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## Article

# Characterizing Neurocardiovascular Responses to an Active Stand Test in Older Women: A Pilot Study Using Functional Data Analysis

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**Abstract:** This observational pilot study investigated neurocardiovascular responses to an active stand test using continuous physiological monitoring and functional data analysis (FDA) in older women. A sample of 25 community-dwelling female adults aged 59–78 years (mean age: 70.3 years) participated. Participants were dichotomized into comparison groups based on five factors: age (<70 vs. ≥70 years), presence of initial orthostatic hypotension (IOH, yes/no), body mass index (BMI <25 vs. ≥25 kg/m<sup>2</sup>), antihypertensive medication use (yes/no), and physical frailty status (SHARE-FI score <−0.5 vs. ≥−0.5). Each participant completed an active stand test during which six physiological signals were continuously recorded: systolic (sBP) and diastolic (dBP) blood pressure and heart rate (HR) via digital artery photoplethysmography, and left frontal oxygenated hemoglobin (O<sub>2</sub>Hb), deoxygenated hemoglobin (HHb), and tissue saturation index (TSI) via near-infrared spectroscopy (NIRS). Signal analysis focused on a standardized 200-second window spanning 50 seconds before to 150 seconds after the stand, with all signals resampled and synchronized at 5 Hz. FDA was used to statistically compare the full time series between groups for each signal. Group-level differences revealed that younger participants (<70 years) exhibited significantly higher HR at multiple periods following the stand (~10 s, ~30 s, ~90 s, and ~140 s post-stand) compared to their older counterparts. Participants with IOH demonstrated significantly lower sBP at ~10 s, ~80 s, and ~130 s post-stand, and lower dBP at ~10 s post-stand. Among participants classified as overweight/obese (BMI ≥25 kg/m<sup>2</sup>), significantly lower levels of HHb were observed at ~10 s, ~30–50 s, and ~60 s post-stand, while O<sub>2</sub>Hb levels were reduced at ~50 s, ~60 s, ~70–110 s, ~130 s, and ~140 s post-stand. No statistically significant group-level differences were observed based on antihypertensive medication use or frailty status. These findings demonstrate the utility of FDA in detecting subtle, time-dependent physiological variations during orthostatic challenge and underscore the value of continuous neurocardiovascular monitoring in assessing orthostatic tolerance in aging populations.

**Keywords:** active stand test; functional data analysis; neurovascular response; cardiovascular monitoring; frailty; initial orthostatic hypotension; BMI; NIRS; photoplethysmography; aging

## 1. Introduction

The ability to maintain blood pressure and cerebral perfusion upon standing is a critical function of the body's neurocardiovascular systems. In older adults, even subtle impairments in these regulatory mechanisms can lead to orthostatic intolerance, characterized by transient hypotension, dizziness, falls, and, in some cases, loss of consciousness [1,2]. These symptoms often occur in the context of underlying age-related changes in vascular compliance, baroreflex sensitivity, and cerebral autoregulation, and may be exacerbated by comorbidities such as obesity, antihypertensive medication use, and frailty [3–5].

The active stand test is a well-established clinical tool for evaluating orthostatic responses. Traditional interpretations typically rely on point estimates or averaged intervals of physiological

data, which may overlook brief but clinically meaningful deviations that occur in the seconds immediately following postural change [6]. This is particularly relevant in detecting initial orthostatic hypotension (IOH), a transient and underdiagnosed form of orthostatic instability associated with adverse outcomes in older adults [7,8].

Recent advances in sensor technologies allow for the continuous collection of cardiovascular and cerebral hemodynamic signals with high temporal resolution. These include beat-to-beat blood pressure and heart rate measurements via photoplethysmography, as well as cerebral oxygenation assessments using near-infrared spectroscopy (NIRS) [9]. While statistical parametric mapping (SPM) has proven useful in large epidemiological datasets for analyzing time-series data [10], its application in smaller clinical samples is limited by reduced statistical power and the need for strong smoothness assumptions. In such contexts, conventional statistical approaches may struggle to detect subtle or time-specific group differences in physiological signals.

Functional data analysis (FDA) offers a flexible alternative by enabling statistical comparisons across entire signal trajectories. Unlike traditional methods that rely on discrete time points or summary measures, FDA models the continuous nature of physiological responses, making it particularly well-suited for capturing transient differences in small-sample studies. This approach has seen growing use in medicine and neuroscience research, where dynamic regulatory processes are often of primary interest [11].

In this pilot study, we applied FDA to investigate neurocardiovascular responses to an active stand test in a cohort of community-dwelling older women. Using continuous recordings of blood pressure, heart rate, and cerebral NIRS, we examined whether specific clinical characteristics—older age, the presence of IOH, higher body mass index (BMI), antihypertensive medication use, and higher physical frailty—were associated with distinct temporal patterns in physiological responses to the orthostatic challenge.

## 2. Materials and Methods

### 2.1. Study Sample

This study involved a small sample of volunteer community-dwelling older women, recruited between May and July 2023 from a local healthy ageing community group in South Dublin, Ireland. Eligibility criteria included age  $\geq 50$  years, the ability to provide written informed consent, independent mobility (with or without a walking aid), and being able to transfer from lying to standing independently or with only minimal assistance. The exclusion criterion was the presence of an indwelling electronic device (e.g., a pacemaker).

