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Keywords: long-COVID; orthostatic stress; active standing test; autonomic responses; cardiovascular responses; orthostatic hypotension; orthostatic intolerance



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Systematic Review

# Using Active Standing Orthostatic Stress Test to Assess Physiological Responses in Individuals with Long-COVID: A Systematic Review

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## Abstract

**Background/Objective:** Individuals experiencing long-COVID frequently report orthostatic intolerance symptoms, which may be linked to autonomic and cardiovascular dysfunction. The active standing test provides a simple, clinically relevant means to assess these impairments. This systematic review aims to determine the use of the active standing orthostatic stress test in evaluating cardiovascular, autonomic, and respiratory responses in people experiencing LC. **Methods:** A systematic search, according to PRISMA guidelines, was conducted in PubMed, MEDLINE, EMBASE, CINAHL, and Scopus for articles published between 2020 and 2025. This study was registered in PROSPERO CRD-42024615872. Studies were included if they used the active standing test, enrolled adults (≥18 years), included both Long-COVID and healthy control groups, used continuous beat-to-beat measurements, and reported physiological outcomes. Risk of bias was assessed using the nine-point Newcastle-Ottawa-Scale. **Results:** Three studies (216 participants with Long-COVID and 186 controls) met the inclusion criteria. Across studies, Long-COVID individuals consistently exhibited elevated heart rate in both supine and standing positions. However, blood pressure findings were more variable: only one study reported 13% of participants met orthostatic hypotension criteria, while another found significant increases in diastolic blood pressure during standing. Long-COVID groups also showed reduced heart rate variability compared to controls. **Conclusions:** Individuals experiencing Long-COVID show elevated heart rate and impaired autonomic function during active standing, with subgroup-specific blood pressure changes. These alterations may contribute to dizziness, fatigue, and reduced activity tolerance. Incorporating active standing into clinical assessment could aid early identification of autonomic dysfunction and inform rehabilitation strategies, though more research is urgently needed.

**Keywords:** long-COVID; orthostatic stress; active standing test; autonomic responses; cardiovascular responses; orthostatic hypotension; orthostatic intolerance

## 1. Introduction

Long-COVID, also called post-acute sequelae of COVID-19, post-COVID-19 condition, or chronic COVID syndrome, is when new, ongoing, or worsening symptoms last for three months or

more after the severe-acute respiratory syndrome coronavirus infection and cannot be explained by other health problems [1,2]. Common issues include dizziness when standing, fatigue, breathlessness, and “brain fog,” which together can greatly affect daily activities and quality of life [3]. A systematic review reported that nearly 38% of people experienced ongoing fatigue, and more than half had reduced quality of life three to six months after infection [4].

A frequent problem in long-COVID (LC) is difficulty remaining upright, known as orthostatic intolerance [5,6]. This occurs when the body struggles to adjust to standing, leading to dizziness, light-headedness, or even fainting. These symptoms are often linked to postural tachycardia syndrome (POTS), which is defined as a rise in heart rate of  $\geq 30$  bpm within 10 minutes of standing without a drop in blood pressure, and orthostatic hypotension, defined as a fall in blood pressure (BP) of  $\geq 20$  mmHg systolic (SBP) or  $\geq 10$  mmHg diastolic (DBP) within three minutes of standing [7–9]. Both conditions increase risks such as falls and injuries.

These problems suggest that LC may disrupt multiple body systems, including the autonomic nervous, cardiovascular, and respiratory systems [3,4,10]. To investigate these changes, researchers use orthostatic stress tests such as the active standing test and the head-up tilt test [11,12]. The active standing test is especially important because it mirrors everyday life as people typically perform around 45–60 postural transitions each day [13]. Unlike the tilt test, which passively moves a person upright, active standing engages leg muscles that help blood flow return to the heart, offering a clearer picture of cardiovascular and autonomic responses [12]. The tilt test may also miss very rapid drops in blood pressure within 30 seconds of standing, known as initial orthostatic hypotension [14,15].

Despite its relevance, studies using the active standing test in people experiencing LC have reported inconsistent results [8,16,17]. For example, Monaghan et al. (2022) found that only 13% of older adults with LC met criteria for POTS, and very few reported symptoms [8]. In contrast, Blitshteyn et al. (2021) reported that 75% of participants showed this response [16]. Studies using the tilt test have also produced highly variable results as González-Hermosillo et al. (2023), for instance, found increases in BP rather than HR [17]. These inconsistencies may reflect small sample sizes, differences in participants’ age or health, timing after infection, or variations in testing methods (e.g., protocols) [18]. Therefore, this review aims to i) identify studies that used the active standing test to measure cardiovascular, autonomic, or respiratory responses in people experiencing LC; ii) describe the physiological measures reported in these studies, and iii) explore how differences in active standing protocols may explain inconsistent findings.

## 2. Materials and Methods

### 2.1. Search Strategy

The Population, Exposure, Comparison, Outcome (PECO) framework was used to guide the research question and search strategy [19]. Published literature indexed in PubMed, MEDLINE, EMBASE, CINAHL & Scopus from January 2020 to August 2024 was initially searched by FO in August 2024, and an updated search was performed in May 2025 using the University of Manitoba Libraries platform, with assistance from an experienced librarian (JW). Combinations of the following terms were used: long -covid’, OR ‘post covid’ OR ‘post-acute sequelae of SARS-CoV-2’ or ‘long-haul covid’, ‘orthostatic stress test’, ‘orthostatic hypotension’, ‘postural transition’, ‘hemodynamic responses’, ‘blood pressure’, ‘heart rate’, ‘cardiovascular’, ‘autonomic’ and ‘respiratory’. The search was limited to studies published in the English language and from 2020 – 2025. The search strategies are presented in Supplemental Material Table S1. The review was registered with PROSPERO (CRD 42024615872) and followed the Preferred Reporting Items for Systematic Review (PRISMA 2020) guidelines (Supplemental Material PRISMA 2020 Checklist).

