

# Autonomic dysfunction in Indonesian patients with Parkinson's disease

<sup>1,2</sup>Dyah Tunjungsari MD, <sup>2</sup>Abraham Al Jody MD, <sup>3</sup>Arden Gabrian MD, <sup>3</sup>Violine Martalia MD, <sup>1,2</sup>Amanda Tiksnadi PhD

<sup>1</sup>Neurology Department, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; <sup>2</sup>Neurology Department, Cipto Mangunkusumo Hospital, Jakarta, Indonesia; <sup>3</sup>Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

## Abstract

**Background & Objective:** Autonomic dysfunction is a prevalent non-motor symptom in Parkinson's disease (PD) and significantly affects patients' quality of life. Despite its clinical importance, data on autonomic dysfunction in Indonesian PD populations were scarce. This study aims to characterize autonomic dysfunction and examine its associations with demographic and clinical subgroups in Indonesian PD patients using the SCOPA-AUT INA instrument. **Methods:** We conducted a cross-sectional study involving 45 PD patients from the outpatient neurology clinic at Dr. Cipto Mangunkusumo Hospital between April 2023 and April 2024. Autonomic dysfunction was assessed using the SCOPA-AUT INA. Patients were grouped by age, sex, disease duration, disease severity, comorbidities, and anti-parkinsonian medications. Statistical analyses included chi-square, Kruskal–Wallis, Mann–Whitney U, and Spearman correlation tests. **Results:** Autonomic dysfunction (SCOPA-AUT INA score  $\geq 10$ ) was present in 77.8% of subjects, with gastrointestinal (93.3%) and urinary (91.1%) symptoms being the most prevalent. Older patients ( $\geq 60$  years) showed significantly higher SCOPA-AUT INA scores and urinary symptom severity. Longer disease duration was significantly associated with cardiovascular symptoms. Discrepancies were noted between categorical and continuous analyses of SCOPA-AUT INA, highlighting the challenge of defining cutoffs.

**Conclusion:** Autonomic dysfunction is highly prevalent in Indonesian PD patients, particularly among older individuals. The findings support the relevance of age and disease duration in shaping autonomic symptom profiles. SCOPA-AUT cutoff scores warrant further validation in larger, multicenter cohorts to improve clinical applicability.

**Keywords:** Parkinson disease, autonomic nervous system diseases, SCOPA-AUT, non-motor symptoms.

## INTRODUCTION

Autonomic dysfunction (dysautonomia) is a common non-motor symptom in Parkinson's disease (PD), affecting multiple systems including urinary, gastrointestinal, cardiovascular, thermoregulatory, pupillomotor, and reproductive functions.<sup>1</sup> Its prevalence increases with disease progression and significantly impacts both patients and caregivers.<sup>1-4</sup> A large-scale study found dysautonomia in 91.3% of PD patients<sup>5</sup> a large multicenter cohort of 2,556 individuals with PD were consecutively recruited to the Parkinson's Disease & Movement Disorders Multicenter Database and Collaborative Network in China (PD-MDCNC, with urinary symptoms being

the most frequent, followed by gastrointestinal complaints.<sup>6,7</sup>

Although  $\alpha$ -synuclein pathology and autonomic nerve denervation have been implicated, the exact mechanisms remain unclear.<sup>3</sup> Parasympathetic and sympathetic dysfunctions produce a spectrum of symptoms, including urinary retention, orthostatic hypotension, and constipation, often progressing in a non-linear pattern.<sup>1</sup> Medications used to treat PD motor dysfunction can also frequently aggravate some of the autonomic features, especially orthostatic hypotension.<sup>8</sup>

Assessment of dysautonomia is challenged by the lack of standardized tools and definitions.<sup>2</sup> While more comprehensive and sometimes more

Address correspondence to: Dr. Dyah Tunjungsari, MD, Neurology Department, Faculty of Medicine, Universitas Indonesia. Jl. Diponegoro No. 71, Jakarta Pusat 10430, Indonesia. Tel: +62 811-9884-224, Email: dytunjungsari@gmail.com

Date of Submission: 10 July 2025; Date of Acceptance: 11 December 2025

<https://doi.org/10.54029/2026sjj>

invasive tests exist, they were often impractical in routine care.<sup>9</sup> SCOPA-AUT, developed by Visser *et al.* (2004)<sup>10</sup>, is a validated questionnaire covering six subdomains and is widely used, including in its Indonesian version (SCOPA-AUT INA), which has demonstrated reliability and validity in the Indonesian population (Basli *et al.*).<sup>11</sup> Other validation studies were conducted in different language versions e.g., Korean (Kim *et al.*, 2017)<sup>12</sup> and Greek (Bostantjopoulou *et al.*, 2016).<sup>13</sup> A cutoff score  $\geq 10$  has been used to indicate significant dysfunction.<sup>14</sup>

Despite global interest, data from Indonesia regarding autonomic dysfunction in PD patients using validated questionnaires remain limited.<sup>11,15</sup> A previous Indonesian study found that higher SCOPA-AUT INA scores were significantly associated with greater disease severity in Parkinsonism patients.<sup>16</sup> This study aims to further characterize autonomic dysfunction in Indonesian PD patients using the SCOPA-AUT INA and explore its clinico-demographic associations.

