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SUPINE HYPERTENSION

Supine Hypertension Is Associated With an Impaired Cerebral Oxygenation Response to Orthostasis: Finding From The Irish Longitudinal Study on Ageing

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ABSTRACT: The cerebrovascular effects of supine hypertension (SH) are still poorly understood. With aging and atherosclerosis of the vascular system, it is not uncommon for SH and non-neurogenic orthostatic hypotension to co-occur. Given evidence for end organ damage and more extreme cerebral dysfunction in those with SH-orthostatic hypotension, we hypothesized that SH would be associated with impaired cerebral autoregulation. The aim of this study was to characterize the cerebrovascular response to orthostasis. Near-infrared spectroscopy was used to quantify the cerebrovascular response. We analyzed data from Wave 3 of TILDA (The Irish Longitudinal Study on Ageing; n=2750). Cerebral oxygenation and blood pressure (BP) were monitored continuously during an active stand. Responses were modeled using multilevel mixed-effects models and adjusted for important covariates such as age, sex, education, antihypertensive medications, and comorbidities. Forty-nine percent of the sample had SH. Those with SH demonstrated an impaired BP response and a slower recovery of BP after standing, graded by severity of SH. The cerebral oxygenation response was similar for both groups, but when standardized to mean arterial BP, the response was impaired in those with SH. A deficit of −0.83% (95% CI, −0.93 to −0.74) remained after 3 minutes of standing. Our study determined that cerebral oxygenation and cerebral autoregulation are impaired in those with SH. In older patients, consideration should be given to measuring SH and screening for orthostatic hypotension. Therapeutic studies are needed to better understand the relationship between cerebral oxygenation, medications, supine BP, and orthostatic hypotension.

Key Words: aging ■ blood pressure ■ cerebral hemodynamics ■ hemodynamics ■ hypotension, orthostatic

Nonstandard Abbreviations and Acronyms

BP	blood pressure
CA	cerebral autoregulation
DBP	diastolic blood pressure

MAP	mean arterial pressure
NIRS	near-infrared spectroscopy
OH	orthostatic hypotension
PWV	pulse wave velocity
SBP	systolic blood pressure
SH	supine hypertension
TILDA	The Irish Longitudinal Study on Ageing
TSI	tissue saturation index
TUG	timed up and go
WMH	white matter hyperintensities

Supine hypertension (SH) is a paradoxical elevation in blood pressure (BP) upon assuming a supine position for 5 to 10 minutes. It is a potential risk factor for end organ damage and poor cardiovascular outcomes, but its cerebrovascular effects are still poorly understood.[1] To date, most research on SH has been conducted in the context of neurogenic orthostatic hypotension (OH).[1] However, with aging and atherosclerosis of the vascular system, it is not uncommon for SH and non-neurogenic OH to co-occur. This poses a therapeutic challenge.[2]

Cerebral autoregulation (CA) is the process that maintains a constant cerebral blood flow and oxygenation despite changes in systemic BP. CA is essential for normal cognitive function and brain health. The autonomic nervous system and the baroreflex are key in adapting to BP fluctuations, such as those induced by postural change, by modulating cardiovascular resistance via vasoconstriction and vasodilation to ensure a constant flow. Maintaining a constant cerebral blood flow may be a challenge at extremes of BP.[3] With age, mechanisms that adapt to maintain peripheral BP can be deficient. These include decreased baroreflex sensitivity[4] and increased vascular stiffness, resulting in increased pulsatility, as well as decreased muscle pump,[5] which can lead to extreme BP and challenge CA.

OH is defined by consensus statement as a sustained drop ≥20 mm Hg in systolic BP (SBP) or ≥10 mm Hg in diastolic BP (DBP) upon assuming the upright position.[6] It is associated with falls,[7] frailty, cognitive impairment,[8] dementia,[9] depression,[10] cardiovascular morbidity, and mortality.[11] Impaired CA and cerebral hypoperfusion is a pathway that has been implicated in these outcomes.

In some cases of SH, BP fails to dip at night.[12] This is associated with natriuresis and consequently volume depletion, all of which exaggerate morning OH, increasing the risk of falls.[13] Nocturnal nondipping is also a risk factor for cardiovascular damage, including cerebrovascular damage.[14]

Our group has already demonstrated, both cross-sectionally and longitudinally, that those with SH-OH display poorer cognitive performance alone across multiple cognitive domains than those with SH alone.[8,15] In a small synucleinopathy cohort (n=57; 67% had SH), SH was associated with increased white matter hyperintensities (WMH), decreased renal function, greater left ventricular hypertrophy, earlier cardiovascular events, and shorter survival times from these events.[16] A previous study by TILDA (The Irish Longitudinal Study on Ageing) using cardiac beat-to-beat recording technology identified a pattern in those with SH, which demonstrated a large drop in BP and nonrecovery to baseline upon standing.[17] This pattern was a predictor of orthostatic intolerance, suggesting a higher hypotensive burden in those with SH. The cerebrovascular response remains to be examined directly.