Participants were invited to attend a dedicated research assessment at the Falls and Syncope Unit, Mercer's Institute for Successful Ageing (MISA), St. James's Hospital, Dublin. The full research setup has been described in detail elsewhere [12]. Ethical approval was obtained, all participants provided written informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

### 2.2. Participant Characteristics

For the comparison of continuous orthostatic physiological responses, the sample was dichotomously classified based on age, presence of IOH, body mass index (BMI), antihypertensive medication use, and physical frailty status. Participants were grouped by age using a threshold of 70 years (younger:  $<70$ ; older:  $\geq 70$ ). IOH was defined based on hemodynamic criteria—regardless of reported orthostatic symptoms—as a transient drop in systolic blood pressure ( $\geq 40$  mmHg) or diastolic blood pressure ( $\geq 20$  mmHg) within 15 seconds of standing [7], measured during the active stand test. BMI was used to categorize participants as overweight ( $\geq 25$  kg/m<sup>2</sup>) or obese ( $\geq 30$  kg/m<sup>2</sup>) (vs. non-overweight), in accordance with World Health Organization (WHO) standards [13]. Antihypertensive use was determined based on self-reported current medication and classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification system. This included

medications in the following ATC classes: C02 (antihypertensives), C03 (diuretics), C07 (beta-blockers), C08 (calcium channel blockers), and C09 (agents acting on the renin-angiotensin system) [12]. Higher physical frailty was defined using the continuous SHARE-FI score [14], with a threshold based on the sample median.

### 2.3. Active Stand

Participants underwent an active stand test in a quiet, temperature-controlled room (maintained at 21–23 °C). Prior to standing, each participant rested in a supine position for approximately 5 minutes while the Finapres® Nova device was calibrated using oscillometric brachial measurements. This calibration ensured accurate beat-to-beat blood pressure monitoring via a finger cuff on the left hand, with continuous signal adjustment using the device's PhysioCal function and height correction unit. Following the supine rest and calibration, participants were instructed to stand up promptly—unaided unless minimal assistance was required—and to remain standing for 3 minutes. Throughout the entire procedure, continuous recordings of cardiovascular and neurovascular signals were collected. Cardiovascular signals included beat-to-beat systolic (sBP) and diastolic (dBP) blood pressure and heart rate (HR), captured via digital photoplethysmography. Neurovascular signals included frontal cerebral oxygenation parameters—oxygenated hemoglobin (O<sub>2</sub>Hb), deoxygenated hemoglobin (HHb), and tissue saturation index (TSI)—measured using near-infrared spectroscopy (NIRS). Full details on the active stand protocol are reported elsewhere [12].

### 2.4. Instrumentation

#### 2.4.1. Continuous Cardiovascular Signals

A Finometer device (Finometer MIDI, Finapres® Medical Systems, Amsterdam, The Netherlands) was used to noninvasively monitor the reconstructed arterial pressure on a beat-to-beat basis. This photoplethysmography-based device records the pressure waveform of the digital arteries at a sampling rate of 200 Hz using the volume-clamp method. The volume of the finger artery, detected by optical sensors embedded in the finger cuff, is kept constant throughout the assessment via a pneumatic control system that dynamically adjusts cuff pressure [15]. Importantly, the volume-clamp method has shown strong agreement with both intra-arterial blood pressure monitoring [16] and the auscultatory method [17]. The Finometer also accounts for hydrostatic pressure differences between the finger and heart level using a height correction unit, which includes a position sensor mounted to the finger.

#### 2.4.2. Continuous Neurovascular Signals

NIRS is a non-invasive, non-ionizing optical technique widely employed for monitoring changes in oxygenated and deoxygenated hemoglobin concentrations across various human tissues [18–20]. Previous studies have demonstrated that NIRS readings are consistent with other measurement modalities in various applications, such as cerebral blood flow [21] and skeletal muscle contractions [22]. NIRS' versatility and high temporal resolution, facilitated by capabilities in time-resolved, frequency-domain, and continuous wave spectroscopic implementations, render its potential for a wide range of applications in both research and clinical settings [23].

Based on optical sensing principles, NIRS measures light absorption at multiple wavelengths to estimate chromophore concentrations. Absorption near 850 nm is primarily associated with oxygenated hemoglobin (O<sub>2</sub>Hb), while absorption around 760 nm corresponds to deoxygenated hemoglobin (HHb). Derived indices such as the tissue saturation index (TSI) are commonly reported and are typically calculated as  $TSI = 100 \times O_2Hb / (O_2Hb + HHb)$  [24].

A wireless NIRS device, the PortaLite® (Artinis Medical Systems, Elst, The Netherlands), was used to measure O<sub>2</sub>Hb, HHb and TSI signals, via a relative concentration method based on Beer-Lambert Law. With an optical sensor comprised of an emitter and three long-range receivers, the PortaLite® has a capability of transmitting multi-channel, real-time data through Bluetooth® at a



maximum sampling frequency of 50 Hz. The user interface for the setup, recording, and export of NIRS data was accommodated by Oxysoft v3.0.53. The NIRS sensor was affixed approximately 2 cm above the left eye (approximately the FP1 (left frontal) position of the 10 to 20 electrode system (3 cm lateral and 3.5 cm superior to the nasion) [25] and the sampling frequency was set at 50 Hz for all recordings. The noise caused by the ambient light was minimized and kept consistent via a black headband covering the sensor.