## METHODS

All PD patients who were on their routine checkup at the neurology outpatient clinic at Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, were consecutively recruited to this study from April 2023 to April 2024. Inclusion criteria were: (1) Subjects with an established PD diagnosis using UKPDSBB (Gibb & Lees, 1988)<sup>17</sup> by neurologists, (2)  $>18$  years old, and (3) willing to participate in our study. The exclusion criteria for this study are (1) verbal inability to comprehend instructions and (2) inability to be fluent in Bahasa Indonesia. Univariate analysis was based on basic demographic and clinical data, including gender, age, disease duration, comorbidities, types of anti-parkinsonian medications, and where available, total levodopa equivalent daily dose (LEDD) and dopamine agonist only LEDD, as well as H&Y, Movement Disorder Society-sponsored revision of Unified Parkinson's Disease Rating Scale (MDS-UPDRS) score, and SCOPA-AUT INA score. Subgroups included gender (female & male), age ( $\geq 60$  &  $<60$  years old), disease duration ( $\geq 5$  &  $<5$  years), H&Y (H&Y 1-2/mild; H&Y 3/moderate; H&Y 4-5/severe), comorbidities (hypertension/HT; type 2 diabetes mellitus/T2DM), and types of anti-parkinsonian drugs consumed (levodopa-based preparations/levodopa; dopamine agonists/DA; anticholinergics/AC). Subjects were determined to have an overall impaired autonomic function

if the SCOPA-AUT INA score was  $\geq 10$ .<sup>14</sup> We performed a chi-square test to find the association between dysautonomia prevalence, including the prevalence of its subdomain, in the subgroups mentioned above. In addition, the Kruskal-Wallis test was performed when the H&Y variable was involved in the association analysis. We performed a normality test using the Shapiro-Wilk test. Continuous variables with normal distribution were observed only in age, MDS-UPDRS, and SCOPA-AUT INA total score. Mann-Whitney U test was performed to analyze the severity of dysautonomia and its subdomains across subgroups of gender, age, disease duration, H&Y, comorbidities, and types of anti-parkinsonian drugs taken. Correlation analysis was performed using Spearman's rho between age, disease duration, H&Y staging, MDS-UPDRS score, and SCOPA-AUT INA score. All analyses were performed using SPSS version 29.

## RESULTS

### Univariates

The majority of the subjects were male (66.7%) and at least 60 years old (55.6%), with a mean age of  $58.6 \pm 13.4$  [Table 1]. A majority (51.1%) of the subjects had less than 5 years of disease duration, with a median disease duration of 4 years (range: 1–18). The median H&Y of the subjects was 2 (1-5), with mild severity (H&Y 1-2) being the most frequently found (71.1%). Fifteen subjects had a history of HT (33.3%), and nine subjects had a history of T2DM (20%). The most frequently consumed anti-parkinsonian medication was Levodopa (80%). The mean MDS-UPDRS score of the subjects was  $30.49 \pm 16.02$ . The mean SCOPA-AUT INA score was  $15.4 \pm 7.8$ . Based on the SCOPA-AUT INA subdomain score that is more than zero, gastrointestinal symptoms were the most frequently found (93.33%), followed by urinary (91.11%) and thermoregulation (55.56%).

### Bivariates

According to the chi-square independence test of SCOPA-AUT INA subdomains, only the urinary subdomain had a significant difference; the urinary subdomain had a higher prevalence (34/35 vs 7/10) in subjects with SCOPA-AUT INA score of  $\geq 10$  [Table 2]. Subjects who were  $\geq 60$  years old significantly more experienced urinary symptoms (25/25 vs 16/20) and had SCOPA-AUT INA total score of  $\geq 10$  (23/25 vs 12/20), compared to  $<60$  years old subjects

**Table 1: Overview of the basic demographic and clinical characteristics of the subjects**

| Variables                               | Proportions,<br>n = 45; n (%) | Mean ± SD   | Median<br>(range) |
|---|-------------------------------|-------------|-------------------|
| Gender                                  |                               |             |                   |
| Female                                  | 15 (33.3)                     |             |                   |
| Male                                    | 30 (66.7)                     |             |                   |
| Age                                     |                               | 58.6 ± 13.4 | 61 (22-84)        |
| ≥60 years old                           | 25 (55.6)                     |             |                   |
| <60 years old                           | 20 (44.4)                     |             |                   |
| Disease duration                        |                               | 5.4 ± 3.8   | 4 (1-18)          |
| ≥5 years                                | 22 (48.9)                     |             |                   |
| <5 years                                | 23 (51.1)                     |             |                   |
| Disease severity                        |                               |             |                   |
| MDS-UPDRS Total                         |                               | 30.5 ± 16.0 | 32 (5-77)         |
| H&Y                                     |                               | 3.0 ± 1.0   | 2 (1-5)           |
| Mild (HY 1-2)                           | 32 (71.1)                     |             |                   |
| Moderate (HY 3)                         | 10 (22.2)                     |             |                   |
| Severe (HY 4-5)                         | 3 (6.7)                       |             |                   |
| Types of anti-parkinsonian medication   |                               |             |                   |
| Levodopa                                | 36 (80)                       |             |                   |
| DA                                      | 27 (60)                       |             |                   |
| AC                                      | 23 (51.1)                     |             |                   |
| Number of anti-parkinsonian medications |                               |             |                   |
| Single                                  | 15 (33.3)                     |             |                   |
| Multiple                                | 30 (66.7)                     |             |                   |
| Comorbidity                             |                               |             |                   |
| HT                                      | 15 (33.3)                     |             |                   |
| T2DM                                    | 9 (20)                        |             |                   |
| SCOPA-AUT INA (0-69)                    |                               | 15.4 ± 7.8  | 15 (1-32)         |
| ≥10                                     | 35 (77.8)                     |             |                   |
| <10                                     | 10 (22.2)                     |             |                   |
| SCOPA-AUT INA subdomains                |                               |             |                   |
| Gastrointestinal (0-21)                 | 42 (93.3)                     | 5.3 ± 3.7   | 5 (0-17)          |
| Urinary (0-14)                          | 41 (91.1)                     | 5.0 ± 3.3   | 4 (0-13)          |
| Cardiovascular (0-9)                    | 21 (46.7)                     | 1.4 ± 2.0   | 0 (0-6)           |
| Thermoregulation (0-7)                  | 25 (55.6)                     | 2.4 ± 3.1   | 1 (0-12)          |
| Pupillomotor (0-6)                      | 11 (24.4)                     | 0.3 ± 0.7   | 0 (0-3)           |
| Sexual (female: 0-6; male: 0-12)        | 14 (31.1)                     | 1.0 ± 1.7   | 0 (0-6)           |

