


SHORT REPORT

Age-related changes in blood pressure and heart rates of patients with Parkinson's disease

Kazumasa Shindo MD  | Yuto Morishima MD | Yumi Suwa MD | Toko Fukao MD | Takafumi Kurita MD | Akane Satake MD | Mai Tsuchiya MD | Yuta Ichinose MD | Takanori Hata MD | Kishin Koh MD | Takamura Nagasaka MD | Yoshihisa Takiyama MD, PhD

Department of Neurology, University of Yamanashi, Yamanashi, Japan

Correspondence

Kazumasa Shindo, Department of Neurology, University of Yamanashi, 1110 Shimokatou, Chuo-city, Yamanashi, 409-3898 Japan.
Email: kshindo@yamanashi.ac.jp

Abstract

This study evaluated yearly changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rates (HR) for patients with Parkinson's disease (PD). Data were collected for the last 10 years from medical records of 28 PD patients and 30 non-PD patients with other neurological disorders. Age-related changes in each group were analyzed by year using mean values of SBP, DBP, and HR obtained at their bi-monthly visits. In results, PD patients had a gradual decrease in SBP with longer disease duration, and mean SBP significantly decreased from Year 7–11 compared to the mean values for Year 1 ($p < .001$ or $p < .01$). In non-PD patients, mean SBP significantly increased from Year 4–11 compared to the mean values for Year 1 ($p < .001$ or $p < .01$). This is the first study to report age-related changes of BP in individual patients with PD over 10 years.

1 | INTRODUCTION

Various degrees of autonomic dysfunction have been reported in patients with Parkinson's disease (PD).^{1,2} Clinical examinations are conducted to evaluate blood pressure changes in PD patients by using the stand-up test, head-up tilt-table test, and 24-h blood pressure monitoring, and cardiovascular autonomic symptoms are commonly observed, including orthostatic hypotension (OH) or dizziness, prandial hypotension, and supine or nocturnal hypertension.^{3,4} While symptoms such as constipation and urinary urgency were observed in some patients, either in the early stages of PD or before diagnosis when motor symptoms begin to appear,^{1-3,5}

many studies have validated that OH and OH-related symptoms are more frequent in PD patients with longer disease duration or higher on the disability scale.^{1,3,6} In our previous study, we confirmed these findings by using a microneurographic technique to record muscle sympathetic nerve activity controlling the blood pressure (BP).⁷ However, age-related changes in BP and heart rates (HR) of individual patients with PD have not been reported to date.

To evaluate yearly changes in BP and HR of patients with idiopathic PD for more than 10 years, we retrospectively calculated the average values of systolic BP (SBP), diastolic BP (DBP), and HR for each year and then analyzed these parameters for age-related changes.

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TABLE 1 Background and clinical findings in patients with Parkinson's disease (PD)

Group	Age (years)	Gender	Disease duration (years)	Change of body weight (Kg)	Body mass index (kg/m ²)	The number of OH	Antiparkinson drugs
PD (n = 28)	66. (11.6)	M:F = 10:18	13.5 (2.9)	+2.6(1.2)	22.7 (3.2)	n = 7	L (n = 28), ROT (n = 10), ROP (n = 10), I (n = 3), E (n = 2), S (n = 2)
Control (n = 30)	66.7 (10.7)	M:F = 10:20	21.6 (6.8)	+3.1 (1.8)	23.1 (2.9)	n = 0	

Note: Values are mean (SD).

Abbreviations: E, entacapone; F, female; I, istradefylline; L, levodopa; M, male; OH, orthostatic hypotension; ROP, ropinirole; ROT, rotigotine; S, selegiline.

2 | METHODS

2.1 | 1 Patients

We evaluated 28 patients (10 men and 18 women) with PD. The mean age was 66.7 ± 11.6 years (range: 51–88 years), and the mean body mass index was 22.7 ± 3.2 kg/m² (range: 16.4–29.8 kg/m²). The mean disease duration was 13.5 ± 2.9 years (range: 11–22 years) as of December 2019. During the study period, we used the Unified Parkinson's disease rating scale as the disability scale of PD patients. The mean rating was 29.7 ± 19.0 and ranged from 8 to 88 in Year 1. In Year 11, the mean rating was 59.0 ± 30.0 and ranged from 19 to 128 (Table 1).

