bloem BR. Neurological disorders of gait, balance and posture: a sign-based approach. Nature Reviews Neurology. 2018 Mar;14(3):183-9.
- Oeda T, Umemura A, Tomita S, Hayashi R, Kohsaka M, Sawada H. Clinical factors associated with abnormal postures in Parkinson's disease. PLoS One. 2013 Sep 19;8(9): e73547.
- Pandey S, Garg H. Postural & striatal deformities in Parkinson's disease: Are these rare?. The Indian journal of medical research. 2016 Jan;143(1):11.
- Pandey S, Kumar H. Assessment of striatal & postural deformities in patients with Parkinson's disease. The Indian journal of medical research. 2016 Nov;144(5):682.Parkinson J. An Essay on the Shaking Palsy. London: Sherwood, Neely, and Jones; 1817.
- Parkinson J. An Essay on the Shaking Palsy. London: Sherwood, Neely, and Jones; 1817.
- Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015 Oct;30(12):1591-601.
- Puig-Diví A, Escalona-Marfil C, Padullés-Riu JM, Busquets A, Padullés-Chando X, Marcos-Ruiz D. Validity and reliability of the Kinovea program in obtaining angles and distances using coordinates in 4 perspectives. PloS one. 2019 Jun 5;14(6): e0216448.
- Richards KV, Beales DJ, Smith AJ, O'Sullivan PB, Straker LM. Neck posture clusters and their association with biopsychosocial factors and neck pain in Australian adolescents.
- Ruttiman R, Eltorai AE, Daniels AH. Etiology and management of spinal deformity in patients with Parkinson's disease. International journal of spine surgery. 2018 Jan 1;12(1):15-21.
- Schlenstedt C, Gavriliuc O, Boße K, Wolke R, Granert O, Deuschl G, Margraf NG. The effect of medication and deep brain stimulation on posture in parkinson's disease. Frontiers in neurology. 2019 Dec 3; 10:1254.
- Seki M, Takahashi K, Koto A, Mihara B, Morita Y, Isozumi K, Ohta K, Muramatsu K, Gotoh J, Yamaguchi K, Tomita Y. Camptocormia in Japanese patients with Parkinson's disease: a multicenter study. Movement disorders. 2011 Dec;26(14):2567-71.

- Srivanitchapoom P, Hallett M. Camptocormia in Parkinson's disease: definition, epidemiology, pathogenesis and treatment modalities. J Neurol Neurosurg Psychiatry. 2016 Jan;87(1):75-85.
- 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. Movement Disorders. 2013 May 1;28(5):668-70.
- Suzuki T, Matsuzaka H. Drug-induced Pisa syndrome (pleurothotonus): epidemiology and management. CNS Drugs. 2002;16(3):165-74.
- The prevention of falls in later life. A report of the Kellogg International Work Group on the Prevention of Falls by the Elderly. Dan Med Bull. Denmark; 1987 Apr;34 Suppl 4:1–24.
- Tinazzi M, Fasano A, Geroin C, Morgante F, Ceravolo R, Rossi S, Thomas A, Fabbrini G, Bentivoglio A, Tamma F, Cossu G, Modugno N, Zappia M, Volontè MA, Dallocchio C, Abbruzzese G, Pacchetti C, Marconi R, Defazio G, Canesi M, Cannas A, Pisani A, Mirandola R, Barone P, Vitale C; Italian Pisa Syndrome Study Group. Pisa syndrome in Parkinson disease: An observational multicenter Italian study. Neurology. 2015 Nov 17;85(20):1769-79.
- Tinazzi M, Gandolfi M, Ceravolo R, Capecci M, Andrenelli E, Ceravolo MG, Bonanni L, Onofrj M, Vitale M, Catalan M, Polverino P. Postural Abnormalities in Parkinson's Disease: An Epidemiological and Clinical Multicenter Study. Movement disorders clinical practice. 2019 Sep;6(7):576-85.
- Tinazzi M, Gandolfi M, Artusi CA, Lanzafame R, Zanolin E, Ceravolo R, Capecci M, Andrenelli E, Ceravolo MG, Bonanni L, Onofrj M. Validity of the wall goniometer as a screening tool to detect postural abnormalities in Parkinson's disease. Parkinsonism & related disorders. 2019 Dec 1;69:159-65.
- Tiple D, Fabbrini G, Colosimo C, Ottaviani D, Camerota F, Defazio G, Berardelli A. Camptocormia in Parkinson disease: an epidemiological and clinical study. Journal of Neurology, Neurosurgery & Psychiatry. 2009 Feb 1;80(2):145-8.