MDS-UPDRS: Movement Disorder Society-sponsored revision of Unified Parkinson's Disease Rating Scale; H&Y: Hoehn & Yahr staging; Levodopa: levodopa-based preparations; DA: dopamine agonists; ACs: anticholinergic; HT: hypertension; T2DM: type 2 diabetes mellitus

SCOPA-AUT INA: Indonesian version of Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction

[Table 3]. The cardiovascular subdomain was found to have a significant difference (14/22 vs 7/23) within the disease duration subgroup, with more PD subjects of ≥5 years experiencing cardiovascular-related symptoms compared to subjects with <5 years of disease duration. Based on the Mann-Whitney U test, urinary symptoms had a significant correlation within the subgroups of age and DA-consuming subjects, with urinary

symptoms found to be more severe in subjects who were ≥60 years old (Mean Rank (MR) = 28.64 vs 15.95) and not consuming DA (MR = 18.5 vs 29.75) [Table 4]. Using Spearman correlation analysis, the SCOPA-AUT INA score did not have any correlation with either age, disease duration, H&Y, MDS-UPDRS Part I, or MDS-UPDRS total score [Table 5]. Meanwhile, H&Y is significantly correlated with MDS-UPDRS Part

I and MDS-UPDRS Total score ( $r = 0.33, p < 0.05$ ;  $r = 0.43, p < 0.01$ ).

**DISCUSSION**

*Basic demographic & clinical profile*

The majority of the sample were male (66.7%) and aged  $\geq 60$  years (55.6%), consistent with previous PD cohorts that reported similar demographic trends.<sup>5,6,15,16</sup> The median disease duration was 4 years and the median H and Y stage was 2, which aligns with earlier reports although prior studies noted slightly longer disease duration.<sup>5,6</sup> Hypertension and T2DM were found in 33.3 percent and 20 percent of subjects, comparable with published data on metabolic comorbidities in PD.<sup>18–20</sup> L-dopa, dopamine agonists, and anticholinergics were the most prescribed medications (80, 60, and 51.1 percent), consistent with national availability but different from Japanese use where AC prescription is low.<sup>21,22</sup> The mean MDS UPDRS score of  $30.49 \pm 16.02$  fell within previously reported ranges.<sup>5,23,24</sup> Variations from earlier studies likely reflect demographic differences, disease severity, comorbidity burden, and regional treatment patterns.

*SCOPA-AUT INA overview*

The mean SCOPA AUT INA score of  $15.36 \pm 7.76$  was higher than most earlier reports.<sup>5,24–26</sup> A larger proportion of subjects exceeded the cutoff of 10 than in a prior study using the same threshold.<sup>14</sup> Gastrointestinal symptoms were found in 93.3 percent, urinary symptoms in 91.1 percent, and thermoregulation symptoms in 55.6 percent, consistent with earlier studies that reported these domains as the most affected.<sup>24,25</sup> More recent work showed different symptom distribution patterns.<sup>26</sup> Differences in findings may reflect population heterogeneity and known contributors to autonomic burden such as higher H and Y and MDS UPDRS scores or dopamine agonist exposure.<sup>24</sup>

*Relations with aging*

Dysautonomia was more prevalent in older participants, consistent with earlier clinical findings.<sup>3,14</sup> Experimental models have shown that ageing facilitates alpha synuclein propagation and autonomic injury<sup>27</sup> and clinical studies confirm similar trends.<sup>3,5</sup> Age related changes in mitochondrial function, protein homeostasis, and inflammation may further contribute to autonomic impairment.<sup>28</sup>