### 2.5. Signal Acquisition and Synchronization

This study focused on a standardized 200-second segment of the active stand test, spanning from 50 seconds before to 150 seconds after the initiation of standing. Beat-to-beat cardiovascular signals acquired from the Finapres® MIDI device were interpolated to 5 Hz. Neurovascular signals recorded by the PortaLite® NIRS device were downsampled to the same frequency (5 Hz) for consistency. Signal synchronization was achieved using multiple manual event markers inserted throughout the recordings. The precise onset of the stand—defined as the moment participants began transitioning from supine to standing—was identified by triggering a keyboard event marker labelled “active stand”. These neurovascular synchronization followed the same methodology as described elsewhere [9].

### 2.6. Functional Data Analysis

Functional Data Analysis (FDA) is a statistical framework for analyzing data that take the form of functions, such as time-series or other continuous processes [26]. Unlike traditional approaches that treat observations as discrete points, FDA represents each time series as a smooth, continuous curve. This enables the analysis of overall trajectories, derivatives, and temporal patterns, while accounting for measurement noise and irregular sampling intervals [27]. FDA has been applied in a range of fields—including neuroscience, biomechanics, and finance—where understanding and comparing dynamic processes is essential. By leveraging the smoothness and continuity of functional data, FDA provides a robust method for detecting meaningful differences between time-varying signals [28].

In this study, FDA was implemented using R (version 4.2.2) within RStudio (version 2024.12.0+467; Boston, MA, USA). The open-source fda package (version 6.1.8) was used for analysis. For each dichotomous grouping variable, the observed test statistic curve  $F^2(t)$  was computed and plotted. This statistic reflects, at each time point  $t$ , the squared difference between the group mean curves relative to the within-group variance. Larger spikes in the  $F^2(t)$  curve indicate greater divergence between group means at that specific time. Statistical significance was determined at a threshold of  $p < 0.05$ , using the  $F^2(t)$  curve. To maximize clinical relevance and reduce the risk of false positives due to transient signal artifacts, a finding was considered statistically significant only if the test statistic exceeded the critical threshold for at least 5 consecutive seconds post-stand.

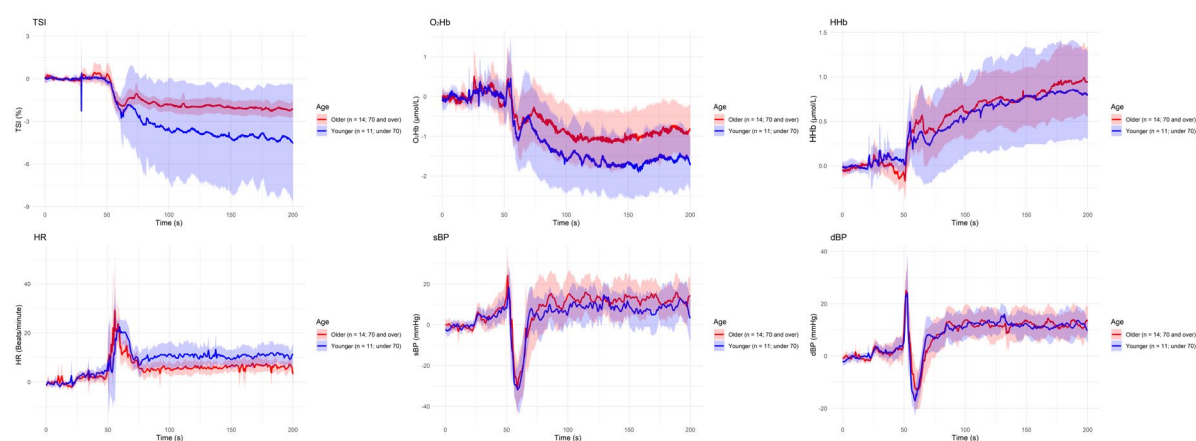
## 3. Results

A total of 25 community-dwelling women were included in the study, with a mean age of 70.3 years (range: 59–82). Participants were dichotomized into an older group ( $n = 14$ , age  $\geq 70$  years) and a younger group ( $n = 11$ , age  $< 70$  years). IOH was present in 14 participants, while 11 did not meet the criteria for IOH. Based on BMI, 15 participants were classified as overweight or obese ( $\text{BMI} \geq 25 \text{ kg/m}^2$ , range: 25–36), and 10 were considered non-overweight ( $\text{BMI} 17$  to  $< 25 \text{ kg/m}^2$ ). Regarding medication use, 8 participants reported current use of antihypertensive medications, while 17 were not taking any such medications. Physical frailty was assessed using the continuous SHARE-FI score; 12 participants had a score  $< -0.5$  (classified as less frail), while 13 scored  $\geq -0.5$  and were considered to have higher frailty.

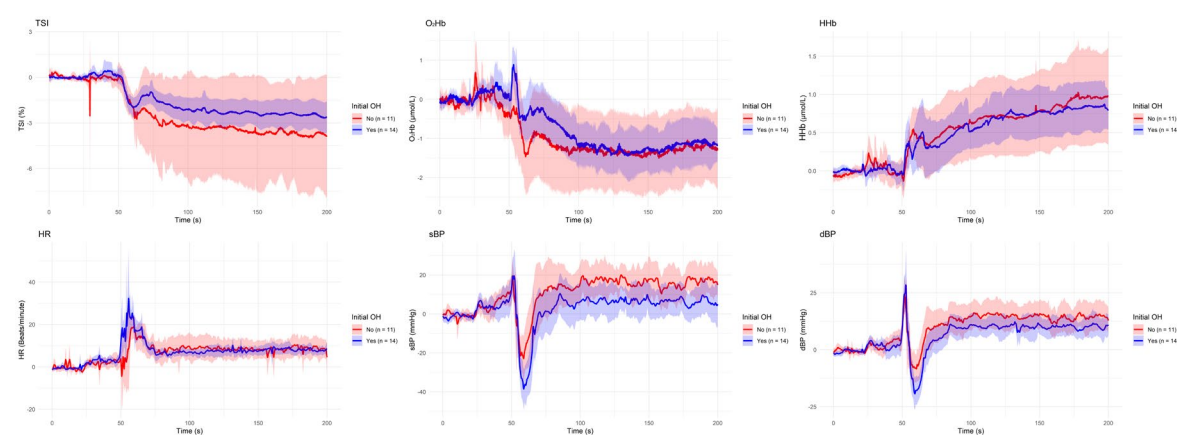
Figures 1 through 5 present the group-level time-series plots of six physiological signals—TSI,  $\text{O}_2\text{Hb}$ , HHb, HR, sBP, and dBP—during the active stand test, stratified by the characteristics of

