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Postural abnormalities in Asian and Caucasian Parkinson's disease patients: A multicenter study

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Abstract

Introduction

Postural abnormalities (PA) 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.

Methods

An international, multicenter, cross-sectional study was performed in 6 European and Asian movement disorders centers with the aim to clarify differences and similarities of prevalence and characteristics of PA in Asian vs. Caucasian PD patients. Axial PA, encompassing antecollis (AC), camptocormia (CC), and Pisa syndrome (PS), and appendicular PA (appPA) were systematically searched and analysed in consecutive patients.

Results

88 (27%) of 326 PD patients had PA (29.1% in Asians and 24.3% in Caucasians, p: 0.331). 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 (OR, 4.036; 95% CI, 1.926–8.456; $p < 0.005$), a longer disease duration (OR, 2.61; 95% CI, 1.024–6.653; $p = 0.044$), and a higher axial score (OR, 1.242; 95% CI, 1.122–1.375; $p < 0.0005$) were the factors associated with axial PA.

Conclusion

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.

Keywords

Parkinson's disease

Postural abnormalities

Axial symptoms

Ethnicity

1. Introduction

Postural abnormalities (PA) are frequent and disabling clinical features of Parkinson's disease (PD) [1]. A recent cross-sectional study showed that over 20% of PD patients have an abnormal neck or trunk posture [2]. The most common type of PA is the stooped posture, firstly described by James Parkinson, and characterized by an anterior trunk bending with rounding of the shoulders and flexed knees [1,3]. More severe PA, namely camptocormia (CC), antecollis (AC), Pisa syndrome (PS), and scoliosis [1,4], proved to be disabling PD features and impair the patients' quality of life (QoL) [2]. In addition to axial PA, abnormal postures of limbs, encompassing striatal foot or hand, can be observed in PD patients and these deformities are typically referred to as appendicular PA (appPA).

PA prevalence is variable across studies because of the different diagnostic criteria and measurement methods employed. CC prevalence has been estimated to range from 3% to 17.7%, according to the cut-off values considered for the anterior trunk flexion, ranging

between 15 and 45° [4]. Likely, different criteria and methods of assessment have been applied over time for the diagnosis of AC and PS [1].

In this context of high heterogeneity, the majority of PD patients reported with CC and AC in the literature originated from Asia [[5], [6], [7], [8], [9]] and some studies suggested that PA could be more prevalent in Asian patients if compared to Caucasian ones [1,10]. 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.

This international, multicenter, cross-sectional study was designed to systemically analyze PA in a large cohort of consecutive PD patients in Europe and Asia with the aim to clarify differences and similarities of prevalence and characteristics of PA in Asian and Caucasian people.

2. Methods

2.1. 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. Recruitment was consecutive being May 2019–May 2021 the global enrollment period. However, a break of variable duration in the recruitment occurred in each center, due to the COVID-19 pandemic, between March 2020 and January 2021. The inclusion criteria were a diagnosis of idiopathic PD [11], at least 3 years of disease duration, and age less than 80 years old. Patients with concomitant neurologic diseases known to negatively affect posture, a history of major spinal surgery or muscle and/or skeletal diseases, and 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) [12] in the 6 months before enrollment were excluded from the study.

The study protocol was reviewed and approved by the institutional review boards from every center. Written informed consent was obtained by all patients, also considering the possibility of taking photographs and walking records for this research.

2.2. Procedures

In each center, all patients were assessed 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). All evaluations were carried out during a single outpatient visit. A retrospective review of medical records was performed to retrieve demographic, clinical, and relevant data.

All patients with any kind of abnormal posture, defined as an MDS-UPDRS III item 3.13 posture score >0, underwent an additional assessment encompassing photographs to characterize the type and degrees of axial PA and a clinical assessment of appPA. Photos were taken in a standing position in the frontal (posterior) and sagittal plane. Full-body

photographs were taken in a standardized manner, in front of a baseline adjustable wall mounted goniometer (https://www.ncmedical.com/item_2631.html

) with the patient standing in front of the wall, 2 m from the camera set at a height of about 1 m from the ground [2]. Kinovea® software, a freeware program already used for the postural analysis of PD patients [2,13,14] was used to analyze postural angles from the pictures.

2.3. Study aims and outcome measures

The main aim of the study was to compare the prevalence of PA between Caucasian and Asian PD patients, separately considering axial and app PA.