**Table 3: Comparison of autonomic dysfunction subdomains across clinical and demographic Variables**

|   | Gender (female vs male) | Age ( $\geq 60$ vs $< 60$ ) | Disease duration ( $\geq 5$ vs $< 5$ ) | H&Y (mild vs moderate vs severe) | HT (yes vs no)        | T2DM (yes vs no)     | Anti-parkinsonian medications |                       |                       |
|---|-------------------------|-----------------------------|--|----------------------------------|-----------------------|----------------------|-------------------------------|-----------------------|-----------------------|
|   |                         |                             |  |                                  |                       |                      | Levodopa (yes vs no)          | DA (yes vs no)        | AC (yes vs no)        |
| <b>Gastrointestinal</b>                   | 14 vs 28 <sup>a</sup>   | 23 vs 19 <sup>a</sup>       | 21 vs 21 <sup>a</sup>                  | 30 vs 9 vs 3 <sup>c</sup>        | 13 vs 29 <sup>a</sup> | 8 vs 34 <sup>a</sup> | 33 vs 9 <sup>a</sup>          | 25 vs 17 <sup>a</sup> | 21 vs 21 <sup>a</sup> |
| <b>Urinary</b>                            | 13 vs 28 <sup>a</sup>   | 25 vs 16 <sup>a*</sup>      | 21 vs 20 <sup>a</sup>                  | 29 vs 9 vs 3 <sup>c</sup>        | 15 vs 26 <sup>a</sup> | 9 vs 32 <sup>a</sup> | 32 vs 9 <sup>a</sup>          | 24 vs 17 <sup>a</sup> | 20 vs 21 <sup>a</sup> |
| <b>Cardiovascular</b>                     | 4 vs 17 <sup>a</sup>    | 12 vs 9 <sup>b</sup>        | 14 vs 7 <sup>b*</sup>                  | 16 vs 5 vs 0 <sup>c</sup>        | 8 vs 13 <sup>b</sup>  | 7 vs 14 <sup>a</sup> | 17 vs 4 <sup>a</sup>          | 10 vs 11 <sup>b</sup> | 11 vs 10 <sup>b</sup> |
| <b>Thermoregulation</b>                   | 7 vs 18 <sup>b</sup>    | 12 vs 13 <sup>b</sup>       | 11 vs 14 <sup>b</sup>                  | 18 vs 5 vs 2 <sup>c</sup>        | 9 vs 16 <sup>b</sup>  | 6 vs 19 <sup>a</sup> | 22 vs 3 <sup>a</sup>          | 15 vs 10 <sup>b</sup> | 12 vs 13 <sup>b</sup> |
| <b>Pupillomotor</b>                       | 3 vs 8 <sup>a</sup>     | 4 vs 7 <sup>a</sup>         | 7 vs 4 <sup>a</sup>                    | 7 vs 3 vs 1 <sup>c</sup>         | 4 vs 7 <sup>a</sup>   | 3 vs 8 <sup>a</sup>  | 9 vs 2 <sup>a</sup>           | 6 vs 5 <sup>b</sup>   | 5 v 6 <sup>b</sup>    |
| <b>Sexual</b>                             | 3 vs 11 <sup>a</sup>    | 7 vs 7 <sup>b</sup>         | 6 vs 8 <sup>b</sup>                    | 9 vs 3 vs 2 <sup>c</sup>         | 3 vs 11 <sup>a</sup>  | 4 vs 10 <sup>a</sup> | 9 vs 5 <sup>a</sup>           | 11 vs 3 <sup>a</sup>  | 8 vs 6 <sup>b</sup>   |
| <b>SCOPA-AUT INA <math>\geq 10</math></b> | 12 vs 23 <sup>a</sup>   | 23 vs 12 <sup>a*</sup>      | 18 vs 17 <sup>a</sup>                  | 24 vs 8 vs 3 <sup>c</sup>        | 13 vs 22 <sup>a</sup> | 8 vs 27 <sup>a</sup> | 29 vs 6 <sup>a</sup>          | 20 vs 15 <sup>a</sup> | 17 vs 18 <sup>a</sup> |

H&Y: Hoehn & Yahr staging; HT: hypertension; T2DM: type 2 diabetes mellitus; SCOPA-AUT INA: Indonesian version of Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction; Levodopa: levodopa-based preparations; DA: dopamine agonists; ACs: anticholinergic \* =  $p < 0.05$ . Association analyses were performed using chi-square independence tests to compare the prevalence of each autonomic subdomain across independent variable subgroups. The chi-square outcomes reflect the prevalence of subjects in each subgroup. Depending on the data, either Fisher's exact test (a) or Pearson's chi-square test (b) was employed; for the H&Y variable, the Kruskal-Wallis test (c) was used. The composite SCOPA-AUT INA score was treated as a binomial outcome, with scores  $\geq 10$  indicating the presence of autonomic dysfunction and scores  $< 10$  indicating its absence.

**Table 4: Associations between clinical characteristics and SCOPA-AUT INA subdomain severity**

|                                  | Gender, female vs male (mean rank) | Age, ≥60 years vs <60 years old (mean rank) | Disease duration, ≥5 years vs <5 years (mean rank) | H&Y, mild vs moderate vs severe (mean rank) | HT, with vs without (mean rank) | T2DM, with vs without (mean rank) | Anti-parkinsonian medications         |                                 |                                 |                                 |
|----------------------------------|------------------------------------|---|--|---|---------------------------------|-----------------------------------|---------------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                  |                                    |   |  |   |                                 |                                   | Levodopa, with vs without (mean rank) | DA, with vs without (mean rank) | AC, with vs without (mean rank) | AC, with vs without (mean rank) |
| <b>Gastrointestinal</b>          | 26.5 vs 21.2                       | 25.6 vs 19.7                                | 24.2 vs 21.8                                       | 22.5 vs 21.6 vs 32.5                        | 22.0 vs 23.5                    | 24.4 vs 22.6                      | 24.4 vs 17.4                          | 21.7 vs 25                      | 21.1 vs 25.0                    |                                 |
| <b>Urinary</b>                   | 21.6 vs 23.7                       | 28.6 vs 15.9*                               | 24.7 vs 21.3                                       | 22.8 vs 23.4 vs 23.7                        | 26.5 vs 21.2                    | 28.3 vs 21.7                      | 23.6 vs 20.5                          | 18.5 vs 29.7*                   | 22.9 vs 23.1                    |                                 |
| <b>Cardiovascular</b>            | 19.0 vs 25.0                       | 23.3 vs 22.6                                | 26.3 vs 19.8                                       | 23.7 vs 23.8 vs 12.5                        | 23 vs 23                        | 28.3 vs 21.7                      | 23.2 vs 22                            | 21.3 vs 25.6                    | 21.7 vs 24.3                    |                                 |
| <b>Thermoregulation</b>          | 21.5 vs 23.8                       | 21.4 vs 24.9                                | 21.9 vs 24.0                                       | 22.9 vs 21.3 vs 30                          | 23.7 vs 22.7                    | 24 vs 22.7                        | 23.9 vs 19.4                          | 23.4 vs 22.4                    | 22.4 vs 23.6                    |                                 |
| <b>Pupillomotor</b>              | 21.8 vs 23.6                       | 20.9 vs 25.6                                | 24.6 vs 21.5                                       | 22.4 vs 24.5 vs 24.7                        | 23.2 vs 22.9                    | 25.3 vs 22.4                      | 23.2 vs 22.3                          | 22.5 vs 23.8                    | 22.4 vs 23.6                    |                                 |
| <b>Sexual</b>                    | 20.1 vs 24.4                       | 22.3 vs 23.9                                | 22.3 vs 23.7                                       | 22.4 vs 23.1 vs 28.9                        | 21.1 vs 24.0                    | 27.0 vs 22.0                      | 21.7 vs 28.2                          | 24.9 vs 20.1                    | 23.8 vs 22.1                    |                                 |
| <b>SCOPA-AUT INA Total score</b> | 22 vs 23.5                         | 25.9 vs 19.4                                | 25.0 vs 21.0                                       | 22.8 vs 22.0 vs 28.2                        | 23.0 vs 23.0                    | 29.4 vs 21.4                      | 24.3 vs 17.8                          | 20.3 vs 27                      | 21.5 vs 24.6                    |                                 |