- 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 Nov 15;25(15):2649-53.
- Tramonti C, Di Martino S, Unti E, Frosini D, Bonuccelli U, Rossi B, Ceravolo R, Chisari C. Gait dynamics in Pisa syndrome and Camptocormia: the role of stride length and hip kinematics. Gait & posture. 2017 Sep 1;57:130-5.Uzawa A, Mori M, Kojima S, et al. Dopamine agonist-induced antecollis in Parkinson's disease. Mov Disord 2009; 24: 2408–11.
- Wenning GK, Krismer F, Poewe W. New insights into atypical parkinsonism. Curr Opin Neurol. 2011 Aug;24(4):331-8.
- Yamada H, Katayama Y, Yamamoto T. Parkinson's disease and dropped head. Rinsho Shinkeigaku. 2003;43:955.
- Yoshii F, Moriya Y, Ohnuki T, Ryo M, Takahashi W. Postural deformities in Parkinson ' s disease – Mutual relationships among neck flexion , fore-bent , knee-bent and lateral-bent angles and correlations with clinical predictors. 2016;3–9.

10. Appendix

10.1. Case Record Form (CRF)

Case No. ……

Case Record Form

Postural deformities in patients with Parkinson's disease:

an observational multicenter study

Part I: General data

Age(years) ☐☐ **Sex:** ☐ Male ☐ Female

Height (cm) ☐☐☐.☐ **Weight (kg):** ☐☐.☐ **BMI:** ☐☐.☐

Age at PD onset (years): ☐☐ **Disease duration (years)** ☐☐(yr)

Associated medical conditions: …….

Laterality of motor symptoms at PD onset: ☐ Right ☐ Left ☐ Bilateral

PD phenotype ☐ Postural instability/ gait difficulty ☐ Tremor-dominant ☐ Mixed type

Modified H&Y score: ☐.☐ **MDS-UPDRS**: Part II☐☐ Part III☐☐

MDS-UPDRS item 3.13 (posture):

☐ 0 Normal ☐ 1 Slight ☐ 2 Mild ☐ 3 Moderate ☐ 4 Severe

First pharmacological therapy:	**Current pharmacological therapy:**
☐ Levodopa: ……..…….……	☐ Levodopa: ……..……..
☐ Dopamine agonists: ……	☐ Dopamine agonists: ……
☐ L-dopa + DA: ……	☐ L-dopa+DA: ……..……..……
☐ Other antiparkinsonian drugs: ……..…….	☐ Other antiparkinsonian drugs: ….…..…….

Levodopa equivalent daily dose (LEDD) (mg): ☐☐☐☐.☐

Falls in the previous month: ☐ Yes, if yes: number of falling ☐☐

Direction ☐ Anterior ☐ Posterior ☐ Right ☐ Left

☐ No

Measured Angle from Goniometer:

☐ Sagittal plane (degrees)…… ☐ Coronal plane (degrees)……

Part II: Parkinson's Disease Quality of Life Questionnaire (PDQ-8)

Many people with Parkinson's Disease report problems from time to time. We are interested in how you have been in your general health over the last four weeks.