Secondary aims were: i) to compare the characteristics of different PA, ii) to describe clinical features of PD patients with PA, and iii) to evaluate risk factors for developing PA.

All patients underwent an extensive cross-sectional clinical assessment including demographic and clinical data, levodopa equivalent daily dose (LEDD) [15], Hoehn and Yahr Stage (HY) [16], MDS-sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part II-III scale [17], the pain NRS scale [18], and Parkinson's disease questionnaire 8 (PDQ-8) [19] 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) [20].

AC was diagnosed in patients with neck flexion (NF) ≥ 45° [21,22].

Total CC was diagnosed in patients with total trunk flexion (TTF) ≥ 30° [23,24].

Upper CC was diagnosed in patients with upper trunk flexion (UTF) ≥ 45°. (Fig. 1) [23,24].

PS was diagnosed in patients with lateral trunk flexion (LF) ≥ 10°. (Fig. 1) [1,25,26]. The explanation for NF, TTF, UTF and LF angle calculations are detailed in Fig. 1 legend.

Patients having a mixed form of axial PA (i.e., a combination of AC, PS or CC) were considered in both categories and a category for combined PA was also considered.

AppPA was defined as the fixed deformity of the angle at hand (metacarpophalangeal, proximal interphalangeal (extension), and distal interphalangeal joints (flexion)) or foot (great toe (flexion or extension) and other toes (plantar flexion)) [9].

Latency to develop PA after PD onset, PA duration, pattern of PA onset, awareness of PA by asking patients if they felt trunk bending or leaning, striatal hand and foot deformities were recorded. In the case of lateral trunk flexion, the side and direction of PD symptoms onset and inclination in patients with PS were also recorded.

2.4. Statistical analysis

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 [27]. A sample size of at least 322 PD patients (182 Asian PD patients and 140 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, respectively; no dropout rate was considered due to the cross-sectional design of the study.

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 axial PA, AC, CC, PS, appPA as the dependent variable and the sociodemographic and clinical features (ethnicity, sex, age, body mass index (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 falls) 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 independent variables and with axial PA, AC, CC, PS, appPA as the dependent variable, were used to calculate an adjusted OR (95% CI) for all possible confounding effects. Multicollinearity analysis was used to find the correlation between variables before performing Multiple regression analysis.

All tests were two-tailed with a P-value set at 0.05. Statistical analyses were performed using SPSS (version 27) statistical software.

3. Results

We recruited a total of 326 PD patients, 182 of Asian (Thailand = 76, South Korea = 81, and Saudi Arabia = 25) and 144 of Caucasian ethnicity (Italy = 77, Germany = 30, Portugal = 37).

Considering all patients, 23.9% (n = 78) presented axial PA and 4.9% (n = 16) appPA; 15.3% of patients had an isolated PA (12.9% axial PA and 2.4% app PA); 11.6% of patients had a combined PA (9.2% combined axial PA, 0.6% combined app PA, and 1.8% combined axial PA and app PA). Among combined axial PA, 6.8% was AC and CC followed by 1.5% of AC and PS, 0.3% of CC and PS, and 0.6% of AC combined with CC and PS. The most common type of axial PA was AC (19.9% of all patients), followed by CC (11.7%), and PS (3.7%) (Table 1 and Table S1).

The average PA duration at the time of study enrolment was 3.21 ± 4.11 years and the onset were 4.49 ± 4.29 years after PD diagnosis.

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 ($p = 0.007$) than PD patients without PA; moreover, PD patients with axial PA showed a higher LEDD ($p < 0.0005$). PD patients with appPA were more often found in Asian ($p = 0.036$), had a lower BMI ($p < 0.0005$), a longer disease duration ($p = 0.002$), a higher H&Y stage ($p = 0.012$), a higher axial score ($p = 0.046$), more clinical symmetry ($p = 0.023$), and a higher LEDD ($p = 0.045$) than patients without appPA.

Patients with appPA had a lower BMI (p = 0.001), a younger age (p = 0.041) and earlier age at PD onset (p = 0.013) than patients with axial PA (Table 2 and Tables S2–S3).

3.1. Differences between Asian and Caucasian patients

No significant difference in the PA prevalence was found between Asian and Caucasian patients (29.1% vs. 24.3%, p = 0.331) neither when considering only axial PA (23.6% vs. 24.3%, p = 0.886).