Given evidence for end organ damage and more extreme cerebral dysfunction in those with SH-OH, we hypothesized that SH would be associated with impaired CA. The aim of this study was to characterize the cerebrovascular response to orthostasis in a large cohort of older adults with SH. Near-infrared spectroscopy (NIRS) was used to quantify the cerebrovascular response.

METHODOLOGY

Data Availability

Due to the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers should be directed to TILDA, Trinity College Dublin, Dublin 2, via email at tilda@tcd.ie.

Sample

This was a cross-sectional study that utilized data from Wave 3 (2014–2015) of TILDA. TILDA is a large prospective cohort study collecting a range of health, social, and economic data on those aged ≥50 years living in Ireland. The sampling and design have been described previously.[18,19] Data collection began in 2009 with 8504 community-dwelling adults. Participants complete a computer-assisted personal interview and self-completion questionnaire every 2 years and every ≈4 years are invited for a comprehensive health assessment. The study was granted ethical approval by the Research Ethics Committee at Trinity College Dublin and complied with the Declaration of Helsinki. Written informed consent was obtained from all participants. Participants who completed an active stand challenge at Wave 3 were eligible for this analysis. Those with known Alzheimer, dementia, or Parkinson disease were excluded due to known effects on cerebral blood flow and autonomic control.

Active Stand Protocol

Participants lay supine for ≈10 minutes in a room at ambient temperature before being asked to stand as quickly as possible. They were aided by a nurse when required. They remained standing quietly for a further 3 minutes. Cerebral oxygenation was continuously recorded by an NIRS Portalite system (Artinis Medical Systems, Zetten, the Netherlands) at 50 Hz. A single probe was placed on the left forehead, approximately at a position corresponding to FP1 of the international 10- to 20-electrode placement system.[20] Using 2 different wavelengths (nominally 760 and 850 nm), the device determines concentrations of oxygenated hemoglobin and deoxygenated hemoglobin based on the principle of the modified Beer-Lambert law.[21] Multiple transmitters with inter-optode distances of 30, 35, and 40 mm allow determination of absolute values of cerebral oxygenation using spatially resolved spectroscopy. Based on inter-optode distances, measurements are at a maximum depth of 20 mm. Spatially resolved spectroscopy minimizes the extracerebral influences.[22] The output, tissue saturation index (TSI), was calculated as oxygenated hemoglobin expressed as a percentage of total oxygenated hemoglobin and deoxygenated hemoglobin. BP, heart rate, and cardiac output were continuously monitored using digital photoplethysmography (Finometer; Finapres Medical Systems, Arnhem, the Netherlands) sampled at 200 Hz. The height correction unit, which is part of the Finometer, corrected for hydrostatic pressure differences between the finger cuff and the heart level. At the start of each test, the height sensors were calibrated by nulling.[23] Then

one was sensor placed on the finger cuff and one placed on an arm sling at heart level. Mean arterial pressure (MAP) was determined by the Finometer as the true integrated mean pressure between the current and the next upstroke.[23,24]

Signal Processing

NIRS and Finometer data were resampled to 1 Hz and smoothed using a 10-s moving average filter and an 11-point median filter. These were implemented in MATLAB R2016b. The onset of the stand and time to transition from supine to standing (standing speed) were determined by applying an algorithm using the Finometer height correction unit data.[25] Baseline was calculated from the average response 60 to 30 s before stand onset. Data from a number of participants were excluded due to technical problems with equipment or signal processing. These cases can reasonably be assumed to be random occurrences.

Supine Hypertension

SH was first classified as binary yes (SBP ≥140 mm Hg and DBP ≥90 mm Hg) or no (SBP <140 mm Hg and DBP <90 mm Hg) using baseline values. A graded severity classification of none (SBP <140 mm Hg and DBP <90 mm Hg), mild (SBP, 140–159 mm Hg and DBP, 90–99 mm Hg), moderate (SBP, 160–179 mm Hg and DBP, 100–109 mm Hg), or severe (SBP ≥180 mm Hg and DBP ≥110 mm Hg) was also used. These cutoffs are in line with recent guidelines for neurogenic SH[26] in the absence of established non-neurogenic SH cutoffs.