## 2.2. Eligibility and Screening Criteria

Studies were included if they: (1) reported on cardiovascular, autonomic or respiratory responses during the active standing test in adults ( $\geq 18$  years old) experiencing LC; (2) included a healthy control group for comparison; (3) published between 2020-2025; (4) used continuous beat-to-beat measurements of BP or HR; (5) published in the English language, and were excluded if they did not use an active standing test, only used manual measurements of BP and HR, focused on assessing immunophenotypical biomarkers of LC, used only self-reported surveys or questionnaires (e.g., DePaul symptom questionnaire, COMPASS-32), were published as systematic, scoping, narrative reviews, case studies, qualitative studies, poster or conference abstracts, letters to editors, or editorials.

Title and abstract screening criteria were independently screened by two review authors (FO and AN) using Covidence ([www.covidence.org](http://www.covidence.org); Melbourne, Australia). Articles identified as potentially eligible by the two review authors were retrieved, and duplicates were either manually (when identified) or automatically (by Covidence) removed. Full texts of potentially eligible studies were screened independently by FO and AN, and RV resolved conflicts when necessary.

## 2.3. Data Extraction

A standardized extraction form was used by two authors (FO and AN) to extract relevant information pertaining to reference data (author, title, journal, year, and country), study characteristics (objective, design, testing setting), participant characteristics (age, sex, race, number of participants, and health status prior to COVID-19 infection). Study details, including the inclusion and exclusion criteria, proportion of participants who were hospitalized (severity of COVID-19 infection), current medication use, and reported symptoms, were also extracted. The instrumented (devices, active standing protocol, questionnaires), outcome measures (cardiovascular, autonomic, and respiratory variables), the definition of LC used, conclusions and limitations as identified by the study authors, and funding sources were also extracted (Supplementary Material Table S2). No automation tool was used in this process.

## 2.4. Quality and Risk of Bias Assessment

Two reviewers (FO and AN) independently evaluated the quality and risk of bias for each included study using the nine-point Newcastle–Ottawa Quality Assessment Scale (NOS) for case-control studies [20]. Disagreements were resolved by the supervising author (RV). The NOS was tailored to long-COVID studies. Studies were categorized based on the NOS score as follows: 0–3 points were considered low quality, 4–6 points moderate quality, and 7–9 points as high quality across the categories of (i) selection, (ii) comparability, and (iii) exposure [20].

Since the NOS was originally designed for cohort and case-control studies, we adapted the case-control scoring tool for long-COVID observational cross-sectional studies by modifying some of its domains to better assess exposure and outcome, as described in previous work in the healthcare field [21,22]. Specifically, we interpreted the domain ‘representative of long-COVID cases’ as meeting recognized definitions of long-COVID and if the sample recruited from relevant populations (e.g., community, outpatient clinics, tertiary care units, or post-COVID recovery programs), and interpreted ‘exposure’ as encompassing the process by which a study confirmed COVID-19 infection in its participants and whether the statistical test used was appropriate, fully described or incomplete. A meta-analysis could not be performed due to the small number of studies and heterogeneity across the studies. The modified scoring criteria are provided in Supplemental Material Table S3.

## 2.5. Data Analysis and Synthesis

Descriptive characteristics were used to describe trials and participants. Means, medians, and associated measures of variability (e.g., 95% confidence intervals, interquartile ranges [IQR], were applied to continuous variables, while counts and proportions were used for dichotomous and

categorical variables. Given the novelty of LC, the anticipated heterogeneity in study designs, and the scarcity of data related to the research question, conducting a meta-analysis was not feasible. Descriptions of individual studies were extracted and presented to show methodological similarities and differences. A narrative summary of results was used to summarize and interpret findings.

3. Results

3.1. Study Selection and Search Strategy

In total, 2145 references were identified and imported into Covidence for screening through database searches, with 1189 references removed as duplicates. 956 studies were screened by title and abstract following duplicate removal, and 41 studies were screened on the full-text level. Three studies were included in the review following full-text screening. The PRISMA flowchart of study selection is provided in Figure 1.