Caucasian patients with axial PA were older (p = 0.042) and with longer PD duration (p = 0.009) than Asian ones, who conversely showed a longer PA duration (p = 0.013) (Table 3). This reflected in a longer though not significant latency for PA appearance among Caucasian patients if compared to the Asian ones (5.35 ± 4.44 vs. 3.58 ± 3.81 years; p = 0.115).

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), axial score (adjusted OR, 1.264; 95% CI, 1.149–1.39; p < 0.0005), and clinical asymmetry (adjusted OR, 1.236; 95% CI, 1.121–1.362; p < 0.005) were significantly associated with the presence of PA.

When considering axial PA, the multiple logistic regression analysis showed that male sex (adjusted OR, 3.658; 95% CI, 1.782–7.512; p < 0.005), an older age (adjusted OR, 1.047; 95% CI, 1.007–1.088; p = 0.022), and a higher axial score (adjusted OR, 1.236; 95% CI, 1.117–1.368; p < 0.0005) were variables significantly associated with the presence of axial PA (Tables 4 and S4).

Differences in ethnicity did not prove to be associated with a different risk of axial PA, appPA (Table S4), nor for the axial PA considered singularly (i.e., AC, CC, and PS) (Table S5).

Considering Caucasian and Asian patients separately, male sex (adjusted OR, 3.684,95%CI, 1.02–13.301; p = 0.047), longer disease duration (adjusted OR, 1.181, 95% CI, 1.034–1.349; p = 0.014) and higher axial score (adjusted OR, 1.21, 95% CI, 1.058–1.383; p = 0.006) were related to PA among Caucasian ones, while male Backspacesex (adjusted OR, 2.616, 95% CI, 1.195–5.727; p = 0.016) and higher axial score (adjusted OR, 1.248, 95% CI, 1.085–1.435; p = 0.002) among Asian ones.

3.1.1. Antecollis (AC)

AC prevalence was 17.6% in Asian patients and 22.9% in Caucasian patients (p = 0.231) (Table S2, Supplementary material). The average degree of 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) (Table 2). 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) (Table S3).

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 (Table S1). While AC patients in Asians had a longer PA duration (p = 0.035) than Caucasian patients.

The multiple logistic regression analysis showed that male sex (adjusted OR, 3.336; 95% CI, 1.588–7.004; p = 0.001), an older age (adjusted OR, 1.071; 95% CI, 1.026–1.117; p = 0.002), a longer disease duration (adjusted OR, 1.079; 95% CI, 1.000–1.163; p = 0.049), and severe axial score (adjusted OR, 1.240; 95% CI, 1.117–1.376; p < 0.0005) were significantly associated with the presence of AC (Table S5).

3.1.2. Camptocormia (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 S3).

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 S5).

3.1.3. Pisa syndrome (PS)

PS prevalence was 3.3% in Asian patients and 4.2% in Caucasian patients (p = 0.679) (Table S2, Supplementary material). 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) (Table 2). 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) (Table S3).

PS patients in Caucasians took more LEDD than in Asian patients (p = 0.03) (Table S1).

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 S5).

3.1.4. Appendicular 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) (Table S2).

AppPA patients in Asian were younger than Caucasian patients (p = 0.043).

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 S3).

4. Discussion

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 [1,10]. 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, confirmed 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%) [2].

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 previous studies (1% and 3.6% respectively) [28,29]. 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%) [2,25]. 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 [2,25]. 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 [2,25]. Once comparing our Italian PD patients with the other enrolled patients of our study, including Caucasians and Asians, we do not find those differences (Table S1).

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 findings from an Italian multicenter study reporting a 6.5% prevalence [2]. We explain 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. This prevalence is lower than the reported in previous studies [9]. At the same time, the clinical features associated with appPA, encompassing a lower BMI, a younger age at PD onset, higher clinical symmetry, and a smaller 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 [9]. Shared diagnostic criteria for the identification of striatal hands and feet are missing. This 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, confirming the impact of PA 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, similarly to data reported in previous studies [2,6], though not confirming the association with a higher LEDD. Once stratifying this analysis for ethnicity, different variables appear to be significant, being male gender and a higher axial score significant in both groups but a longer disease duration significant only for Caucasian patients. This finding highlights the role of disease duration for axial PA development among Caucasian patients, while this is 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 years). However, latency for PA development was a secondary, retrospectively collected outcome and it should be considered that self-reported PA occurrence could be overlooked.