We selected patients with idiopathic PD who met the following criteria: diagnosis that was confirmed by at least 3 years of clinical observation, good response to levodopa treatment, and absence of demonstrable atrophy of the brainstem or cerebellum on magnetic resonance imaging. All patients were diagnosed with clinically definite PD using the British Brain Bank criteria.⁸

Autonomic symptoms were present in 24 out of 28 patients during Year 11: constipation ($n = 22$), urinary urgency ($n = 11$), limb coldness ($n = 9$), orthostatic dizziness ($n = 7$), and sweating dysfunction ($n = 5$). Although seven patients with PD had OH, defined as a reduction in systolic pressure of at least 20 mm Hg or a reduction in diastolic pressure of at least 10 mm Hg within 3 min of standing, no patients had any severe manifestations of autonomic failure such as frequent syncope due to OH. The levodopa-equivalent daily dose (LEDD) ranged from 250 to 1262 mg, with a mean of 593.7 ± 260.6 mg. Twenty patients received both levodopa and dopamine agonists, and eight patients received levodopa only (Table 1).

The control group of 30 non-PD patients consisted of 10 men and 20 women with diagnoses that included epilepsy, migraine, focal myopathy, hemifacial spasm, carpal tunnel syndrome, trigeminal neuralgia, idiopathic dizziness, and lumbar canal stenosis. The mean age in the control group was 66.7 ± 10.7 years old (range: 48–89 years), and the mean body mass index was 23.1 ± 2.9 kg/m² (range: 18.3–28.3 kg/m²). No patient had associated OH (Table 1).

The patients in this study did not have any co-morbidities such as hypertension, cardiovascular disease, or cerebrovascular disease. We excluded patients who were taking other drugs that might affect the autonomic nervous system, including blood pressure agents, muscle relaxants, vasodilators, or antidepressants. Patients with body weight fluctuations over 5 kg were also excluded. The present study was approved by the institutional review board of the University of Yamanashi, and written informed consent was obtained from all patients who participated in this study.

2.2 | 2 Measurements

We reviewed the medical records of 28 patients with PD and 30 patients with other neurological disorders. These patients made bi-monthly outpatient clinic visits to the Department of Neurology at the University of Yamanashi Hospital from January 2009 to

December 2019. We confirmed that all patients were examined at rest and in a sitting position while an automated sphygmomanometer took SBP, DBP, and HR measurements. The mean values of SBP, DBP, and HR obtained at the bi-monthly visits were calculated for each year. These data were considered to be yearly quantitative values for each individual patient that were calculated in both PD and control patients for 10 years or more. Age-related changes in each group were measured and statistically analyzed by year. Correlations between age and SBP, DBP, or HR were also analyzed for both groups. In the PD group, correlations between the increase of LEDD and SBP, DBP, or HR were evaluated, and the age-related changes in patients taking only levodopa and in those taking both levodopa and dopamine agonists were also measured.

2.3 | 3 Statistical analysis

Results were expressed as the mean \pm SD. Student's paired *t* test was used to evaluate differences in the results. Spearman's rank correlation coefficient was used to assess the relationships between age or LEDD and SBP, DBP, or HR. For all analyses, $p < .05$ was considered to indicate statistical significance.

3 | RESULTS

In the PD group, there was a gradual decrease in SBP with longer disease duration (-0.65 mm Hg/year), and the mean SBP significantly

decreased from Year 7 to 11 compared to the mean values for Year 1 (Figure 1A $p < .001$ or $p < .01$). In the non-PD group, there was a gradual increase in SBP over the duration (1.30 mm Hg/year), and the mean SBP significantly increased from Year 4 to 11 compared to the mean values for Year 1 (Figure 1B $p < .001$ or $p < .01$). A gradual decrease in DBP in the PD group was observed (-0.08 mm Hg/year), but this was not significant. The DBP in the non-PD group showed a gradual increase over the duration (0.70 mm Hg/year), and the mean DBP from Year 4 to 11 significantly increased compared to mean values for Year 1 ($p < .001$ or $p < .01$). There were no significant HR changes in either group. In addition, there were no significant correlations between age and SBP, DBP, or HR for both groups. In the PD group, similar changes with longer disease durations were observed in patients taking only levodopa and in those taking both levodopa and dopamine agonists. No significant correlations between the increase of LEDD and SBP, DBP, or HR were found from Year 1 to Year 11.