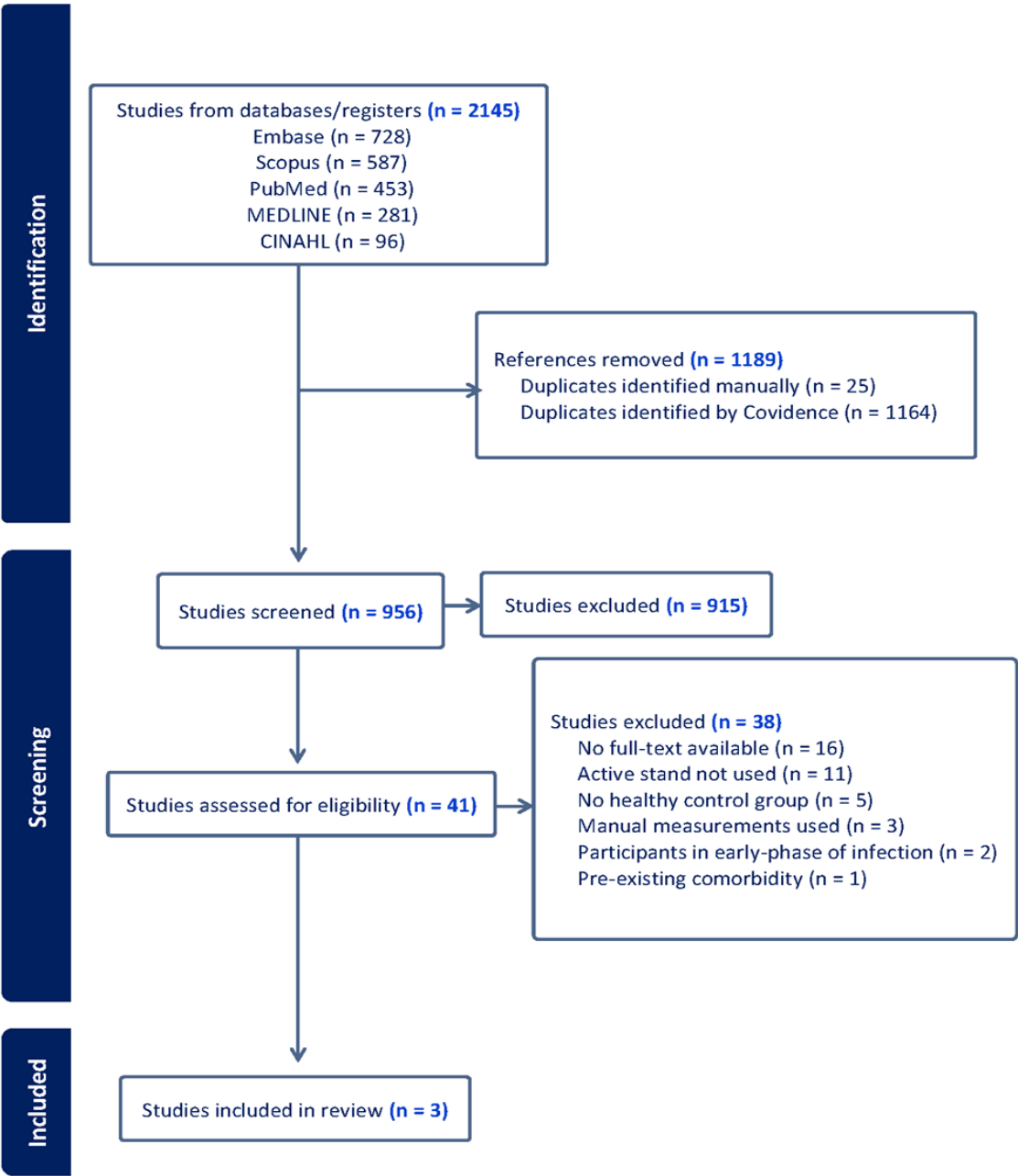


Figure 1. PRISMA flowchart – study selection.

3.2. Study Characteristics

We identified 3 studies that used the active standing test to evaluate physiological responses in individuals experiencing LC [23–25]. These studies included assessments of cardiovascular (e.g., HR, BP), autonomic (e.g., heart rate variability, baroreflex sensitivity) and cardiorespiratory (respiratory sinus arrhythmia) variables. Sample sizes varied across studies, ranging from 30-92 LC participants and 33-120 healthy control participants.

Methodological approaches differed in terms of data collection protocols (5 mins supine and 3 mins standing *vs.* 10 mins supine and 10 mins standing), and the definition of LC used (WHO’s definition *vs.* NICE) [23–25]. Study design and classification was based on the descriptions provided by the original authors. Study characteristics are presented in Table 1.

Table 1. Study characteristics.

| Study (Year)         | Country   | Study Design              | Sample size                       | Proportion of females (%) | Age (mean ± SD, median [IQR])/[CI] (years)       | Definition of long-COVID                         | Active standing protocol (Timeframe) | Outcome Measures                                                                                                    |
|----------------------|-----------|---------------------------|-----------------------------------|---------------------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| Shah et al. (2022)   | India     | Prospective single center | PASC = 92<br>HC = 120             | 41%<br>46%                | PASC = 50.6 ± 12.1<br>HC = 51.8 ± 4.2            | Descriptive definition; no organizational source | 5 min supine, 3 min. stand           | Heart rate variability                                                                                              |
| Seeley et al. (2023) | Australia | Prospective comparative   | PASC = 30<br>POTS = 33<br>HC = 33 | 82%<br>94%<br>82%         | PASC = 37 [15]<br>POTS = 28 [14]<br>HC = 28 [23] | WHO’s Delphi Consensus                           | 10 min supine, 10 min standing       | Respiratory sinus arrhythmia, heart rate and blood pressure responses                                               |
| Hira et al. (2025)   | Canada    | Cross-sectional           | PASC = 94<br>HC = 33              | 81%<br>76%                | PASC = 42 [36, 53]<br>HC = 49 [30, 62]           | NICE guideline                                   | 10 min supine, 10 min standing       | Heart rate variability, blood pressure variability, Baroreflex sensitivity, Blood pressure and heart rate responses |

**Note:** SD: standard deviation; IQR: inter-quartile range; CI: confidence interval; PASC: post-acute sequelae of SARS-CoV-2 infection; HC: healthy control; POTS: postural orthostatic tachycardia syndrome; WHO: World Health Organization; NICE: National Institutes for Health and Care Excellence.

Risk of bias was assessed using the nine-point Newcastle-Ottawa Quality Assessment Scale (NOS) adapted for cross-sectional long-COVID studies. All studies were classified as high quality [23–25]. The quality of included studies is presented in Supplementary Material Table S4.

3.3. Definitions and Diagnostic Criteria

All three studies defined POTS as an increase in HR of ≥ 30 bpm within 10 minutes of standing, in the absence of orthostatic hypotension [23–25]. Orthostatic hypotension (OH) was defined by Seeley et al. (2023) and Shah et al. (2022) as a ≥ 20 mmHg drop in SBP or ≥ 10 mmHg drop in DBP within 3 minutes of standing [24,25]. Hira et al. (2025) only evaluated initial orthostatic hypotension (IOH), defined as a transient SBP drop of ≥ 40 mmHg within 15 seconds of standing, with recovery within 45–60 seconds and DBP was not considered in this definition [23].

3.4. Heart Rate Responses

All three studies reported elevated HR in LC participants compared to healthy controls in both supine and upright positions [23–25]. Supine HR was significantly higher in LC groups, with reported averages ranging from 67 to 88 bpm, compared to 61 to 78 bpm in controls [23–25]. The increase in

HR following standing was also significantly higher in LC participants, particularly for those meeting the POTS criteria, with standing HR ranging from 99 to 114 bpm compared to 78-83 bpm in controls. Subgroup analysis comparisons in Hira et al. (2025) study showed significant differences in supine and standing HR across LC phenotypes, with the LC-POTS group showing the highest increase after standing [23]. Detailed HR responses across studies and subgroups are presented in Table 2.