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. On a related note, differences in the delay of appearance of PA, which seems earlier in Asian patients, even if Caucasians seem to have more severe AC, merit to be further investigated by means of prospective studies, which could adequately consider possible differences in environmental and genetic factors and comorbidities and not only antiparkinsonian treatment approaches. Indeed, also regarding environmental factors, there is a scarcity of large epidemiological studies in the Western Pacific Region; moreover, lower level of physical activities, and higher risk of type 2 diabetes seem to characterize Western PD patients if compared to Eastern ones, and these factors could contribute to delay in PA appearance [30].

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 [1,2].

The interpretation of results should consider our study shortcomings. First, the cross-sectional design and the fact that 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. Finally, we assessed PA in the Med On condition as several patients lived in rural area far from the hospital and it was logistically not possible to perform an outpatient assessment in the Med Off condition. This could partly have induced un underestimation of PA prevalence, inducing a specific focus on dopaminergic unresponsive PA.

In conclusion, our study does not confirm the role of ethnicity as a risk factor for axial and app PA development when comparing Asian vs. Caucasian PD patients. However, it is possible that Asian patients tend to develop PA earlier and with a higher prevalence of striatal hand and foot deformities than Caucasian ones. We confirm that the most relevant demographic/clinical features associated with PA in both ethnicities is male sex (ratio 2.3:1), with disease duration being a risk factor only for Caucasian patients. 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.

Authorship disclosure

All authors have materially participated in the research and/or article preparation (see roles, below). All authors have approved the final submitted article. This article represents original

work by the authors, has not been published elsewhere, and is not under consideration for publication elsewhere.

Author statement

Chatkaew Pongmala: Conception, Organization, Execution, Design, Execution, Writing of the first draft, Dr.Carlo Alberto Artusi: Conception, Organization, Execution, Review and Critique, Writing of the first draft, Dr.Maurizio Zibetti: Organization, Execution, Review and Critique, Review and Critique, Dr. Yuvadee pitakpatapee: Organization, Execution, Review and Critique, Review and Critique, Dr. Takarn Wangthumrong: Organization, Execution, Review and Critique, Review and Critique, Dr. Tanita Sangpeamsook: Organization, Execution, Review and Critique, Review and Critique, Dr. Jindapa Srikajon: Organization, Execution, Review and Critique, Review and Critique, Dr. Prachaya Srivanitchapoom: Organization, Execution, Review and Critique, Review and Critique, Dr. Jinyoung Youn: Organization, Execution, Review and Critique, Review and Critique, Dr. Jin Whan Cho: Organization, Execution, Review and Critique, Review and Critique, Dr. Minkyeong Kim: Organization, Execution, Review and Critique, Review and Critique, Dr. Heba M.Zamil Shinawi: Organization, Execution, Review and Critique, Review and Critique, Dr. Mona Talib Obaid: Organization, Execution, Review and Critique, Review and Critique, Dr. Nils G. Margraf: Organization, Execution, Review and Critique, Review and Critique, Dr. Alexander Baumann: Organization, Execution, Review and Critique, Review and Critique, Filipa Pona-Ferreira: Organization, Execution, Review and Critique, Review and Critique, Mariana Leitão: Organization, Execution, Review and Critique, Review and Critique, Teresa Lobo: Organization, Execution, Review and Critique, Review and Critique, Dr.Joaquim J Ferreira: Organization, Execution, Review and Critique, Review and Critique, Dr.Margherita Fabbri: Organization, Execution, Review and Critique, Review and Critique, Conception, Writing of the first draft, Dr.Leonardo Lopiano: Organization, Execution, Review and Critique, Review and Critique.