interest. Each plot displays mean trajectories with 95% confidence intervals for two comparison groups, covering a 200-second window (0–200 s) with the stand occurring at 50 seconds. Specifically, Figure 1 compares responses between younger (<70 years) and older ( $\geq 70$  years) participants; Figure 2 compares those with and without initial orthostatic hypotension (IOH); Figure 3 compares non-overweight (BMI <25 kg/m<sup>2</sup>) and overweight/obese (BMI  $\geq 25$  kg/m<sup>2</sup>) participants; Figure 4 contrasts participants based on antihypertensive medication use; and Figure 5 shows trajectories by physical frailty status based on median SHARE-FI score.

Figures 6 and 7 present the results of the FDA conducted on the neurovascular (Figure 6) and cardiovascular (Figure 7) signals, respectively. Each plot displays the  $F^2(t)$  test statistic curve for the relevant grouping variables, illustrating the moments in time where statistically significant differences between groups emerged. Peaks that exceed the permutation-derived significance threshold (dotted line) indicate time intervals of meaningful group-level divergence. Figure 6 focuses on the NIRS-derived signals, while Figure 7 shows the results for the cardiovascular signals. Table 1 provides a summary of these significant findings, including the direction of differences and the approximate time periods post-stand where group-level divergences lasting at least 5 consecutive seconds were observed.

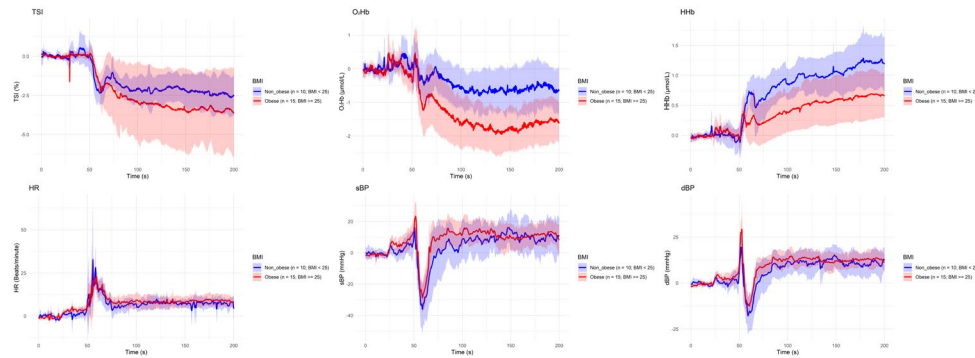


**Figure 1.** Group-level mean trajectories with 95% confidence intervals for neurovascular and cardiovascular signals during the active stand test, stratified by age group. Participants were classified as younger (<70 years, n = 11; blue line) or older ( $\geq 70$  years, n = 14; red line). The active stand was initiated at 50 seconds. Signals shown include tissue saturation index (TSI), oxygenated hemoglobin (O<sub>2</sub>Hb), deoxygenated hemoglobin (HHb), heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP).

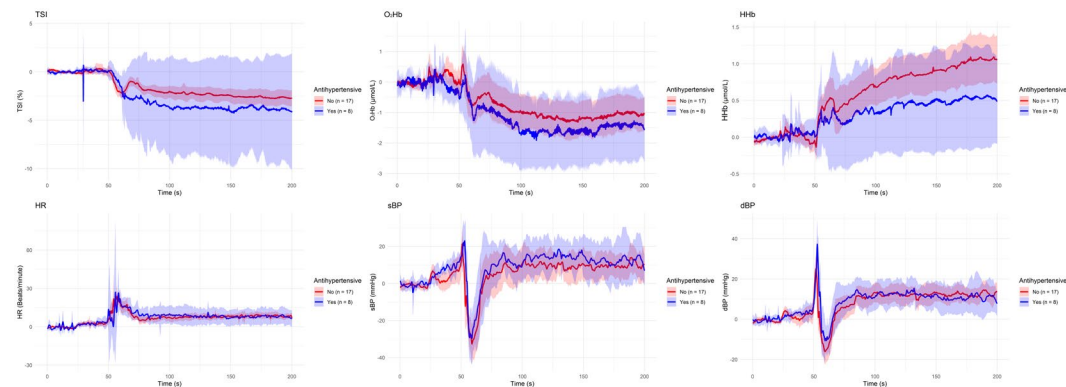


**Figure 2.** Group-level mean trajectories with 95% confidence intervals for neurovascular and cardiovascular signals during the active stand test, stratified by presence of initial orthostatic hypotension (IOH). Participants were classified as IOH positive (n = 14; blue line) or IOH negative (n = 11; red line) based on standard hemodynamic criteria. The active stand was initiated at 50 seconds. Signals shown include tissue saturation