**Table 2.** Comparison of heart rate findings across studies.

| Study (Year)         | Supine HR Findings                                                                                                                                                                                                                                                                                                                                                        | Standing HR Findings                                                                                                                                                                                                                                                                                                                                                            |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Shah et al. (2022)   | LC: 88 ± 15 bpm<br>HC: 78 ± 11 bpm<br><i>p</i> = 0.0001                                                                                                                                                                                                                                                                                                                   | LC-OH: 99 ± 18 bpm<br>No-OH: 86 ± 14 bpm<br><i>p</i> = 0.006<br>HC: not reported.                                                                                                                                                                                                                                                                                               |
| Seeley et al. (2023) | PASC: 72 ± 13 bpm<br>POTS: 79 ± 12 bpm<br>HC: 68 ± 9 bpm<br>Group ( <i>p</i> = 0.003)<br>PASC > HC ( <i>p</i> = 0.05)<br>PASC < POTS <i>p</i> : not reported                                                                                                                                                                                                              | ΔHR (0-10 min)<br>PASC: 36 [30–47] bpm<br>POTS: 46 [34–59] bpm<br>HC: 15 [9–20] bpm<br>Group ( <i>p</i> = 0.001)<br>PASC > HC ( <i>p</i> = 0.001)<br>PASC ~ POTS ( <i>p</i> = 0.1)                                                                                                                                                                                              |
| Hira et al. (2025)   | LC: 67 [62–75] bpm<br>HC: 61 [56–70] bpm<br><i>p</i> = 0.01<br>Subgroups:<br>LC-IOH: 67 [61–77] bpm<br>LC-POTS: 68 [65–75] bpm<br>LC-none: 63 [57–73] bpm<br>HC: 61 [56–70] bpm<br>Group ( <i>p</i> = 0.023)<br>LC-none ~ HC ( <i>p</i> = 0.999)<br>LC-none ~ LC-POTS ( <i>p</i> = 0.283)<br>LC-none ~ LC-IOH ( <i>p</i> = 0.063)<br>LC-POTS ~ LC-IOH ( <i>p</i> = 0.999) | LC: 89 [77–106] bpm<br>HC: 78 [69–87] bpm<br><i>p</i> = 0.001<br>Subgroups:<br>LC-IOH: 85 [77–93] bpm<br>LC-POTS: 114 [103–131] bpm<br>LC-none: 80 [70–88] bpm<br>HC: 78 [69–87] bpm<br>Group ( <i>p</i> < 0.001)<br>LC-none ~ HC ( <i>p</i> = 0.999)<br>LC-none < LC-POTS ( <i>p</i> = 0.001)<br>LC-none ~ LC- IOH ( <i>p</i> = 0.279)<br>LC-POTS > LC-IOH ( <i>p</i> = 0.001) |

**Note:** Long-COVID terminology is presented as reported in each article. *OH*: orthostatic hypotension; *LC*: Long-COVID; *HC*: healthy controls; *LC-OH*: Long-COVID with orthostatic hypotension; *no-OH*: participants without orthostatic hypotension; *PASC*: post-acute sequelae of COVID-19; *POTS*: postural orthostatic tachycardia syndrome; *HR*: heart rate; *LC-IOH*: participants with long-COVID and initial orthostatic hypotension; *LC-POTS*: participants with long-COVID and postural orthostatic tachycardia syndrome; *LC-none*: participants with long-COVID but no abnormalities.

3.5. Blood Pressure Responses

Blood pressure findings were less consistent across studies. Shah et al. (2022) reported that 13% of LC participants (*n* = 12/92) met the criteria for OH, though absolute values and *p*-values were not reported [25]. Similarly, Seeley et al. (2023) reported no absolute values but found no significant group differences in supine and standing BP (*p* = 0.12) but observed a time-dependent increase in DBP in PASC and participants with POTS compared to controls (*p* = 0.03) [24]. In contrast, Hira et al. (2025) reported absolute values and found no overall BP differences between LC and controls. However, subgroup analysis showed higher SBP, DBP and mean arterial pressure (MAP) in LC participants who met the criteria of initial orthostatic hypotension (LC-IOH) compared to both LC with no abnormalities (LC-none) and LC-POTS groups (all *p* < 0.001). After standing, the LC-IOH showed lower SBP and MAP responses. Additionally, vascular sympathetic modulation, measured by low-frequency systolic blood pressure variability (LF<sub>SBP</sub>), was significantly reduced in LC-none compared to controls during supine and standing positions. Standing LF<sub>SBP</sub> was also significantly

lower in the LC-none group compared to the LC-POTS group. Detailed responses are summarized in Table 3.

**Table 3.** Comparison of blood pressure response findings across studies.

| Variable                                      | Shah et al.<br>(2022)        | Seeley et al.<br>(2023)                                                   | Hira et al.<br>(2025)                                                                                                                                                                                                                                |
|-----------------------------------------------|------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SBP-supine (mmHg)                             | Absolute values not reported | No significant differences ( $p = 0.12$ ).<br>No absolute values reported | LC: 119 [109–132] mmHg<br>HC: 119 [114–124] mmHg<br>$p = 0.683$ .<br>Subgroup:<br>LC-IOH: 130 [123–143] mmHg<br>LC-none: 113 [105–119] mmHg<br>LC-POTS: 112 [103–123] mmHg<br>LC-IOH > LC-none ( $p = 0.001$ ).<br>LC-IOH > LC-POTS ( $p = 0.001$ ). |
| DBP-supine (mmHg)                             | Absolute values not reported | No data reported for DBP in supine                                        | LC: 71 [64–77] mmHg<br>HC: 67 [64–72] mmHg<br>$p = 0.065$<br>Subgroup:<br>LC-IOH: 76 [67–79] mmHg<br>LC-none: 67 [63–73] mmHg<br>LC-POTS: 66 [63–73] mmHg<br>LC-IOH > LC-none ( $p = 0.001$ ).<br>LC-IOH > LC-POTS ( $p = 0.009$ ).                  |
| MAP-supine (mmHg)                             | Not reported                 | Not reported                                                              | LC: 87 [80–95] mmHg<br>HC: 85 [80–91] mmHg<br>$p = 0.268$<br>Subgroup:<br>LC-IOH: 94 [87–100] mmHg<br>LC-none: 81 [78–89] mmHg<br>LC-POTS: 81 [77–92] mmHg<br>LC-IOH > LC-none ( $p = 0.001$ ).<br>LC-IOH > LC-POTS ( $p = 0.001$ ).                 |
| LF <sub>SBP</sub> supine (mmHg <sup>2</sup> ) | Not reported                 | Not reported                                                              | LC: 4.06 [2.69–6.62] mmHg <sup>2</sup><br>HC: 5.15 [3.77–9.37] mmHg <sup>2</sup><br>LC-none < HC ( $p = 0.001$ )                                                                                                                                     |

**Note:** SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; LF<sub>SBP</sub>: Low-frequency systolic blood pressure; LC: long-COVID; HC: healthy control; LC-IOH: participants with long-COVID and initial orthostatic hypotension; LC-POTS: participants with long-COVID and postural orthostatic tachycardia syndrome; LC-none: participants with long-COVID but no abnormalities.