H&Y: Hoehn & Yahr staging; HT: hypertension; DM: diabetes mellitus type 2; SCOPA-AUT INA: Indonesian version of Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction; Levodopa: levodopa-based preparations; DA: dopamine agonists; ACs: anticholinergic  
 \* =  $p < 0.05$

Due to the non-normal distribution of the data, analyses were conducted using the Mann-Whitney U test to examine the severity of each autonomic subdomain across independent variable subgroups. The Mann-Whitney U outcomes reflect the mean rank for each subgroup. Statistically significant results ( $p < 0.05$ ) were denoted with an asterisk. The composite SCOPA-AUT INA score was treated as a continuous outcome.

### Urinary subdomain

Urinary symptoms were more severe among older subjects in accordance with previous findings.<sup>13,29</sup> These symptoms likely reflect dysfunction in the putamen caudate pathway due to dopaminergic neuron loss.<sup>29</sup> Subjects not receiving dopamine agonists had worse urinary scores. Prior studies reported mixed effects of dopaminergic therapy on micturition and proposed that differing responses at D1 and D2 receptors may produce an early inhibitory and later facilitatory pattern described as a biphasic effect.<sup>30–36</sup>

### Cardiovascular subdomain

Cardiovascular autonomic symptoms showed an association with longer disease duration, similar to several studies.<sup>37–40</sup> Other reports did not observe such associations.<sup>12,41–43</sup> Proposed mechanisms include accumulation of phosphorylated alpha synuclein within vagal and sympathetic nerves supplying vascular and cardiac tissues.<sup>44</sup> Differences across studies may result from methodological variation and heterogeneous clinical characteristics.

### Discrepancy in association & correlation analyses

Several discrepancies emerged between categorical and continuous SCOPA AUT INA analyses. The cutoff of 10 adopted from Martinez Ramirez *et al.* (2020) may not generalize well because our data distribution was skewed.<sup>14</sup> Prior studies have proposed cutoffs ranging from 9 to 13.<sup>14,45,46</sup> and others used tertile based thresholds. Diagnostic challenges also arise because dysautonomia encompasses a wide spectrum of symptoms and optimal assessment requires comprehensive autonomic function testing.<sup>3</sup> Small sample size and uneven symptom distribution may have further contributed to analytic inconsistencies.

In conclusion, this study provides an in-depth characterization of dysautonomia in Indonesian PD subjects, highlighting its correlation with demographic and clinical subgroups. The findings reveal that dysautonomia is highly prevalent, with gastrointestinal, urinary, and thermoregulation symptoms being the most commonly reported. SCOPA-AUT INA scores in this study were generally higher than in prior studies, suggesting possible regional or methodological differences. Age emerged as a key factor, with general dysautonomia and urinary symptoms being more prevalent in older patients. The relationship between disease duration and cardiovascular symptoms showed variability across studies,

emphasizing the need for standardized assessment approaches. Additionally, discrepancies between association and correlation analyses underscore the challenges in defining dysautonomia using SCOPA-AUT cutoff scores, reflecting the complexities of autonomic impairment assessment in PD.

The limitations of our study were (1) small sample size, (2) a cross-sectional design, which precludes causal inference and longitudinal assessment of symptom progression, and (3) lack of an established cutoff score for SCOPA-AUT. Future studies should employ larger, multicenter cohorts to enhance generalizability and monitor dysautonomia progression in PD. Patient-reported outcomes may also sometimes lack accuracy compared with more objective testing of dysautonomia, for example for orthostatic hypotension or gastrointestinal motility.<sup>48–51</sup>

Overall, this study contributes to the understanding of autonomic dysfunction in Indonesian PD patients, reinforcing the importance of demographic and clinical factors in shaping dysautonomic profiles. Future research with larger sample sizes and more comprehensive autonomic function testing is needed to refine diagnostic and management strategies for dysautonomia in PD.