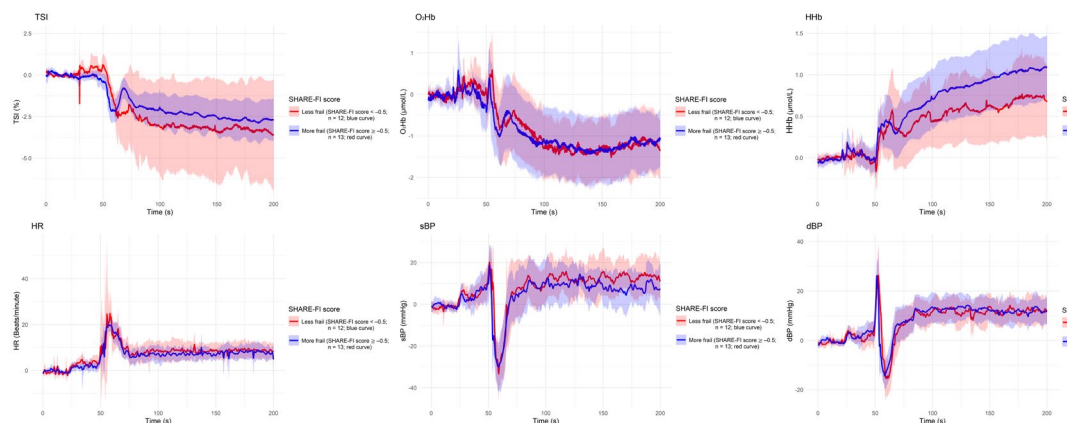
index (TSI), oxygenated hemoglobin ( $O_2Hb$ ), deoxygenated hemoglobin (HHb), heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP).



**Figure 3.** Group-level mean trajectories with 95% confidence intervals for neurovascular and cardiovascular signals during the active stand test, stratified by body mass index (BMI). Participants were classified as non-overweight (BMI < 25 kg/m<sup>2</sup>, n = 10; blue line) or overweight/obese (BMI ≥ 25 kg/m<sup>2</sup>, n = 15; red line). The active stand was initiated at 50 seconds. Signals shown include tissue saturation index (TSI), oxygenated hemoglobin ( $O_2Hb$ ), deoxygenated hemoglobin (HHb), heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP).



**Figure 4.** Group-level mean trajectories with 95% confidence intervals for neurovascular and cardiovascular signals during the active stand test, stratified by antihypertensive medication use. Participants were categorized as not using antihypertensive medication (n = 17; red line) or currently using antihypertensive medication (n = 8; blue line). The active stand was initiated at 50 seconds. Signals shown include tissue saturation index (TSI), oxygenated hemoglobin ( $O_2Hb$ ), deoxygenated hemoglobin (HHb), heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP).