3.6. Time Domain Heart Rate Variability Responses

Shah et al. (2022) and Hira et al. (2025) reported decreases in heart rate variability (HRV) in individuals experiencing LC compared to healthy controls [23,25]. Time-domain HRV indices, such as root-mean square of successive R-R interval differences (RMSSD) and standard deviation of R-R intervals (SDNN), were consistently lower in LC participants compared to healthy controls. Shah et al. (2022) also reported a reduction in RMSSD based on COVID-19 severity, finding that the values were lowest in those with severe and moderate illness, with higher values in the mild and asymptomatic groups ( $p < 0.0001$ ). Similarly, subgroup analysis by Hira et al. (2025) also showed significant reductions in heart rate variability indices in the LC-IOH and LC-POTS subgroups compared to LC-none group during standing. Standing RMSSD was lowest in LC-POTS group (9.72 [7.37–13] ms) and highest in LC-none group (19 [16–38] ms), with similar patterns observed for SDNN

and pNN50 (percentage of successive R-R intervals differing by more than 50 ms). Detailed time-domain HRV across studies and subgroups are presented in Table 4 below.

**Table 4.** Time-domain heart rate variability indices.

| Variable | (Shah et al., 2022)                                                                                                                                                                                                                 | (Hira et al., 2025)                                                                                                                                                                                                                                                                                                                  |
|----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RMSSD    | LC:13.9 ± 11.8 ms<br>HC: 19.9 ± 19.5 ms<br>LC < Controls ( <i>p</i> = 0.01)<br>Subgroup:<br>Graded reduction by COVID severity ( <i>p</i> = 0.0001)<br>Asymptomatic: 24.2 ms<br>Mild: 16.3 ms<br>Moderate: 9.3 ms<br>Severe: 7.2 ms | Supine:<br>No significant group-level differences.<br>Standing:<br>LC: 15 [8.9–22] ms<br>HC: 18 [13–32] ms<br>LC < HC ( <i>p</i> = 0.011).<br>Subgroup:<br>LC-IOH: 15 [9.60–27] ms<br>LC-none: 19 [16–38] ms<br>LC-POTS: 9.72 [7.37–13] ms<br>LC-POTS < LC-none ( <i>p</i> = 0.001)<br>LC-POTS < LC-IOH ( <i>p</i> = 0.024)          |
|          | SDNN                                                                                                                                                                                                                                | Supine:<br>No significant group-level differences.<br>Standing:<br>LC: 31 [22–43] ms<br>HC: 40 [32–55] ms;<br>LC < HC ( <i>p</i> = 0.001).<br>Subgroup:<br>LC-none: 37 [28–51] ms<br>LC-POTS: 27 [20–33] ms<br>LC-POTS < LC-none ( <i>p</i> = 0.018)                                                                                 |
| pNN50    | Not reported                                                                                                                                                                                                                        | Supine:<br>No significant group-level differences.<br>Standing:<br>LC: 0.23 [0–0.87] ms<br>HC: 0.78 [0.11–2.72] ms<br>LC < HC ( <i>p</i> = 0.011).<br>Subgroup:<br>LC-IOH: 2.46 [0.32–7.44]%<br>LC-none: 0.83 [0–2.50]%<br>LC-POTS: 8.12 [3.10–13]%<br>LC-POTS > LC-none ( <i>p</i> = 0.039)<br>LC-POTS > LC-IOH ( <i>p</i> = 0.026) |

**Note:** LC: long-COVID; HC: healthy controls; RMSSD: root-mean square of successive R-R interval differences; SDNN: standard deviation of R-R intervals; pNN50: percentage of successive R-R intervals differing by more than 50ms. LC-IOH: participants with long-COVID and initial orthostatic hypotension; LC-POTS: participants with long-COVID and postural orthostatic tachycardia syndrome; LC-none: participants with long-COVID but no abnormalities.

3.7. Frequency Domain Heart Rate Variability Responses

Frequency-domain HRV indices, including high-frequency (HF), low-frequency (LF), total power (TP), low-frequency to high-frequency ratio (LF/HF) and vagal baroreflex sensitivity (BRSv), were reported only by Hira et al. (2025). No significant differences were found between LC and control participants during supine. However, after standing, LC participants demonstrated significantly lower HF, LF, and TP compared to controls, with no group differences found in LF/HF ratio or BRSv. Subgroup analysis revealed significant differences in HF, LF, TP, and BRSv across LC phenotypes (LC-IOH, LC-POTS, LC-none) in both supine and standing positions. During supine, the

LC-IOH group showed significantly lower HF, LF, and BRSv compared to LC-POTS (all  $p < 0.05$ ), and BRSv was also significantly reduced in LC-IOH compared to LC-none ( $p = .01$ ). Following standing, the LC-POTS group had significantly lower HF, LF, and TP compared to LC-none (all  $p < 0.01$ ). BRSv was also significantly lower in both LC-POTS and LC-IOH compared to LC-none. LF/HF ratio did not significantly differ between groups. Detailed frequency-domain HRV across studies and subgroups are presented in Table 5.