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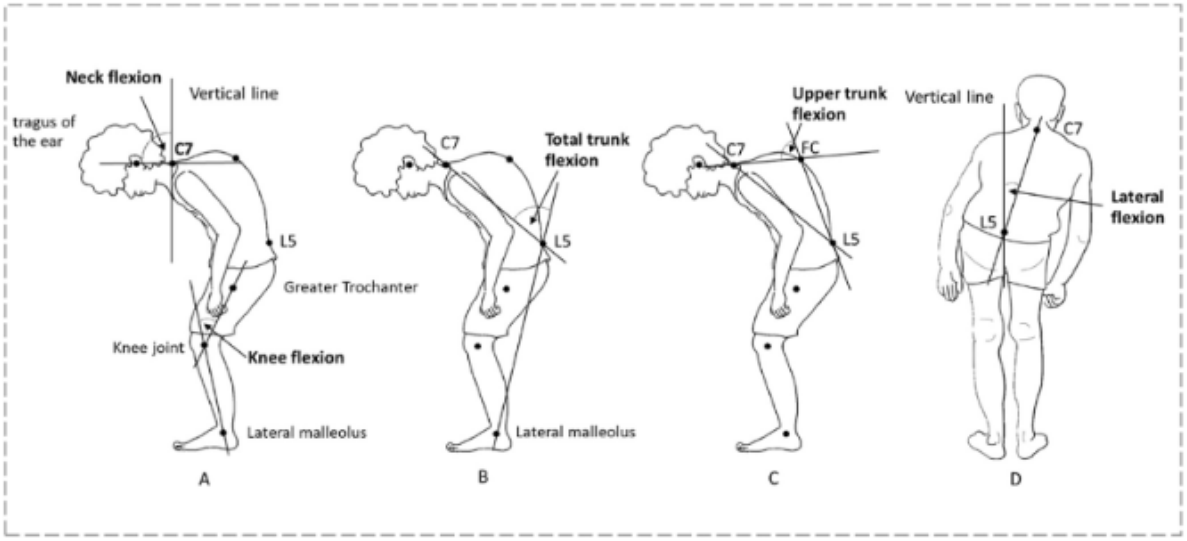

Fig. 1. The measurement of body angles. In lateral view, neck flexion (NF) and knee flexion (KF) (A), total trunk flexion (TTF) (B), and upper trunk flexion (UTF) (C).

In back view, lateral flexion (LF) (D) is shown. 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. 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. 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. 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.

	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)	
PS direction, n (%)				
Right	5 (41.7%)	3 (50%)	2 (33.3%)	
Left	7 (58.3%)	3 (50%)	4 (66.7%)	
Side of PD symptoms at onset and PS inclination, n (%)				
Ipsilateral	8 (66.7%)	4 (66.7%)	4 (66.7%)	
Contralateral	4 (33.3%)	2 (33.3%)	2 (33.3%)	
Bilateral				

PA: Postural Abnormalities.