## REFERENCES

1. Gu SC, Shi R, Gao C, *et al.* Autonomic function and motor subtypes in Parkinson's disease: a multicentre cross-sectional study. *Sci Rep* 2023;13(1):14548. <https://doi.org/10.1038/s41598-023-41662-9>
2. Schapira AHV, Chaudhuri KR, Jenner P. Non-motor features of Parkinson's disease. *Nat Rev Neurosci* 2017;18(7):435-50. <https://doi.org/10.1038/nrn.2017.62>
3. Chen Z, Li G, Liu J. Autonomic dysfunction in Parkinson's disease: Implications for pathophysiology, diagnosis, and treatment. *Neurobiol Dis* 2020;134:104700. <https://doi.org/10.1016/j.nbd.2019.104700>
4. Ledda C, Montanaro E, Imbalzano G, *et al.* Burden of caregiving for cardiovascular dysautonomia in Parkinson's disease. *Clin Auton Res* 2022;32(6):455-61. <https://doi.org/10.1007/s10286-022-00888-9>
5. Zhou Z, Zhou X, Zhou X, *et al.* Characteristics of autonomic dysfunction in Parkinson's disease: a large Chinese multicenter cohort study. *Front Aging Neurosci* 2021;13:761044. <https://doi.org/10.3389/fnagi.2021.761044>
6. Qin Y, Meng DT, Jin ZH, Du WJ, Fang BY. Association between autonomic dysfunction with motor and non-motor symptoms in patients with Parkinson's disease. *J Neural Transm* 2024;131(4):323-34. <https://doi.org/10.1007/s00702-024-02745-7>
7. Yang L, Gao H, Ye M. Baseline prevalence and longitudinal assessment of autonomic dysfunction

- in early Parkinson's disease. *J Neural Transm* 2024;131(2). <https://doi.org/10.1007/s00702-023-02711-9>
8. Lim SY, Lang AE. The nonmotor symptoms of Parkinson's disease—an overview. *Mov Disord* 2010;25(Suppl 1):S123–S130. <https://doi.org/10.1002/mds.22786>
  9. Diaconu S, Irincu L, Ivan I, Falup-Pecurariu C. Rating scales for dysautonomia in Parkinson's disease. In: Falup-Pecurariu C, Jenner P, eds. *Autonomic Dysfunction in Parkinson's Disease*. Academic Press, 2021:41–89.
  10. Stanković I, Petrović I, Pekmezović T, et al. Longitudinal assessment of autonomic dysfunction in early Parkinson's disease. *Parkinsonism Relat Disord* 2019;66:74–9. <https://doi.org/10.1016/j.parkreldis.2019.07.008>
  11. Basli, Sitorus F, Dewati E, Herqutanto. Uji validitas dan reliabilitas Scales for Outcome in Parkinson's disease autonomic SCOPA-AUT untuk menilai gangguan fungsi otonom pada penyakit Parkinson. *Neurona* 2011. <https://scholar.ui.ac.id/en/publications/uji-validitas-dan-reliabilitas-scales-for-outcome-in-parkinsons-d>
  12. Kim JY, Song IU, Koh SB, et al. Validation of the Korean version of the scale for outcomes in Parkinson's disease-autonomic. *J Mov Disord* 2017;10(1):29–34. <https://doi.org/10.14802/jmd.16057>
  13. Bostantjopoulou S, Katsarou Z, Danglis I, Karakasis H, Milioni D, Falup-Pecurariu C. Self-reported autonomic symptoms in Parkinson's disease: Properties of the SCOPA-AUT scale. *Hippokratia* 2016;20(2):115–20. <https://pubmed.ncbi.nlm.nih.gov/28416907/>
  14. Martinez-Ramirez D, Velazquez-Avila ES, Almaraz-Espinoza A, et al. Lower urinary tract and gastrointestinal dysfunction are common in early Parkinson's disease. *Parkinsons Dis* 2020;2020:1694547. <https://doi.org/10.1155/2020/1694547>
  15. Arasen M. Profile of autonomic symptoms in Parkinson's disease patients in RSUPN Cipto Mangunkusumo and RSUPN Fatmawati [Thesis]. 2012. <https://lib.ui.ac.id/detail?id=20330128&lokasi=lokal>
  16. Floransia I, Mahama CN, Khosama H, Tumewah R. Hubungan disfungsi otonom dengan derajat keparahan penderita parkinsonisme. *J Indonesian Med Assoc* 2019;69(12):349–59. <https://mki-ojs.idionline.org/jurnal/article/download/166/94/>
  17. Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1988;51(6):745–52. <https://doi.org/10.1136/jnnp.51.6.745>
  18. Tulbă D, Cozma L, Bălănescu P, Buzea A, Băicuș C, Popescu BO. Blood pressure patterns in patients with Parkinson's disease: A systematic review. *J Pers Med* 2021;11(2):129. <https://doi.org/10.3390/jpm11020129>
  19. Chmiela T, Węgrzynek J, Kasprzyk A, Waksmundzki D, Wilczek D, Gorzkowska A. If not insulin resistance so what? – Comparison of fasting glycemia in idiopathic Parkinson's disease and atypical parkinsonism. *Diabetes Metab Syndr Obes* 2022;15:1451–60. <https://doi.org/10.2147/dms.s359856>
  20. De Pablo-Fernandez E, Sierra-Hidalgo F, Benito-León J, Bermejo-Pareja F. Association between Parkinson's disease and diabetes: Data from NEDICES study. *Acta Neurol Scand* 2017;136(6):732–6. <https://doi.org/10.1111/ane.12793>
  21. Indonesian Ministry of Health. e-Fornas Kemkes. E-Fornas.kemkes.go.id. 2024. [https://e-fornas.kemkes.go.id/daftar\\_obat.php](https://e-fornas.kemkes.go.id/daftar_obat.php)
  22. Seki M, Kawata Y, Hayashi A, Arai M, Fujimoto S. Prescribing patterns and determinants for elderly patients with Parkinson's disease in Japan: a retrospective observational study using insurance claims databases. *Front Neurol* 2023;14:1162016. <https://doi.org/10.3389/fneur.2023.1162016>
  23. Adams C, Suescun J, Haque A, et al. Updated Parkinson's disease motor subtypes classification and correlation to cerebrospinal homovanillic acid and 5-hydroxyindoleacetic acid levels. *Clin Parkinsonism Relat Disord* 2023;8:100187. <https://doi.org/10.1016/j.prdoa.2023.100187>
  24. Stanković I, Petrović I, Pekmezović T, et al. Longitudinal assessment of autonomic dysfunction in early Parkinson's disease. *Parkinsonism Relat Disord* 2019;66:74–9. <https://doi.org/10.1016/j.parkreldis.2019.07.008>
  25. Merola A, Romagnolo A, Rosso M, et al. Autonomic dysfunction in Parkinson's disease: A prospective cohort study. *Mov Disord* 2018;33(3):391–7. <https://doi.org/10.1002/mds.27268>
  26. Yang Y, Jeong J, Bae SH. A systematic review of social processes and mechanisms in the community that influence risky sexual behaviour among adolescents and young adults. *Nurs Open* 2023;10(9):5868–86. <https://doi.org/10.1002/nop2.1700>
  27. Van Den Berge N, Ferreira N, Mikkelsen TW, et al. Ageing promotes pathological alpha-synuclein propagation and autonomic dysfunction in wild-type rats. *Brain* 2021;144(6):1853–68. <https://doi.org/10.1093/brain/awab061>
  28. Coleman C, Martin I. Unraveling Parkinson's disease neurodegeneration: Does aging hold the clues? *J Parkinsons Dis* 2022;12(8):1–18. <https://doi.org/10.3233/jpd-223363>
  29. Pagano G, Niccolini F, Yousaf T, et al. Urinary dysfunction in early de novo patients with Parkinson's disease. *Mov Disord* 2017;32(6):939–40. <https://doi.org/10.1002/mds.26967>
  30. Winge K, Werdelin LM, Nielsen KK, Stimpel H. Effects of dopaminergic treatment on bladder function in Parkinson's disease. *Neurourol Urodyn* 2004;23(7):689–96. <https://doi.org/10.1002/nau.20054>
  31. Sakakibara R, Tateno F, Nagao T, et al. Bladder function of patients with Parkinson's disease. *Int J Urol* 2014;21(7):638–46. <https://doi.org/10.1111/iju.12421>
  32. Araki I, Kitahara M, Oida T, Kuno S. Voiding dysfunction and Parkinson's disease: Urodynamic abnormalities and urinary symptoms. *J Urol*. 2000;164(5):1640–3. [https://doi.org/10.1016/s0022-5347\(05\)67048-6](https://doi.org/10.1016/s0022-5347(05)67048-6)