Please complete this form by placing a tick or check mark (✓) in one box on each line

	Never	**Occasionally**	**Sometimes**	**Often**	**Always or cannot do at all**
1.Over the past four weeks have you had difficulty getting around in public places?	□	□	□	□	□
2.Over the past four weeks have you had difficulty dressing yourself?	□	□	□	□	□
3.Over the past four weeks have you felt depressed?	□	□	□	□	□
4.Over the past four weeks have you had problems with close relationships?	□	□	□	□	□
5.Over the past four weeks have you had problems with concentration?	□	□	□	□	□
6.Over the past four weeks have you felt unable to communicate properly?	□	□	□	□	□
7.Over the past four weeks have you had painful muscle cramps and pains?	□	□	□	□	□
8.Over the past four weeks have you felt embarrassed by having Parkinson's Disease?	□	□	□	□	□

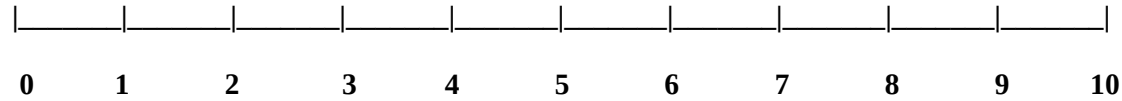
Part III: Postural & Gait deformities (CP=camptocormia; AC=antecollis; PS=Pisa syndrome)

1. **Latency to develop one or more postural deformity after PD onset (months)**: ☐☐
2. **Postural deformity duration (years):** ☐☐
3. **Postural deformity direction**: ☐ right ☐ left ☐ anterior
4. **In case of Pisa syndrome (PS), the presence of metronome sign (defined as an alternate leaning behavior occurring toward both sides):** ☐ Yes ☐ No
5. **The pattern of postural deformity onset**:
   - ☐ Acute (<1 month)
   - ☐ Subchronic (≥1 month <3 months)
   - ☐ Chronic (≥3 months)
6. **Side of PD symptoms at onset and Pisa syndrome (PS) inclination**
   - ☐ PS ipsilateral PD symptoms onset
   - ☐ PS contralateral PD symptoms onset
   - ☐ PS with bilateral PD symptoms onset
7. **Postural deformity after one month of drug modification**:☐ Yes ☐ No
8. **Postural deformity awareness by the patient**: ☐ Yes ☐ No
9. **Head compensation (in case of Pisa syndrome (PS), camptocormia (CP), antecollis (AC)) (defined as head deviation away from the bending side to preserve a horizontal vision):** ☐ Yes ☐ No
10. **Striatal hand**: ☐ Yes ☐ No
11. **Striatal foot**: ☐ Yes ☐ No

Part IV: Pain assessment: Numeric Rating Scale

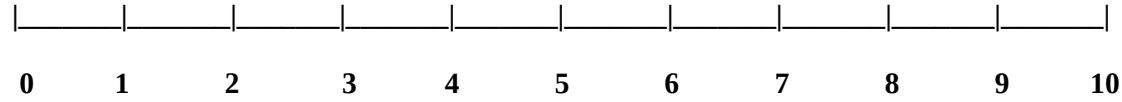
- Head

- Neck



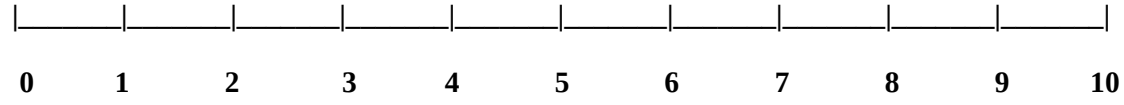
- Right Upper Limb

- Left Upper Limb



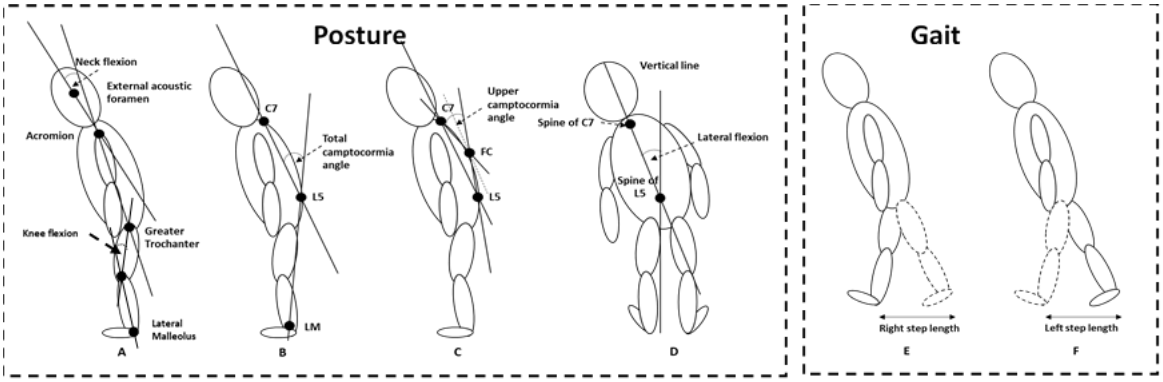
- Back

- Right Lower Limb



- Left Lower Limb

Part V: Posture and gait measurement



Neck flexion angle (degrees): …….…….

