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# Lower body mass index is associated with orthostatic hypotension in Parkinson's disease☆

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ABSTRACT

*Introduction:* Lower body mass index (BMI) is associated with orthostatic hypotension (OH) in the general population, especially in the elderly; however, no studies have addressed this issue in Parkinson's disease (PD).
*Methods:* We investigated the results of the head-up tilt test and BMI of patients with PD, and evaluated whether BMI is related to orthostatic systolic blood pressure (SBP) change during the head-up tilt test. PD patients were divided into male and female groups, and further divided into middle-aged (age < 65 years) and elderly (age ≥ 65 years) subgroups in each sex.
*Results:* OH was observed in 13 of 64 male and 12 of 75 female patients with PD. BMI was lower in patients with OH than in those without, in both men and women. In the elderly group, a significant correlation between BMI and orthostatic SBP change was found (men, $r = 0.47$, $p = 0.006$; women, $r = 0.43$, $p = 0.005$), and a BMI below mean − 0.5 standard deviation increased OH odds (men: BMI < 20.5; odds ratio, 6.79; 95% CI, 1.06–43.36; women: BMI < 18.5; odds ratio, 5.11; 95% CI, 1.05–24.96).
*Conclusion:* Lower BMI is a predisposing factor of OH in elderly patients with PD.


## 1. Introduction

Orthostatic hypotension (OH) is one of the commonly occurring nonmotor symptoms in patients with Parkinson's disease (PD). Older age, male sex, advanced Hoehn-Yahr stage, longer disease duration, higher systolic blood pressure (SBP), and the use of dopaminergic drugs are predisposing factors [1,2]. In the general population, multiple factors have been linked to OH, including bed rest, high blood pressure (BP), stroke, and medication, especially in elderly persons [3,4]. In addition, lower body mass index (BMI) is reported to be associated with OH in elderly populations [4–6]. However, there have been no studies focusing on the association between OH and lower BMI in PD patients. Here, we examined whether BMI differs between PD patients with and without OH, and whether BMI is related to orthostatic BP change during the head-up tilt test. PD patients were divided into male and female groups, and further divided into middle-aged (age < 65 years) and elderly (age ≥ 65 years) subgroups.

## 2. Methods

### 2.1. Subjects

We retrospectively investigated the medical charts of PD patients who underwent the head-up tilt test at Nagoya University Hospital from January 2007 to July 2015. PD was diagnosed according to the diagnostic criteria [7]. We excluded patients who matched the following criteria: (i) age < 40 years; (ii) with severe obesity (BMI ≥35 kg/m$^2$); (iii) with diabetes mellitus; (iv) with a history of myocardial infarction; (v) with cardiac failure; (vi) with other known neurological disorders including suspicion for peripheral neuropathy; or (vii) taking vasopressor drugs, antihypertensive drugs, or selegiline.

The head-up tilt test was performed at 0900 h in a temperature controlled clinical laboratory (average temperature 25 ± 2 °C) after an overnight fast. Any drugs that might influence the cardiovascular system, such as antiparkinsonian drugs, were discontinued at least 12 h before the examination. After resting for at least 5 min in a supine position, patients were tilted up to 60° in a stepwise manner (20° for 5 min, 40° for 5 min, and 60° for 5 min), as described in previous reports [8,9]. BP and heart rate were measured with continuous non-invasive cardiovascular monitoring using the Task Force Monitor (CNSystems Medizintechnik AG, Austria). Electrocardiograms (ECG) were recorded continuously using four spot electrodes. Beat-to-beat BP measurements were obtained by finger plethysmography of the index finger on the

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right hand and continuously corrected to the BP of the brachial artery in the left arm obtained by oscillometric measurements. Baseline BP was defined as the last BP values in the supine position just before the tilt up. As OH may be observed after 3 min of orthostatic stress in autonomic failure, such as PD [10], OH was diagnosed as a reduction in SBP of at least 20 mm Hg and/or diastolic BP of at least 10 mm Hg at the 5 min mark in the 60° position compared to baseline [11]. If the subject reported presyncope symptoms (dizziness, feeling faint, or nausea) during the head-up tilt, and a progressively falling SBP (<80 mm Hg) was observed, the tilt table was returned to the horizontal position before the intended 5 min of head-up tilt were fulfilled; data from just before discontinuation were used for analysis. BMI was recorded at the time of the head-up tilt.

We identified 64 male PD patients (age 64 ± 9 years, disease duration 5.1 ± 4.7 years) and 75 female PD patients (age 64 ± 8 years, disease duration 4.8 ± 4.2 years). We then classified the PD patients into two groups according to the presence or absence of OH, and compared the measured variables including age, disease duration, levodopa equivalent dose [12], or BMI between the groups. We also analyzed the correlation between orthostatic BP change during the head-up tilt test and the measured variables in the PD patients. There were no differences in age, disease duration, Hoehn-Yahr stage, or levodopa equivalent dose between genders; however, BMI differed between men and women (men 21.9 ± 2.7 kg/m$^2$, women 20.1 ± 3.1 kg/m$^2$, $p < 0.001$), and so we analyzed male and female data separately. Furthermore, as OH is reported to be associated with BMI in the elderly [4–6], we divided the patients into the middle-aged (age < 65 years) and elderly (age ≥ 65 years) groups.