Table 1

Prevalence and clinical features of PD patients with PA

	Total			Total		
	Wo axial PA	axial PA	P-value	Wo app PA	app PA	P-value
Patients, n	248 (76.1%)	78 (23.9%)	**<0.0005**	310 (95.1%)	16 (4.9%)	**<0.0005**
Ethnicitiy, n (%)			0.886			**0.036**
Asian	139 (56%)	43 (55.1%)		169 (54.5%)	13 (81.3%)	
Caucasian	109 (44%)	35 (44.9%)		141 (45.5%)	3 (18.8%)	
Gender, n (%)			**<0.0005**			0.306
Male	124 (50%)	59 (75.6%)		176 (56.8%)	7 (43.8%)	
Female	124 (50%)	19 (24.4%)		134 (43.2%)	9 (56.3%)	
Age, y, mean (SD)	63.42 (9.41)	67.97 (7.65)	**<0.0005**	64.48 (9.22)	65.06 (9.31)	0.814
BMI, mean (SD)	24.73 (4.05)	25.23 (4.69)	0.579	25.03 (4.2)	21.31 (2.55)	**<0.0005**
Age of PD onset, y, mean (SD)	56.11 (10.38)	59.03 (8.82)	**0.032**	56.98 (10.05)	53.56 (10.73)	0.212
Disease duration, y, mean (SD)	7.27 (4.05)	9 (4.96)	**0.002**	7.49 (4.12)	11.5 (6.42)	**0.002**
H&Y stage, n (%)			**<0.0005**			**0.012**
I	38 (15.3%)	1 (1.3%)		39 (12.6%)	0 (0%)	
II	136 (54.8%)	30 (38.5%)		160 (51.6%)	6 (37.5%)	
III	72 (29%)	37 (47.4%)		100 (32.2%)	9 (56.3%)	
IV	1 (0.4%)	9 (11.5%)		10 (3.2%)	0 (0%)	
V	1 (0.4%)	1 (1.3%)		1 (0.3%)	1 (6.3%)	
MDS-UPDRS score, mean (SD)						
II	10.43 (6.05)	16.29 (9.49)	**<0.0005**	11.65 (7.18)	15.44 (11.14)	0.183
III	26.91 (12.43)	36.62 (14.26)	**<0.0005**	28.91 (13.33)	35.44 (16.06)	0.106
IV*	3.99 (4.06)	3.58 (3.91)	0.368	3.77 (3.99)	5.88 (4.16)	**0.041**
Axial score	7.22 (4.06)	12.96 (6.03)	**<0.0005**	8.45 (5.12)	11.44 (6.22)	**0.046**
Dominant phenotype, n (%)			**0.015**			0.193
PIGD	121 (48.8%)	52 (66.7%)		161 (51.9%)	12 (75%)	
Tremor	104 (41.9%)	19 (24.4%)		120 (38.7%)	3 (18.8%)	
Mixed	23 (9.3%)	7 (9%)		29 (9.4%)	1 (6.3%)	
Lateral of PD onset, n (%)			0.362			0.228
Right	144 (58.1%)	39 (50%)		177 (57.1%)	6 (37.5%)	
Left	89 (35.9%)	35 (44.9%)		116 (37.4%)	8 (50%)	
Bilateral	15 (6%)	4 (5.1%)		17 (5.5%)	2 (12.5%)	
Clinical asymmetry, n (%)			0.068			**0.023**
Symmetry	143 (57.7%)	54 (69.2%)		183 (59%)	14 (87.5%)	
Asymmetry	105 (42.3%)	24 (30.8%)		127 (41%)	2 (12.5%)	
PDQ-8, mean (SD)	21.36 (15.62)	27.93 (19.19)	**0.007**	22.59 (16.67)	29.49 (17.38)	0.094
LEDD, mg, mean (SD)	671.52 (419.44)	866.42 (393.13)	**<0.0005**	709.58 (422.21)	886.75 (369.58)	**0.045**
Fall, n (%)			0.093			0.065
No	211 (85.1%)	60 (76.9%)		255 (82.3%)	16 (100%)	
Yes	37 (14.9%)	18 (23.1%)		55 (17.7%)	0 (0%)	

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; (*): MDS-UPDRS part IV assessment is

available only for 280 patients, including 158 Asian and 122 Caucasian.

Table 2

Demographic and clinical features and their differences between PD patients without axial PA and app PA and PD patients with axial PA and app PA

	Axial PA		
	Asian	Caucasian	P-value
Patients, n	43 (23.6%)	35 (24.3%)	0.886
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, n (%)			0.596
I	1 (2.3%)	0 (0%)	
II	16 (37.2%)	14 (40%)	
III	22 (51.2%)	15 (42.9%)	
IV	4 (9.3%)	5 (14.3%)	
V	0 (0%)	1 (2.9%)	
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
IV*	3.56 (3.79)	3.61 (4.1)	0.945
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**

Table 3

Demographic and clinical features and their differences between Asian and Caucasian PD patients.

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. (*): MDS-UPDRS part IV assessment is available only for 65 patients, including 34 Asian and 31 Caucasian.

	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**	3.658	1.782–7.512	**<0.0005**
Age, y	1.063	1.029–1.097	**<0.0005**	1.047	1.007–1.088	**0.022**
BMI	1.028	0.969–1.09	0.367			
Disease duration	1.088	1.029–1.15	**0.003**	1.074	0.998–1.155	0.056
H&Y stage	3.186	2.118–4.794	**<0.0005**	1.116	0.643–1.939	0.696
MDS-UPDRS score on state						
II	1.111	1.069–1.154	**<0.0005**	1.031	0.969–1.097	0.331
III	1.055	1.034–1.077	**<0.0005**	1.009	0.978–1.041	0.571
Axial score	1.277	1.194–1.365	**<0.0005**	1.236	1.117–1.368	**<0.0005**
Dominant phenotype						
PIGD vs Tremor	0.425	0.236–0.765	**0.004**	0.839	0.401–1.755	0.641
PIGD vs Mixed	0.708	0.286–1.753	0.456	0.649	0.218–1.932	0.437
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**	0.978	0.954–1.003	0.083
L-dopa equivalent daily dose	1.001	1.000–1.002	**0.001**	1	1–1.001	0.357
Fall, No vs Yes	1.711	0.909–3.219	0.096			

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.

*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.

Table 4

Demographic and clinical features associated with axial PA*