Total camptocormia angle (degrees): …….……

Upper camptocormia angle (degrees): ……..……..…..……

Lateral flexion angle (degrees): ……...……...……

Knee flexion angle (degrees): ……..……

Step Length (cm): Right ……..……..…… Left ……..……..

Stride Length (cm): ……..……..……

Velocity (m/s): ……..……..……

Cadence (steps/min): …….……..…….

…….. Patient Name or Subject ID	…… Site ID	……..-……-…… (mm-dd-yyyy) Assessment Date	…… Investigator's Initials

MDS UPDRS Score Sheet

1.A	Source of information	☐ Patient ☐ Caregiver ☐ Patient + Caregiver	3.3b	Rigidity– RUE	
			3.3c	Rigidity– LUE	
Part I			3.3d	Rigidity– RLE	
1.1	Cognitive impairment		3.3e	Rigidity– LLE	
1.2	Hallucinations and psychosis		3.4a	Finger tapping– Right hand	
1.3	Depressed mood		3.4b	Finger tapping– Left hand	
1.4	Anxious mood		3.5a	Hand movements– Right hand	
1.5	Apathy		3.5b	Hand movements– Left hand	
1.6	Features of DDS		3.6a	Pronation- supination movements– Right hand	
1.6a	Who is filling out questionnaire	☐ Patient ☐ Caregiver ☐ Patient + Caregiver	3.6b	Pronation- supination movements– Left hand	
			3.7a	Toe tapping– Right foot	
1.7	Sleep problems		3.7b	Toe tapping– Left foot	
1.8	Daytime sleepiness		3.8a	Leg agility– Right leg	
1.9	Pain and other sensations		3.8b	Leg agility– Left leg	
1.10	Urinary problems		3.9	Arising from chair	
1.11	Constipation problems		3.10	Gait	
1.12	Light headedness on standing		3.11	Freezing of gait	
1.13	Fatigue		3.12	Postural stability	
Part II			3.13	Posture	
2.1	Speech		3.14	Global spontaneity of movement	
2.2	Saliva and drooling		3.15a	Postural tremor– Right hand	
2.3	Chewing and swallowing		3.15b	Postural tremor– Left hand	
2.4	Eating tasks		3.16a	Kinetic tremor– Right hand	
2.5	Dressing		3.16b	Kinetic tremor– Left hand	
2.6	Hygiene		3.17a	Rest tremor amplitude– RUE	
2.7	Handwriting		3.17b	Rest tremor amplitude– LUE	
2.8	Doing hobbies and other activities		3.17c	Rest tremor amplitude– RLE	
2.9	Turning in bed		3.17d	Rest tremor amplitude– LLE	
2.10	Tremor		3.17e	Rest tremor amplitude– Lip/jaw	
2.11	Getting out of bed		3.18	Constancy of rest	
2.12	Walking and balance			Were dyskinesias present?	☐ No ☐ Yes
2.13	Freezing			Did these movements interfere with ratings?	☐ No ☐ Yes
3a	Is the patient on medication?	☐ No ☐ Yes		Hoehn and Yahr Stage	
3b	Patient's clinical state	☐ Off ☐ On	**Part IV**		
3c	Is the patient on Levodopa?	☐ No ☐ Yes	4.1	Time spent with dyskinesias	
3.C1	If yes, minutes since last dose:		4.2	Functional impact of dyskinesias	
Part III			4.3	Time spent in the OFF state	
3.1	Speech		4.4	Functional impact of fluctuations	
3.2	Facial expression		4.5	Complexity of motor fluctuations	
3.3a	Rigidity– Neck		4.6	Painful OFF-state dystonia	