**Table 5.** Frequency-domain heart rate variability indices from Hira et al. 2025.

| Variable    | Supine Findings                                         | Standing Findings                                       |
|-------------|---------------------------------------------------------|---------------------------------------------------------|
| HF          |                                                         | LC: 315 [95–730] ms <sup>2</sup>                        |
|             | No significant difference between LC and HC.            | HC: 349 [260–1190] ms <sup>2</sup>                      |
|             | Subgroup:                                               | LC < HC ( $p = 0.042$ )                                 |
|             | HC: 1136 [262–3121] ms <sup>2</sup>                     | Subgroup:                                               |
|             | LC-none: 1919 [725–4921] ms <sup>2</sup>                | HC: 349 [260–1190] ms <sup>2</sup>                      |
|             | LC-IOH: 1384 [339–2036]ms <sup>2</sup>                  | LC-none: 578 [337–1881] ms <sup>2</sup>                 |
|             | LC-POTS: 2166 [1112–4419] ms <sup>2</sup>               | LC-IOH: 296 [98–871] ms <sup>2</sup>                    |
|             | Group ( $p = 0.026$ )                                   | LC-POTS: 100 [51–339] ms <sup>2</sup>                   |
| LF          | LC-POTS > LC-IOH ( $p = 0.028$ )                        | Group ( $p < 0.001$ )                                   |
|             |                                                         | LC-none > LC-POTS ( $p = 0.001$ ).                      |
|             |                                                         | LC: 1203 [483–2212] ms <sup>2</sup>                     |
|             | No significant differences between LC and HC.           | HC: 1901 [935–4008] ms <sup>2</sup>                     |
|             | Subgroup:                                               | LC < HC ( $p = 0.008$ )                                 |
|             | HC: 1484 [603–4210] ms <sup>2</sup>                     | Subgroup:                                               |
|             | LC-none: 2130 [1142–4393] ms <sup>2</sup>               | HC: 1901 [935–4008] ms <sup>2</sup>                     |
|             | LC-IOH: 1429 [643–2778] ms <sup>2</sup>                 | LC-none: 1806 [1106–3932] ms <sup>2</sup>               |
| TP          | LC-POTS: 2680 [1889–4938] ms <sup>2</sup>               | LC-IOH: 974 [428–1941] ms <sup>2</sup>                  |
|             | Group ( $p = 0.015$ )                                   | LC-POTS: 1080 [298–1671] ms <sup>2</sup>                |
|             | LC-POTS > LC-IOH ( $p = 0.012$ )                        | Group ( $p = 0.001$ )                                   |
|             |                                                         | LC-POTS < LC-none ( $p = 0.020$ )                       |
|             |                                                         | LC: 3313 [1773–5559] ms <sup>2</sup>                    |
|             | No significant differences between LC and HC.           | HC: 5342 [3410–10550] ms <sup>2</sup>                   |
|             | Subgroup:                                               | LC < HC ( $p < 0.001$ )                                 |
|             | HC: 689 [2547–17839] ms <sup>2</sup>                    | Subgroup:                                               |
| BRSv        | LC-none: 7702 [4681–14480] ms <sup>2</sup>              | HC: 5342 [3410–10550] ms <sup>2</sup>                   |
|             | LC-IOH: 5975 [3321–11206] ms <sup>2</sup>               | LC-none: 4938 [301–9406] ms <sup>2</sup>                |
|             | LC-POTS: 9415 [5096–16398] ms <sup>2</sup>              | LC-IOH: 3269 [1757–5130] ms <sup>2</sup>                |
|             | Group ( $p = 0.057$ )                                   | LC-POTS: 2619 [1413–3949] ms <sup>2</sup>               |
|             | LC-POTS > LC-IOH ( $p = 0.030$ )                        | Group ( $p = 0.001$ )                                   |
|             |                                                         | LC-POTS < LC-none ( $p = 0.006$ )                       |
|             | No significant differences between LC and HC.           | No significant differences between LC and controls.     |
|             | Subgroup:                                               | Subgroup:                                               |
| LF/HF ratio | HC: 6.89 [4.94–11.4] ms/mmHg                            | Controls: 3.97 [2.93–6.41] ms/mmHg]                     |
|             | LC-none: 10.7 [5.35–17.0] ms/mmHg                       | LC-none: 5.33 [3.34–7.06] ms/mmHg                       |
|             | LC-IOH: 6.24 [4.11–10.0] ms/mmHg                        | LC-IOH: 2.77 [1.76–5.11] ms/mmHg                        |
|             | LC-POTS: 9.81 [8.47–16.0] ms/mmHg                       | LC-POTS: 2.85 [1.44–3.93] ms/mmHg                       |
|             | Group ( $p = 0.001$ )                                   | Group $p = 0.001$                                       |
|             | LC-POTS > LC-IOH ( $p = 0.010$ )                        | LC-POTS < LC-none ( $p = 0.001$ )                       |
|             | LC-IOH > LC-none ( $p = 0.001$ )                        | LC-IOH < LC-none ( $p = 0.005$ )                        |
|             | No significant differences between groups or subgroups. | No significant differences between groups or subgroups. |

**Note:** LC: long-COVID; HC: healthy controls; HF: high-frequency; LF: low-frequency; TP: total power; BRSv: baroreflex sensitivity; LF/HF ratio: low-frequency/high-frequency ratio; LC-IOH: participants with long-COVID

and initial orthostatic hypotension; *LC-POTS*: participants with long-COVID and postural orthostatic tachycardia syndrome; *LC-none*: participants with long-COVID but no abnormalities.

### 3.8. Respiratory Responses

Only Seeley et al. (2023) reported respiratory sinus arrhythmia, but no other respiratory system variables were reported. Respiratory sinus arrhythmia was significantly lower in their LC group (9.8 [7.0 – 14.5] breaths/min) compared to the group with POTS (14.0 [12.1 – 19.2] breaths/min) and healthy controls (17.4 [12.0 – 19.5] breaths/min) groups ( $p < 0.001$ ) [24].

## 4. Discussion

This review highlights that the active standing test reveals subtle but clinically relevant cardiovascular and autonomic changes in individuals with LC. Across studies, consistent patterns included elevated HR and reduced HRV indices (RMSSD, SDNN, LF, HF, TP, BRSv), whereas BP responses were highly variable. Notably, the active standing test was able to identify subgroups with exaggerated tachycardic or hypotensive responses, suggesting its value for detecting early autonomic dysfunction. Together, these findings indicate that LC frequently involves disturbances in cardiovascular regulation, with potential implications for symptom burden, safety, and rehabilitation.

Our findings align with growing evidence that autonomic dysfunction is a core feature of long-COVID [26]. While some studies reported high prevalence of postural orthostatic tachycardia syndrome or orthostatic hypotension, others found minimal cases [8,24,25]. Such variation is in line with prior reports of heterogeneous orthostatic intolerance prevalence in post-viral syndromes [6,7]. Several mechanisms may contribute, including persistent inflammation, impaired baroreflex function, microvascular injury, and altered hemodynamics [10,27,28]. Reduced HRV indices across studies supports impaired autonomic control, consistent with prior research in long-COVID and other chronic conditions. These observations reinforce the hypothesis that long-COVID involves dysregulation of both sympathetic and parasympathetic function, which may underline symptoms such as dizziness, fatigue, and exercise intolerance [26,29].