33. Ouchi M, Kitta T, Chiba H, *et al.* Mechanisms of D1/D2-like dopaminergic agonist, rotigotine, on lower urinary tract function in rat model of Parkinson's disease. *Sci Rep* 2022;12(1):4540. <https://doi.org/10.1038/s41598-022-08612-3>
34. Uchiyama T, Sakakibara R, Yamamoto T, *et al.* Comparing bromocriptine effects with levodopa effects on bladder function in Parkinson's disease. *Mov Disord* 2009;24(16):2386-90. <https://doi.org/10.1002/mds.22840>
35. Scanga A, Lafontaine AL, Kaminska M. An overview of the effects of levodopa and dopaminergic agonists on sleep disorders in Parkinson's disease. *J Clin Sleep Med* 2023;19(6):1133-44. <https://doi.org/10.5664/jcsm.10450>
36. Schaeffer E, Berg D. Dopaminergic therapies for non-motor symptoms in Parkinson's disease. *CNS Drugs* 2017;31(7):551-70. <https://doi.org/10.1007/s40263-017-0450-z>
37. Brockmann K, Srulijes K, Hauser AK, *et al.* GBA-associated PD presents with nonmotor characteristics. *Neurology* 2011;77(3):276-80. <https://doi.org/10.1212/WNL.0b013e318225ab77>
38. Carandina A, Lazzari G, Rodrigues GD, *et al.* Dysautonomia in Parkinson's disease: Impact of glucocerebrosidase gene mutations on cardiovascular autonomic control. *Front Neurosci* 2022;16:842498. <https://doi.org/10.3389/fnins.2022.842498>
39. Cilia R, Tunesi S, Marotta G, *et al.* Survival and dementia in GBA-associated Parkinson's disease: The mutation matters. *Ann Neurol* 2016;80(5):662-73. <https://doi.org/10.1002/ana.24777>
40. Giannini G, Minardi R, Barletta G, *et al.* The degree of cardiovascular autonomic dysfunction is not different in GBA-related and idiopathic Parkinson's disease patients: A case-control instrumental evaluation. *J Parkinsons Dis* 2024;14(2):335-46. <https://doi.org/10.3233/jpd-230334>
41. Sebastian I, Kate MP, Khatter H, Singh B, Pandian JD. Spectrum of cardiovascular autonomic dysfunction and 24-hour blood pressure variability in idiopathic Parkinson's disease. *Ann Indian Acad Neurol* 2022;25(5):902. [https://doi.org/10.4103/aian.aian\\_289\\_22](https://doi.org/10.4103/aian.aian_289_22)
42. Wang C, Cai Y, Gu Z, *et al.* Clinical profiles of Parkinson's disease associated with common leucine-rich repeat kinase 2 and glucocerebrosidase genetic variants in Chinese individuals. *Neurobiol Aging* 2014;35(3):725.e1-6. <https://doi.org/10.1016/j.neurobiolaging.2013.08.012>
43. Yalcin A, Atmis V, Karaarslan Cengiz O, *et al.* Evaluation of cardiac autonomic functions in older Parkinson's disease patients: A cross-sectional study. *Aging Dis* 2016;7(1):28. <https://doi.org/10.14336/ad.2015.0819>
44. Xu H, Zheng X, Xing X, *et al.* Advances in autonomic dysfunction research in Parkinson's disease. *Front Aging Neurosci* 2025;17:1468895. <https://doi.org/10.3389/fnagi.2025.1468895>
45. Matsubara T, Suzuki K, Fujita H, *et al.* Autonomic symptoms correlate with non-autonomic non-motor symptoms and sleep problems in patients with Parkinson's disease. *Eur Neurol* 2018;80(3-4):193-9. <https://doi.org/10.1159/000495797>
46. Arnao V, Cinturino A, Valentino F, *et al.* In patient's with Parkinson disease, autonomic symptoms are frequent and associated with other non-motor symptoms. *Clin Auton Res* 2015;25(5):301-7. <https://doi.org/10.1007/s10286-015-0306-x>
47. Chenini S, Barateau L, Rattu AL, *et al.* Systematic assessment of autonomic symptoms in restless legs syndrome. *Sleep Med* 2021;80:30-8. <https://doi.org/10.1016/j.sleep.2021.01.017>
48. Lim KB, Lim SY, Hor JW, *et al.* Orthostatic hypotension in Parkinson's disease: Sit-to-stand vs supine-to-stand protocol and clinical correlates. *Parkinsonism Relat Disord* 2024;123:106980. <https://doi.org/10.1016/j.parkreldis.2024.106980>
49. Wieling W, Kaufmann H, Claydon VE, *et al.* Diagnosis and treatment of orthostatic hypotension. *Lancet Neurol* 2022;21(8):735-46. [https://doi.org/10.1016/S1474-4422\(22\)00169-7](https://doi.org/10.1016/S1474-4422(22)00169-7)
50. Knudsen K, Krogh K, Østergaard K, Borghammer P. Constipation in Parkinson's disease: subjective symptoms, objective markers, and new perspectives. *Mov Disord* 2017;32(1):94-105. <https://doi.org/10.1002/mds.26866>
51. Tan AH, Chuah KH, Beh YY, Schee JP, Mahadeva S, Lim SY. Gastrointestinal dysfunction in Parkinson's disease: neuro-gastroenterology perspectives on a multifaceted problem. *J Mov Disord* 2023;16(2):138-51. <https://doi.org/10.14802/jmd.22220>