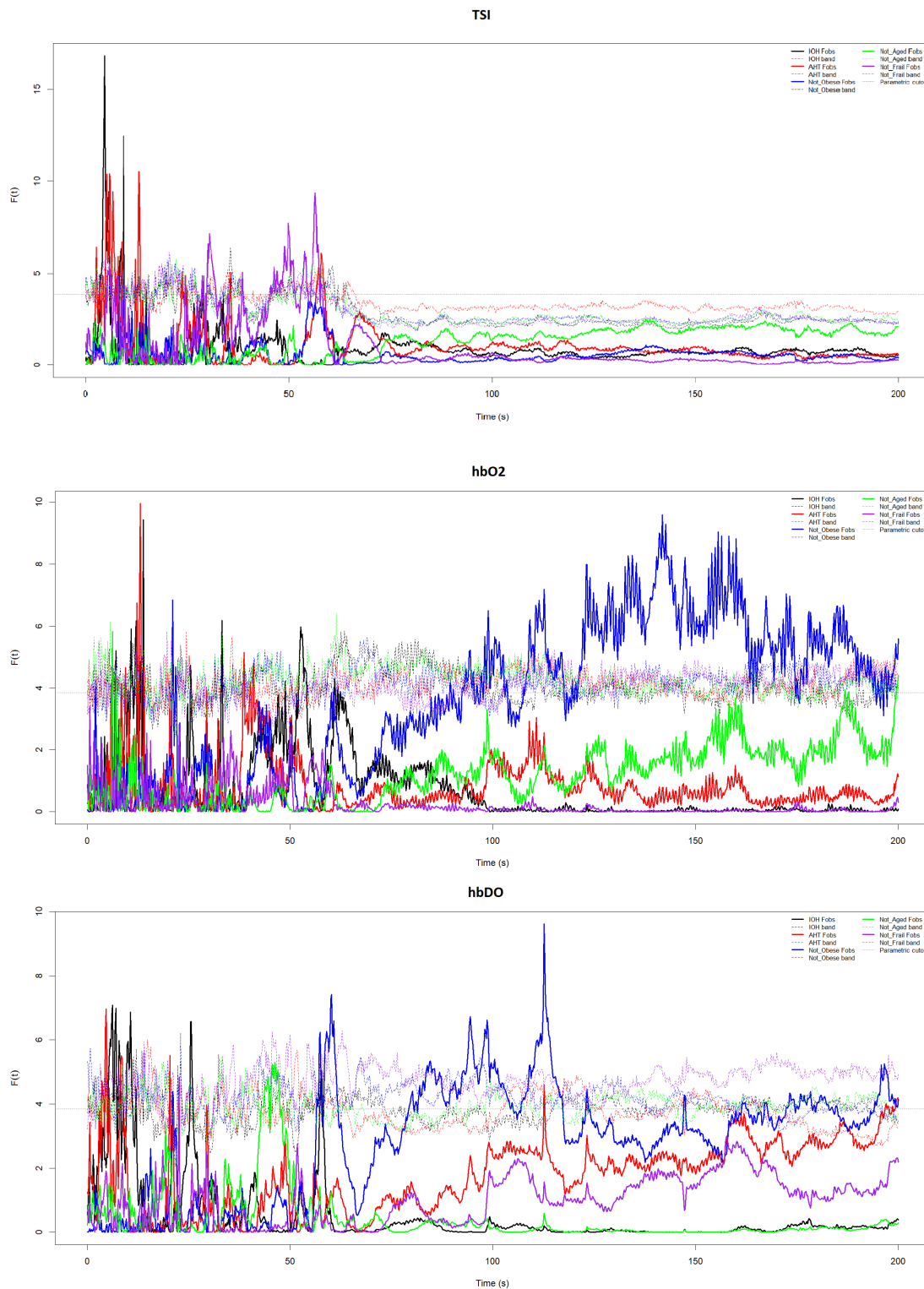


**Figure 5.** Group-level mean trajectories with 95% confidence intervals for neurovascular and cardiovascular signals during the active stand test, stratified by physical frailty status. Participants were classified as less frail (SHARE-FI score < -0.5; n = 12; blue curve) or more frail (SHARE-FI score ≥ -0.5; n = 13; red curve). The active stand was initiated at 50 seconds. Signals shown include tissue saturation index (TSI), oxygenated hemoglobin (O<sub>2</sub>Hb), deoxygenated hemoglobin (HHb), heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP).

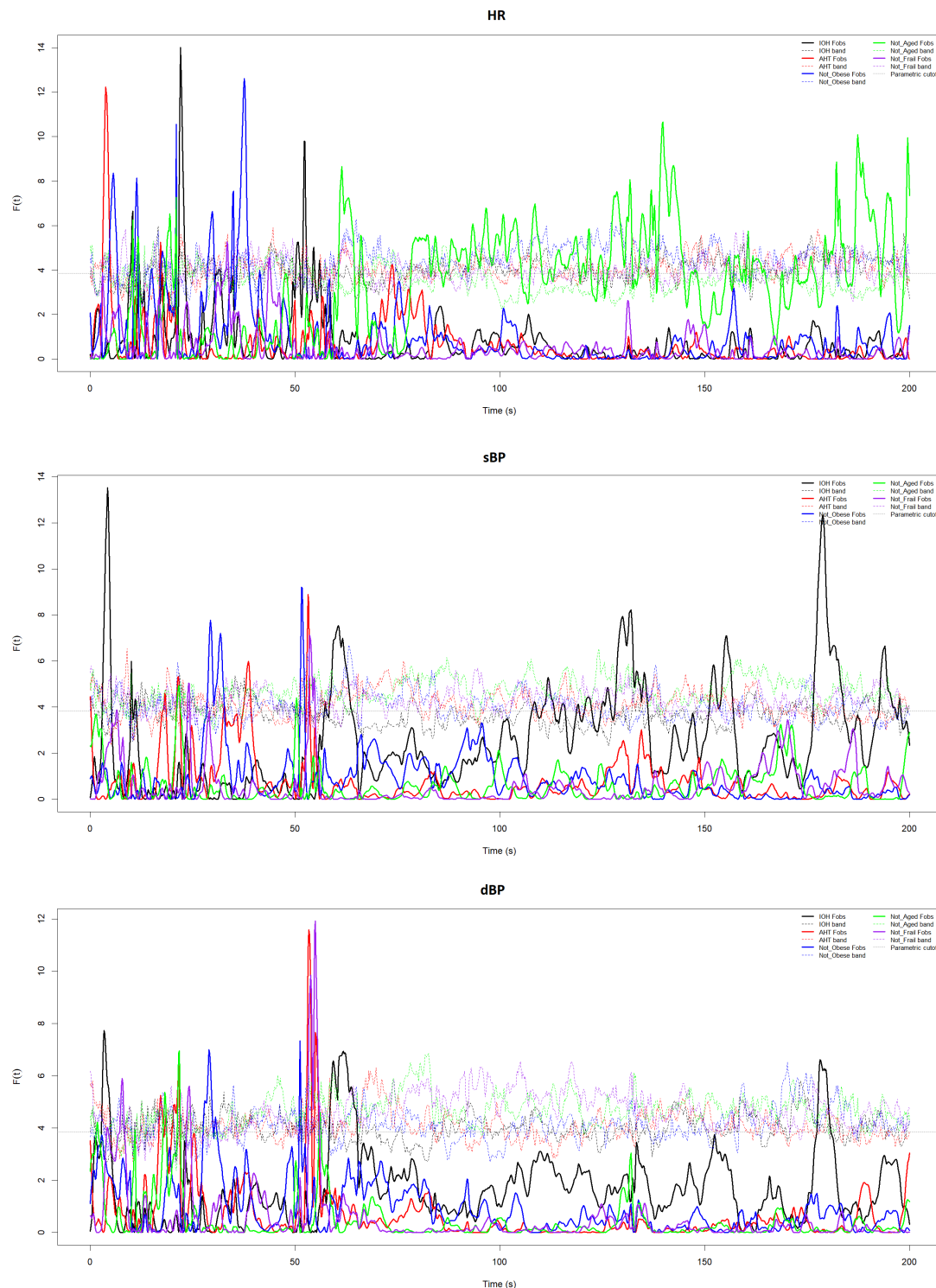
**Table 1.** Summary of statistically significant group-level differences in neurocardiovascular responses during the active stand test as identified by functional data analysis (FDA). Each row represents a dichotomous grouping variable (e.g., age, IOH status) and the corresponding physiological signal(s) where significant differences were observed. The "Direction of Difference" column indicates which group had lower values, and the "Significant Period(s)" column reports approximate time intervals post-stand (in seconds) during which the difference exceeded the permutation-derived threshold for at least 5 consecutive seconds.