Covariates

Selected covariates included age, sex, educational attainment, smoking history, problematic alcohol intake based on the Cut down, Annoyed, Guilty, and Eye-opener questionnaire,[27] diabetes, number of cardiovascular conditions (transient ischemic attack, stroke, hypertension, angina, heart attack, congestive heart failure, high cholesterol, heart murmur, or any abnormal heart rhythm), cancer, kidney disease, antihypertensive medications (anatomical therapeutic chemical codes C02, C03, C07, C08, or C09), antidepressant medications (anatomical therapeutic chemical code N06A), benzodiazepines (anatomical therapeutic chemical code N05BA), antipsychotics (anatomical therapeutic chemical code N05A), timed-up-and-go (TUG) test (time taken to stand up from a chair, walk 3 m, turn, and sit back down), height, body mass index, depressive symptoms (short form of the Centre for Epidemiological Studies Depression) scale,[28] standing speed, change in cardiac output, and pulse wave velocity (PWV). Carotid-femoral PWV was measured using Vicorder (Skidmore Medical, Ltd, Bristol, United Kingdom) and calculated as an average of 2 measurements. Seated BP was calculated as an average of 2 readings from an automatic oscillometric sphygmomanometer (Omron).

Statistical Modeling

Data were analyzed using Stata 14 (StataCorp, TX). Our analysis includes active stand data at 10-s intervals from 0 to 180s, with time 0 s being the onset of the stand. We used linear multilevel mixed-effects models to examine relationships with SH. Fixed and random effects (random intercept) accounted for repeated measurements within participants. Linear splines were fitted to the data with knots at 0, 10, 20, 30, and 50 s, corresponding to the phases of the response (0–10, 10–20, 20–30, 30–50, and 50–180 s). An autoregression covariance matrix with a lag of 1 was applied to model residual variance over time as time points closer together are more strongly correlated.

First, we examined the BP response (absolute and change from baseline) adjusted for age, sex, education, and height by SH severity. Next, we examined change in TSI from baseline in those with and without SH, adjusted for age, sex, education, and height. To assess CA efficiency, we additionally adjusted for beat-to-beat MAP at all time points during the stand, thus examining the TSI response standardized to MAP. This method is similar to transcranial Doppler and NIRS studies, which assess CA via a CA index, that is, a ratio of cerebral blood flow and BP.[29,30] A fully controlled model also adjusted for smoking history, alcohol excess, stand transition time, depressive symptoms, antidepressant medications, antihypertensive medications, benzodiazepines, antipsychotics, diabetes, number of cardiovascular conditions, cancer, kidney disease, body mass index, TUG time, change in beat-to-beat cardiac output, seated SBP, and PWV. Finally, we looked at change in TSI from baseline by SH severity adjusted for the full set of covariates.

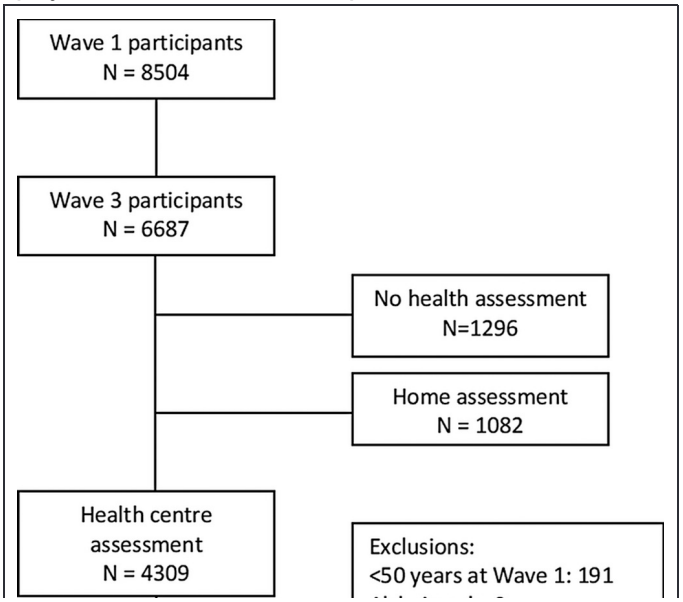
Sensitivity Tests

We included sensitivity tests to examine the effect of cardiac output and heart rate on the TSI response. First, we assessed the cardiac output and heart rate responses after standing by SH category. We examined the effect of cardiac output on the TSI response in a model adjusting for age, sex, height, and change in cardiac output only and then additionally adjusting for MAP. Similarly, we examined the effect of heart rate on the TSI response adjusting for age, sex, height, and heart rate only and then additionally adjusting for MAP.