**Supplementary Table 2: Characteristics of the SCOPA-AUT INA scores, including its subdomains**

| SCOPA-AUT INA subdomains | Mean $\pm$ SD | Median (range) | SCOPA-AUT INA $\geq$ 10, n = 35 (%) | SCOPA-AUT INA <10, n = 10 (%) | p value           |
|--------------------------|---------------|----------------|-------------------------------------|-------------------------------|-------------------|
| Gastrointestinal         | 5.3 $\pm$ 3.7 | 5 (0-17)       | 33 (94.3)                           | 9 (90)                        | .54 <sup>a</sup>  |
| Urinary                  | 5.0 $\pm$ 3.4 | 4 (0-13)       | 34 (97.1)                           | 7 (70)                        | .03 <sup>a*</sup> |
| Cardiovascular           | 1.4 $\pm$ 2.0 | 0 (0-6)        | 17 (48.6)                           | 4 (40)                        | .73 <sup>a</sup>  |
| Thermoregulation         | 2.4 $\pm$ 3.1 | 1 (0-12)       | 22 (62.9)                           | 3 (30)                        | .08 <sup>a</sup>  |
| Pupillomotor             | 0.3 $\pm$ 0.7 | 0 (0-3)        | 8 (22.9)                            | 3 (30)                        | .69 <sup>a</sup>  |
| Sexual                   | 0.9 $\pm$ 1.7 | 0 (0-6)        | 11 (31.4)                           | 3 (30)                        | 1.0 <sup>a</sup>  |

SCOPA-AUT INA: Indonesian version of Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction

\* = p < 0.05

We performed a chi-square independence test to compare the prevalence of each autonomic subdomain across subjects who had a SCOPA-AUT INA score of  $\geq$ 10 and <10. All analyses utilized Fisher's exact test (a).

**Supplementary Table 5: Correlation matrix between age, disease duration, H&Y staging, MDS-UPDRS Part I, MDS-UPDRS Total score, and SCOPA-AUT INA. Spearman's rho was used as the correlation coefficient**

|                       | Age  | Disease duration | H&Y    | MDS-UPDRS Part I | MDS-UPDRS Total score | SCOPA-AUT INA |
|-----------------------|------|------------------|--------|------------------|-----------------------|---------------|
| Age                   | 1.0  |                  |        |                  |                       |               |
| Disease duration      | 0.16 | 1.0              |        |                  |                       |               |
| H&Y                   | 0.2  | 0.14             | 1.0    |                  |                       |               |
| MDS-UPDRS Part I      | 0.25 | 0.04             | 0.33*  | 1.0              |                       |               |
| MDS-UPDRS Total score | 0.12 | 0.07             | 0.43** | 0.51**           | 1.0                   |               |
| SCOPA-AUT INA         | 0.26 | 0.19             | 0.19   | 0.18             | 0.02                  | 1.0           |

H&Y: Hoehn & Yahr staging; MDS-UPDRS: Movement Disorder Society-sponsored revision of Unified Parkinson's Disease Rating Scale; SCOPA-AUT INA: Indonesian version of Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction

\* = p < 0.05; \*\* = p < 0.01