Grouping Criterion	Signal	Direction of Difference (Group with Lower Value)	Significant Period(s)
Younger (<70 years)	HR	Aged (≥70 years) < Younger	~60 s, ~80 s, ~140 s, ~190 s
IOH: Yes	sBP	IOH < Non-IOH	~60 s, ~130 s, ~180 s
IOH: Yes	dBP	IOH < Non-IOH	~60 s
Overweight (BMI ≥25 kg/m <sup>2</sup> )	HHb	Overweight < Non-overweight	~60 s, ~90–100 s, ~110 s
Overweight (BMI ≥25 kg/m <sup>2</sup> )	O <sub>2</sub> Hb	Overweight < Non-overweight	~100 s, ~110 s, ~120–160 s, ~180 s
Antihypertensive Use: Yes	None	—	—
Frailty (SHARE-FI ≥-0.5)	None	—	—





**Figure 6.** Functional data analysis (FDA) test statistic curves ( $F^2(t)$ ) for neurovascular signals—tissue saturation index (TSI), oxygenated hemoglobin ( $O_2Hb$ ), and deoxygenated hemoglobin (HHb)—during the active stand test. Each solid-colored line represents the  $F^2(t)$  curve corresponding to a specific group comparison (age, IOH, BMI, antihypertensive use, and frailty). The dashed horizontal line denotes the permutation-derived critical value ( $p < 0.05$ ). Periods where the  $F^2(t)$  curve exceeds this threshold for  $\geq 25$  consecutive seconds were interpreted as clinically significant differences in signal trajectories between groups. The active stand commenced at 50 seconds.



**Figure 7.** Functional data analysis (FDA) test statistic curves ( $F^2(t)$ ) for cardiovascular signals—heart rate (HR), systolic blood pressure (sBP), and diastolic blood pressure (dBP)—during the active stand test. Each solid-colored line represents the  $F^2(t)$  curve corresponding to a specific group comparison (age, IOH, BMI, antihypertensive use, and frailty). The dashed horizontal line indicates the permutation-derived critical threshold ( $p < 0.05$ ). Time intervals where the  $F^2(t)$  curve exceeds this threshold for  $\geq 5$  consecutive seconds post-stand (initiated at 50 seconds) were interpreted as statistically and clinically significant differences in physiological responses between groups.

## 4. Discussion

This pilot study, conducted in a sample of older women, aimed to examine whether dichotomous participant characteristics—related to age, IOH, BMI, antihypertensive medication use, and physical frailty status—were associated with differential neurocardiovascular responses to an active stand test. Functional data analysis (FDA) was employed to characterize the timing and nature of postural adaptation patterns beyond conventional time-point comparisons. Group-level differences revealed that younger participants (<70 years) exhibited significantly higher HR at multiple periods following the stand (~10 s, ~30 s, ~90 s, and ~140 s post-stand) compared to their older counterparts. Participants with IOH demonstrated significantly lower sBP at ~10 s, ~80 s, and ~130 s post-stand, and lower dBP at ~10 s post-stand. Among participants classified as overweight/obese (BMI  $\geq 25$  kg/m<sup>2</sup>), significantly lower levels of HHb were observed at ~10 s, ~30–50 s, and ~60 s post-stand, while O<sub>2</sub>Hb levels were reduced at ~50 s, ~60 s, ~70–110 s, ~130 s, and ~140 s post-stand. No statistically significant group-level differences were observed based on antihypertensive medication use or frailty status.

The observed group-level differences in HR and blood pressure following the orthostatic challenge are consistent with established physiological mechanisms and prior literature. The finding that younger participants exhibited greater post-stand HR elevations aligns with well-documented age-related declines in baroreflex sensitivity and autonomic responsiveness, which contribute to a diminished chronotropic response in older adults [6,29–31]. Similarly, the lower sBP and dBP observed among participants with IOH is expected and consistent with the diagnostic criteria for IOH—particularly around 10 seconds post-stand—as well as previously published findings [7].

These expected and internally consistent findings support the validity of the BMI-related results and reduce the likelihood that they are spurious. Notably, participants with a BMI  $\geq 25$  kg/m<sup>2</sup> exhibited significantly lower levels of O<sub>2</sub>Hb and HHb in the frontal cortex following the orthostatic challenge, suggesting impaired cerebral oxygenation in individuals with excess adiposity. This observation is in line with work by Knight et al. (2021), who demonstrated that higher BMI, waist circumference (WC), and waist-to-hip ratio (WHR) were each associated with lower cerebral blood flow in older adults, as measured by arterial spin labeling MRI. Their analysis further highlighted that a 1 cm increase in waist circumference had an equivalent impact on cerebral perfusion as one additional year of aging, underscoring the vascular burden of central adiposity. Importantly, they also found that high levels of physical activity moderated the negative associations between obesity metrics and cerebral blood flow. Taken together, these findings reinforce the plausibility of our NIRS-based observations and point to a physiologically grounded mechanism whereby increased adiposity impairs neurovascular function [32].