4 | DISCUSSION

In this study, we investigated age-related changes in the BP and HR of individual patients with idiopathic PD and non-PD associated with other neurological disorders for more than 10 years. In the PD group, SBP showed a significant decrease, whereas there were no significant changes in DBP. In comparison, in the non-PD group, SBP and DBP increased significantly. Also, there were no significant changes in HR. Although antiparkinson drugs such as levodopa or dopamine

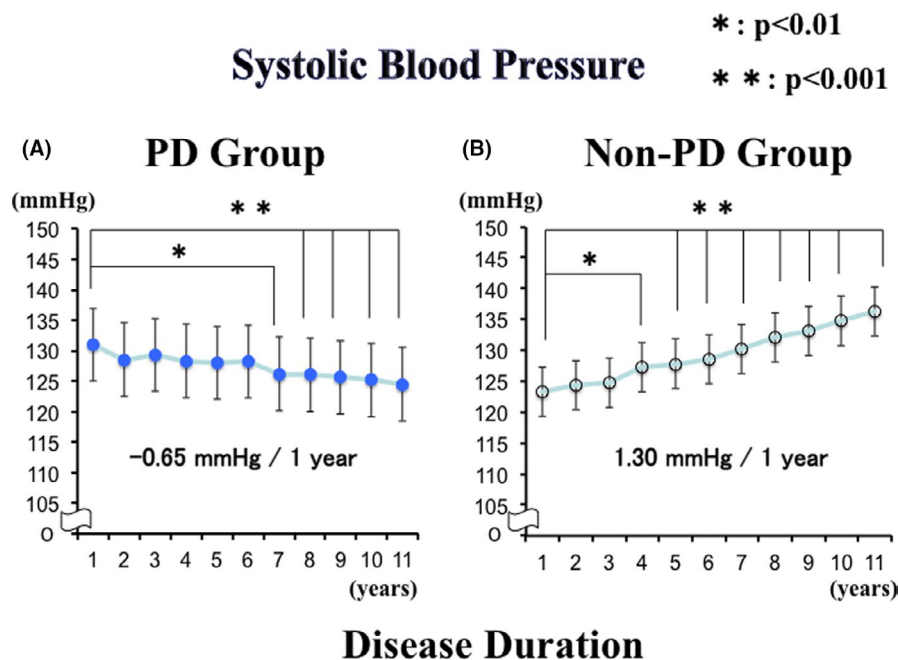


FIGURE 1 Age-related changes in systolic blood pressure (A, B) and diastolic blood pressure (C, D) of Parkinson's disease (PD) group (A, C) and non-PD group (B, D). In PD group, there was a gradual decrease in systolic blood pressure with longer disease duration, and the mean systolic blood pressure significantly decreased from Year 7–11 compared to the mean values for Year 1. In non-PD group, there was a gradual increase in systolic blood pressure over the duration, and the mean systolic blood pressure significantly increased from Year 4–11 compared to the mean values for Year 1

agonists were reported to have some effects on BP in PD patients,^{1,9} these drugs did not influence the results in this study because similar changes were observed in patients taking levodopa only and in those taking both levodopa and dopamine agonists, and no significant correlations between the increase of LEDD and SBP, DBP, or HR were found. SBP and DBP generally tend to increase with age, according to retrospective and prospective studies.^{10,11} However, significant correlations between age and SBP, DBP, or HR were not observed in this study. This may be because patients with cardiovascular or cerebrovascular disorders were strictly excluded in two groups from this study.