### 2.2. Ethics

This study adhered to the Ethical Guidelines for Medical and Health Research Involving Human Subjects endorsed by the Japanese government, and was approved by the Ethics Committee of Nagoya University. Written informed consent was waived because the study involved only a retrospective review of routine clinical tests and medical records. Instead, the study protocol was open to the public to assure the right to withdraw of patients.

### 2.3. Statistical analyses

SPSS software version 23 (SPSS, Chicago, IL, USA) was used for statistical analyses. Values are expressed as mean ± standard deviation (SD). Significant differences were defined as $p < 0.05$. Unpaired *t*-test or Mann–Whitney's *U* test, depending on the data distribution, was used to compare the differences between two independent subgroups. To examine relationships, Pearson's correlation coefficient was used. Multiple regression analysis was used to estimate the predictive factors of SBP changes during the head-up tilt test. The risk of OH associated with lower BMI was determined with odds ratios (OR) and 95% confidence intervals (CI).

## 3. Results

### 3.1. Association with BMI and orthostatic BP change in the whole population

OH was observed in 13 of 64 male PD patients and 12 of 75 female PD patients. Among the 25 patients with OH, 6 patients discontinued the head-up tilt test due to the discontinuance criteria (5 patients felt faint at the 40° position of the head-up tilt test with a SBP of <80 mm Hg, and 1 patient had nausea after 3 min at 60° with a SBP of <80 mm Hg). The results of the comparison between PD patients with and without OH are shown in Table 1. BMI was significantly lower in PD patients with OH than in those without OH in both sexes.

The SBP change during the head-up tilt test did not correlate with age, disease duration, Hoehn–Yahr score, or levodopa equivalent dose in both male and female patients; however, it correlated with baseline SBP and BMI in both male (baseline SBP, $r = -0.35$, $p = 0.004$; BMI, $r = 0.32$, $p = 0.010$) and female (baseline SBP, $r = -0.37$, $p = 0.002$; BMI, $r = 0.33$, $p = 0.005$) groups. In addition, diastolic BP (DBP) change during the head-up tilt test also correlated with BMI in male patients ($r = 0.35$, $p = 0.005$) but not female patients ($r = 0.13$, $p = 0.33$).

We subsequently investigated the variables that were related to orthostatic SBP change. Stepwise regression analysis adjusted for age, disease duration, levodopa equivalent dose, baseline SBP, and BMI confirmed that baseline SBP and BMI were independently related to SBP changes during the head-up tilt test in both male ($R = 0.492$, $p < 0.001$) and female ($R = 0.457$, $p < 0.001$) PD patients.

In patients with a BMI < mean − 0.5 SD (men: BMI < 20.5, women: BMI < 18.5), the OR associated with OH was 3.20 in male patients (95% CI, 0.91 to 11.28) and 3.24 in female patients (95% CI, 0.91 to 11.51), with a non-significant difference compared to patients with a BMI ≥ mean − 0.5 SD.

### 3.2. Association with BMI and orthostatic SBP change in middle-aged and elderly patients

The patients were further divided into the middle-aged and elderly groups. There were no differences in disease duration, Hoehn-Yahr score, levodopa equivalent dose, BMI, or BP and HR changes in the head-up tilt test between middle-aged and elderly patients irrespective of whether they were male or female patients. The results of this subgroup analysis demonstrated that in the middle-aged group (31 men

**Table 1**
Comparison of the demographics and the results of the head-up tilt test between PD patients with and without OH.

| | Male | | | Female | | |
|---|---|---|---|---|---|---|
| | OH ($n = 13$) | No OH ($n = 51$) | *p* | OH ($n = 12$) | No OH ($n = 63$) | *p* |
| Age (y) | 64 ± 9 | 64 ± 10 | 0.923 | 66 ± 7 | 63 ± 8 | 0.356 |
| Disease duration (y) | 7.4 ± 5.1 | 4.5 ± 4.4 | 0.077 | 5.0 ± 4.3 | 4.8 ± 4.3 | 0.883 |
| HY | 2.5 ± 1.3 | 2.3 ± 1.0 | 0.560 | 2.1 ± 0.8 | 2.3 ± 1.2 | 0.525 |
| LED (mg) | 403 ± 331 | 221 ± 294 | 0.056 | 282 ± 318 | 322 ± 352 | 0.727 |
| Body mass index | 20.3 ± 3.1 | 22.3 ± 2.5 | 0.020 | 18.5 ± 2.5 | 20.5 ± 3.1 | 0.035 |
| Baseline | | | | | | |
| SBP (mm Hg) | 129 ± 19 | 115 ± 1 | 0.003 | 130 ± 23 | 114 ± 20 | 0.025 |
| DBP (mm Hg) | 73 ± 15 | 71 ± 18 | 0.775 | 69 ± 7 | 69 ± 15 | 0.882 |
| HR (bpm) | 67 ± 10 | 64 ± 10 | 0.450 | 70 ± 12 | 68 ± 10 | 0.633 |
| Head-up tilt test | | | | | | |
| ΔSBP (mm Hg) | −29 ± 7 | 2 ± 10 | <0.001 | −26 ± 13 | 4 ± 12 | <0.001 |
| ΔDBP (mm Hg) | −11 ± 9 | 6 ± 8 | <0.001 | −9 ± 5 | 7 ± 10 | <0.001 |
| ΔHR (bpm) | 10 ± 10 | 12 ± 8 | 0.378 | 15 ± 11 | 10 ± 7 | 0.071 |

PD, Parkinson's disease; OH, orthostatic hypotension; HY, The Hoehn and Yahr scale; LED, levodopa equivalent dose; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.