In contrast, no statistically significant differences were observed based on antihypertensive medication use or frailty status. The absence of medication-related effects may reflect the heterogeneity of antihypertensive drug classes represented in the sample, or the varying influence of these agents on autonomic and vascular tone. Similarly, the binary classification of frailty using the SHARE-FI threshold may have lacked the sensitivity to detect more nuanced differences in physiological reserve, particularly within this relatively high-functioning cohort. Indeed, according to the original SHARE-FI classification [14], only four participants met criteria for pre-frailty, while the remainder were classified as non-frail. Although the use of a median split allowed for the construction of two approximately equal-sized comparison groups, it may not have captured a clinically meaningful distinction in physical frailty status in a sample composed predominantly of robust individuals.

Although this finding did not reach statistical significance in our analysis, the observation that younger adults exhibited a larger post-stand drop in O<sub>2</sub>Hb—remaining lower during the recovery phase compared to older participants—has also been noted by Klop et al. in small samples of both community-dwelling individuals and geriatric outpatients, although it was not formally tested for statistical significance in their work [33]. In addition, Klop et al. reported that cerebral oxygenation recovery values were lower in participants with orthostatic hypotension (OH), and that those who

experienced symptomatic OH exhibited a deeper maximum O<sub>2</sub>Hb drop than those with asymptomatic responses [34]; however, in their study, OH was defined as a drop in systolic BP of  $\geq 20$  mmHg and/or diastolic BP of  $\geq 10$  mmHg occurring 1 to 3 minutes after standing, based on a 5-second moving average—consistent with the classical OH definition [35], not initial IOH. Notably, none of our included participants met criteria for classical OH. In relatively healthy individuals, IOH has been associated with faster standing speeds and may reflect effective compensatory mechanisms rather than pathological dysregulation [36–38]. It is therefore possible that the suggested trend toward higher O<sub>2</sub>Hb levels at 10–20 seconds post-stand in our sample may represent a compensatory response in otherwise healthy individuals adapting to a transient BP drop. This potential relationship warrants further investigation in larger, well-characterized cohorts. Furthermore, although not statistically significant in our analysis, there was a possible trend toward an exaggerated orthostatic sBP pressor response in participants with elevated BMI. This is consistent with prior evidence linking obesity and related conditions—such as diabetes, hypertension, and aging—with exaggerated orthostatic pressor responses (ERTS) or orthostatic hypertension (OHT), likely due to heightened sympathetic activity and baroreflex dysregulation [39]. Again, further investigation in larger samples is warranted.

Several methodological considerations merit acknowledgment. First, the modest sample size limited statistical power, particularly for subgroup comparisons. Although FDA improves sensitivity to time-localized effects in small samples, it remains susceptible to signal noise and individual variability—especially when multiple physiological signals are analyzed concurrently. Second, the study cohort was restricted to community-dwelling older women, which limits the generalizability of the findings to men and to more frail or institutionalized populations. Third, while NIRS provides a valuable, non-invasive proxy of cortical oxygenation, it is influenced by extracranial blood flow and does not offer a direct measure of cerebral perfusion. Additionally, the cross-sectional observational design precludes causal inference and limits conclusions about the long-term clinical implications of the observed responses.

Furthermore, although continuous physiological monitoring provides high temporal resolution, such data are vulnerable to motion-related and technical artifacts—particularly around the transition from supine to standing. In this study, transient fluctuations were observed both pre- and post-stand, which may reflect artifacts rather than true physiological changes. To mitigate this, a conservative approach was adopted: only group differences that statistically persisted for at least five consecutive seconds were considered clinically meaningful. While this criterion helped reduce the influence of brief, potentially spurious spikes, it may also have excluded short-duration responses of physiological relevance. Future work should incorporate automated artifact detection algorithms and larger, more diverse cohorts to validate and extend these exploratory findings.

Despite the study's limitations, the findings support the feasibility and utility of FDA for evaluating continuous physiological responses under clinically relevant testing conditions. FDA enables time-resolved analysis of complete signal trajectories, providing a valuable alternative to conventional methods—especially in studies with limited sample sizes or exploratory aims. The results indicate that elevated BMI, older age, and the presence of IOH may be associated with distinct neurocardiovascular response patterns during orthostatic challenge. These physiological differences may help explain increased susceptibility to falls, syncope, and cognitive impairment in older adults, particularly among those older and with higher adiposity. However, further research involving larger, more diverse populations and longitudinal follow-up is needed to validate these observations and clarify their clinical relevance.

**Author Contributions:** Conceptualization, F.X. and R.R.O.; methodology, F.X. and R.R.O.; formal analysis, F.X. and R.R.O.; investigation, F.X. and R.R.O.; resources, R.R.O.; data curation, F.X. and R.R.O.; writing—original draft preparation, F.X. and R.R.O.; writing—review and editing, F.X. and R.R.O.; visualization, F.X.; supervision, R.R.O.; funding acquisition, R.R.O. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Tallaght University Hospital/St. James's Hospital Joint Research Ethics Committee as an amendment to the original FRAILMatics study (Project ID: 0221; approval date: 2 August 2022).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are available on reasonable request from the corresponding author. The data are not publicly available due to ethical and privacy restrictions, as they contain identifiable information collected from human participants.

**Conflicts of Interest:** The authors declare no conflicts of interest. The funder had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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