Correlations between OH or OH-related symptoms and either disease duration or disability level have been thoroughly evaluated in PD patients. Even though some investigators reported there were no significant relationships between OH and disease duration,¹² many studies have demonstrated a significant correlation between OH or OH-related symptoms and the duration of the disability.^{1-3,5} Moreover, prospective studies have shown that the frequency of OH by head-up tilt tests or OH symptoms scores gradually increased with longer durations of PD.^{1-3,6} Other studies have also reported a smaller increase in BP after head-up tilting,^{1,3,6} accelerated decreases of postprandial BP,^{1,13} and higher frequency of supine hypertension according to the longer duration or higher severity of the disease in PD patients.^{1,4} This is the first study to report the age-related changes of BP and HR in individual patients with PD for over 10 years.

5 | CONCLUSION

Patients with PD frequently undergo physiological examinations and clinical tests involving the cardiovascular system and peripheral circulation to assess impaired autonomic functions. The influence of age-related BP changes in patients with long PD durations should be considered in the analysis of the quantitative data obtained in these precise laboratory tests. Because this study was conducted only at our hospital with strict exclusion criteria, the sample size was comparatively small. Further prospective studies with large sample populations are necessary to perform precise and accurate medical management of cardiovascular autonomic dysfunctions and to provide daily life guidance for patients with PD.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

K Shindo and Y Takiyama are the primary authors. K Shindo, K Koh, and Y Takiyama were responsible for study design. Y Morishima, Y Suwa, T Fukao, N Kurita, A Satake, M Tsuchiya, and Y Ichinose

were responsible for patient data collection. T Hata, K Koh, and T Nagasaka undertook statistical analysis. All authors contributed to manuscript preparation.

ORCID

Kazumasa Shindo  <https://orcid.org/0000-0001-8237-3916>

REFERENCES

- Goldstein DS. Dysautonomia in Parkinson's disease: neurocardiological abnormalities. *Lancet Neurol*. 2003;2:669-676.
- Merola A, Romagnolo A, Rosso M, et al. Autonomic dysfunction in Parkinson's disease: a prospective cohort study. *Mov Disord*. 2018;33:391-397.
- Van Dijk JG, Haan J, Zwinderman K, Kremer B, van Hilten BJ, Roos RAC. Autonomic nervous system dysfunction in Parkinson's disease: relationships with age, medication, duration, and severity. *J Neurol Neurosurg Psychiatry*. 1993;56:1090-1095.
- Vichayanrat E, Low DA, Iodice V, Stuebner E, Hagen EM, Mathias CJ. Twenty-four-hour ambulatory blood pressure and heart rate profiles in diagnosing orthostatic hypotension in Parkinson's disease and multiple system atrophy. *Eur J Neurol*. 2017;24:90-97.
- Postuma R, Gagnon J-F, Pelletier A, Montplaisir J. Prodromal autonomic symptoms and signs in Parkinson's disease and dementia with Lewy bodies. *Mov Disord*. 2013;28:597-604.
- Hiorth YH, Pedersen KF, Dalen I, Tysnes O-B, Alves G. Orthostatic hypotension in Parkinson's disease. *Neurology*. 2019;93:e1526-e1534.
- Shindo K, Watanabe H, Tanaka H, Ohashi K, Nagasaka T, Shiozawa Z. Age and duration related changes in muscle sympathetic nerve activity in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2003;74:1407-1411.
- Gibb WRG, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1988;51:745-752.
- Kulisevsky J, Pagonabarraga J. Tolerability and safety of ropinirole versus other dopamine agonists and levodopa in the treatment of Parkinson's disease. Meta-analysis of randomized controlled trials. *Drug Saf*. 2010;33:147-161.
- Ueda K, Omae T, Fujishima M. Physiological and biochemical changes in ageing - based on a population survey in a Japanese community, Hisayama. *Ann Acad Med Singapore*. 1987;16:35-41.
- Franklin SS, Gustin IV W, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure. The Framingham Heart Study. *Circulation*. 1997;96:308-315.
- Jost WH, Augustis S. Severity of orthostatic hypotension in the course of Parkinson's disease: no correlation with the duration of the disease. *Parkinsonism Relat Disord*. 2015;21:314-316.
- Chaudhuri KR, Ellis C, Love-Jones S, et al. Postprandial hypotension and Parkinsonian state in Parkinson's disease. *Mov Disord*. 1997;12:877-884.

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