A key challenge identified in this review is methodological heterogeneity across studies. Active standing test protocols differed in duration and timing of measurements limiting comparability [23,25]. Definitions of long-COVID also varied, with some studies relying on self-report while others required a positive polymerase chain reaction or rapid kit confirmation of infection [23–25]. Physiological measures were largely restricted to HR and BP, with few assessments of stroke volume, systemic vascular resistance, or cerebral blood flow, which are factors critical for understanding OI pathophysiology [30,31]. These inconsistencies likely explain much of the variability in prevalence estimates and underscore the need for standardized approaches.

This review has several limitations that need to be acknowledged. The number of eligible studies is small, restricting generalizability and precluding meta-analysis. Although our inclusion criteria strengthened rigor by requiring continuous cardiovascular monitoring and the inclusion of healthy controls, this may have excluded relevant but less detailed studies. Publication bias may also favor studies reporting positive findings. Finally, the limited representation of diverse populations reduces the ability to draw conclusions about sex, age, or comorbidity effects. Despite these limitations, this review provides important implications for both research and clinical practice.

Future studies should adopt standardized definitions of long-COVID (e.g., National Academies of Sciences, Engineering, and Medicine 2024 consensus definition), consistent active standing test protocols, and beat-to-beat monitoring to capture rapid hemodynamic changes. Expanding beyond heart rate and blood pressure to include stroke volume, systemic vascular resistance, and cerebral blood flow will clarify mechanisms of orthostatic intolerance and guide targeted interventions. Comparative research across post-viral syndromes could also help determine whether these autonomic disturbances are specific to long-COVID or reflect broader post-infectious processes.

Ultimately, the active standing test offers a simple and physiologically relevant tool to advance understanding of cardiovascular dysregulation in long-COVID, with potential to inform both diagnosis and rehabilitation strategies. Individuals with long-COVID show consistent elevations in heart rate and impaired autonomic function during active standing, with varied blood pressure abnormalities. These findings suggest altered autonomic-cardiovascular integration that may contribute to symptoms such as dizziness, fatigue, and reduced tolerance of daily activities. Incorporating active standing into clinical assessment could support earlier identification of autonomic dysfunction, guide rehabilitation strategies, and help tailor management to improve functional recovery in long-COVID. The limited evidence base also emphasizes an urgent need for further research evaluating hemodynamic and multisystem responses in this population.

## 5. Conclusions

This systematic review synthesized studies using the active standing test to assess cardiovascular, autonomic, or respiratory responses in long-COVID. While limited in number, findings show increased heart rate responses and reduced heart rate variability indices in individuals experiencing long-COVID, suggesting persistent autonomic dysfunction. Blood pressure responses were inconsistent, with some subgroup-level differences in systolic and mean arterial pressure. Key gaps included the absence of standardized long-COVID definitions, incomplete reporting of absolute values, and the absence of other hemodynamic variables (e.g., cardiac output, stroke volume, systemic vascular resistance) and respiratory measures, limiting comparability. Future research should consider adopting the use of standardized definitions (e.g., National Academies of Sciences, Engineering, and Medicine consensus criteria), using continuous hemodynamic measurement tools, and including broader physiological assessment of variables beyond BP and HR, and incorporate appropriate control groups. A multi-system assessment approach may better characterize dysregulation and inform targeted interventions for long-COVID.

**Supplementary Materials:** The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Table S1, Table S2, Table S3, Table S4 and PRISMA 2020 Checklist.

**Author Contributions:** Faith Olarinde - Conceptualization, Formal analysis, Methodology, Writing – review & editing, Writing – original draft. Albená Nunes-Silva - Formal analysis and revisions. Diana C. Sanchez-Ramirez – Validation and revisions. Yannick Molgat-Seon – Validation and revisions. Rodrigo Villar - Conceptualization, Formal analysis, Methodology, Supervision, Validation, and revisions.

**Identifying information:** Faith Olarinde has moved to a new institution (affiliated as a PhD student at the Department of Kinesiology and Physical Education at McGill University, Montreal, Quebec, Canada) since completing this project.

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Abbreviations

The following abbreviations are used in this manuscript:

|                   |                                                                    |
|-------------------|--------------------------------------------------------------------|
| BRSv              | Vagal baroreflex sensitivity                                       |
| CI                | Confidence interval                                                |
| DBP               | Diastolic blood pressure                                           |
| HC                | Health controls                                                    |
| HF                | High frequency                                                     |
| HR                | Heart rate                                                         |
| HR                | Heart rate variability                                             |
| IQR               | Inter-quartile range                                               |
| LC                | Long-COVID                                                         |
| LC-IOH            | Long-COVID and initial orthostatic hypotension                     |
| LC-None           | Long-COVID but no abnormalities                                    |
| LC-POTS           | Long-COVID and post orthostatic tachycardia syndrome               |
| LF                | Lower frequency                                                    |
| LF/HF ratio       | Lower to higher frequency ratio                                    |
| LF <sub>SBP</sub> | Low-frequency systolic blood pressure                              |
| MAP               | Mean arterial pressure                                             |
| NASEM             | National Academies of Sciences, Engineering, and Medicine          |
| NICE              | National Institutes for Health and Care Excellence.                |
| OH                | Orthostatic hypotension                                            |
| PASC              | Post-acute sequelae of SARS-CoV-2 infection                        |
| pNN50             | Percentage of successive R-R intervals differing by more than 50ms |
| POTS              | Post orthostatic tachycardia syndrome                              |
| RMSSD             | Root-mean square of successive R-R interval differences            |
| SBP               | Systolic blood pressure                                            |
| SD                | Standard deviation                                                 |
| SDNN              | Standard deviation of R-R intervals                                |
| TP                | Total Power                                                        |
| WHO               | World Health Organization                                          |

References

1. National Academies of Sciences, Engineering, and Medicine. A Long COVID Definition: A Chronic, Systemic Disease State with Profound Consequences. Washington, DC: The National Academies Press; 2024.
2. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis* 2022;22(4):e102–107.
3. Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. 2023;21(3):133–146.
4. Sanchez-Ramirez DC, Normand K, Yang Z, Torres-Castro R. Long-term impact of COVID-19: A systematic review of the literature and meta-analysis. *Biomedicines* 2021;9(8).
5. Ricci F, De Caterina R, Fedorowski A. Orthostatic hypotension epidemiology, prognosis, and treatment. *J AM Coll Cardiol* 2015;66:848–860.
6. Vernon SD, Funk S, Bateman L, Stoddard GJ, Hammer S, Sullivan K, et al. Orthostatic challenge causes distinctive symptomatic, hemodynamic and cognitive responses in long COVID and myalgic encephalomyelitis/chronic fatigue syndrome. *Front Med* 2022;9:917019.
7. Ormiston CK, Świątkiewicz I, Taub PR. Postural orthostatic tachycardia syndrome as a sequela of COVID-19. *Heart Rhythm* 2022;19(11):1880–1889.

8. Monaghan A, Jennings G, Xue F, Byrne L, Duggan E, Romero-Ortuno R. Orthostatic intolerance in adults reporting long COVID symptoms was not associated with postural orthostatic tachycardia syndrome. *Front Phys* 2022;13:833650.
9. Freeman R, Wieling W, Axelrod FB, Benditt DG, Benarroch E, Biaggioni I, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Clin Auton Res* 2011;21(2):69–72.
10. Diab AM, Carleton BC, Goralski KB. COVID-19 pathophysiology and pharmacology: what do we know and how did Canadians respond? A review of Health Canada authorized clinical vaccine and drug trials. *Can J Physiol Pharmacol* 2021;99(6):577–588.
11. Finucane C, van Wijnen VK, Fan CW, Soraghan C, Byrne L, Westerhof BE, et al. A practical guide to active stand testing and analysis using continuous beat-to-beat non-invasive blood pressure monitoring. *Clin Auton Res* 2019;29(4):427–441.
12. McJunkin B, Rose B, Amin O, Shah N, Sharma S, Modi S, et al. Detecting initial orthostatic hypotension: A novel approach. *J Am Soc Hypertens* 2015;9(5):365–369.
13. Dall PM, Kerr A. Frequency of the sit to stand task: An observational study of free-living adults. *Appl Ergon* 2010;41(1):58–61.
14. Wieling W, Kaufmann H, Claydon VE, van Wijnen VK, Harms MPM, Juraschek SP, et al. Diagnosis and treatment of orthostatic hypotension. *Lancet Neurol* 2022;21(8):735–746.
15. Wieling W, Krediet CTP, van Dijk N, Linzer M, Tschakovsky ME. Initial orthostatic hypotension: review of a forgotten condition. *Clin Sci* 2007;112(3):157–165.
16. Blitshteyn S, Whitelaw S. Postural orthostatic tachycardia syndrome (POTS) and other autonomic disorders after COVID-19 infection: a case series of 20 patients. *Immunol Res* 2021;69(2):205–211.
17. González-Hermosillo GJA, Galarza EJ, Fermín OV, González JMN, Tostado LMFÁ, Lozano MAE, et al. Exaggerated blood pressure elevation in response to orthostatic challenge, a post-acute sequelae of SARS-CoV-2 infection (PASC) after hospitalization. *Autonom Neurosci* 2023;247:103094.
18. Osuchowski MF, Winkler MS, Skirecki T, Cajander S, Shankar-Hari M, Lachmann G, et al. The COVID-19 puzzle: deciphering pathophysiology and phenotypes of a new disease entity. *Lancet Respir Med* 2021;9(6):622–642.
19. Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. *Environ Int* 2018;121:1027–1031.
20. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. The Ottawa Hospital Research Institute, Our Research. 2000.
21. Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. *BMC Public Health*. 2013;13(1).
22. Modesti PA, Reboldi G, Cappuccio FP, Agyemang C, Remuzzi G, Rapi S, et al. Panethnic differences in blood pressure in Europe: A systematic review and meta-analysis. *PLoS ONE*. 2016;11(1):e0147601.
23. Hira R, Baker JR, Siddiqui T, Patel A, Valani FGA, Lloyd MG, et al. Attenuated cardiac autonomic function in patients with long-COVID with impaired orthostatic hemodynamics. *Clin Auton Res* 2025;35(2):301–314.
24. Seeley MC, Gallagher C, Ong E, Langdon A, Chieng J, Bailey D, et al. High incidence of autonomic dysfunction and postural orthostatic tachycardia syndrome in patients with long COVID: Implications for management and health care planning. *Am J Med* 2025;138(2):354–361.
25. Shah B, Kunal S, Bansal A, Jain J, Poundrik S, Shetty MK, et al. Heart rate variability as a marker of cardiovascular dysautonomia in post-COVID-19 syndrome using artificial intelligence. *Indian Pacing Electrophysiol J* 2022;22(2):70–76.
26. Novak P, Mukerji SS, Alabsi HS, Systrom D, Marciano SP, Felsenstein D, et al. Multisystem involvement in post-acute sequelae of coronavirus disease 19. *Ann Neurol* 2022;91(3):367–379.
27. Bielecka E, Sielatycki P, Pietraszko P, Zapora-Kurel A, Zbroch E. Elevated arterial blood pressure as a delayed complication following COVID-19 – a narrative review. *Int J Mol Sci* 2024;25(3):1837

28. van Campen CLMC, Rowe PC, Visser FC. Two different hemodynamic responses in ME/CFS patients with postural orthostatic tachycardia syndrome during head-up tilt testing. *J Clin Med* 2024;13(24):7726.
29. Fedorowski A, Olsén MF, Nikesjö F, Janson C, Bruchfeld J, Lerm M, et al. Cardiorespiratory dysautonomia in post-COVID-19 condition: Manifestations, mechanisms and management. *J Intern Med* 2023;294(5):548–562.
30. Khan MS, Miller AJ, Ejaz A, Molinger J, Goyal P, MacLeod DB, et al. Cerebral blood flow in orthostatic intolerance. *J Am Heart Assoc* 2025;14(3):e036752.
31. De Matos DG, De Santana JL, Aidar FJ, Cornish SM, Giesbrecht GG, Mendelson AA, et al. Cardiovascular regulation during active standing orthostatic stress in older adults living with frailty: a systematic review. *Arch Gerontol Geriatr.* 2025;136:105894.

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