RESULTS

Participant Characteristics

Valid data were available for 2750 participants (Figure 1). Almost half the sample (49%) had SH. Table S1 in the Data Supplement displays the severity of SH. Those with SH were older, more likely to be women, taking antihypertensive medications, have a higher PWV, and a slower TUG. Supine TSI was not different in those with or without SH. Full characteristics by SH are shown in Table S2. Characteristics of excluded cases are shown in Table S3. Compared with the final sample, they were older, had a higher percentage of current smokers, and were more likely to rate their physical health as fair or poor.



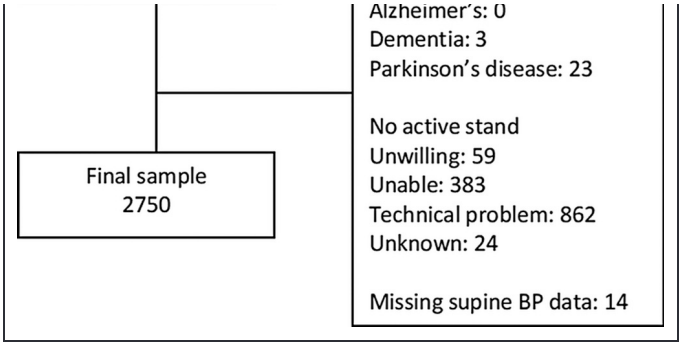


Figure 1. **Data available for analysis.** BP indicates blood pressure.

BP Response

Those with SH maintained significantly higher absolute levels of MAP throughout the stand, graded by severity of SH (Figure 2, top). The change in MAP from baseline after standing revealed a graded pattern of impaired and slower recovery in those with SH (Figure 2, bottom). Those with SH experienced a larger initial drop after standing (at 10 s), which is also graded by severity of SH. After 180 s (3 minutes) of standing, those without SH and those with mild/moderate SH had returned to baseline MAP levels (Figure 2, bottom), but those with severe SH had not recovered to baseline level. Those without SH quickly returned to baseline (by 30 s).

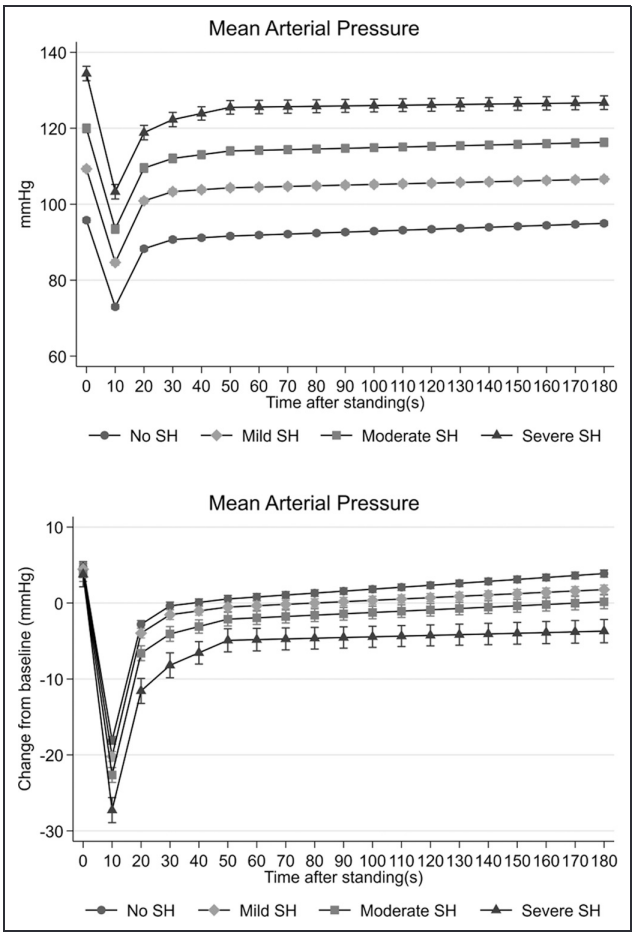


Figure 2. **Conditional means and 95% CIs for absolute mean arterial pressure by supine hypertension (SH) category, estimated from mixed-effects models, adjusted for age, sex, education, and height.** Absolute values (top) and change from baseline (bottom) are shown. As baseline is calculated as an average of readings 60 to 30 s before standing, it may not always be at 0.

Cerebral Oxygenation Response

Those with SH maintained TSI and recovered in a similar manner to those without SH (with only minor differences observed at 10- and 20-s time points; Figure 3, top). However, when the TSI response was standardized to orthostatic MAP at each time point, a graded pattern of impaired recovery emerged (Figure 3, middle), that is, when presented with the same MAP deficit (held at mean MAP values at each time point over the stand), TSI was impaired in those with SH, indicating impaired cerebral regulation. As reported above, those with SH have differing MAP profiles, and we wanted to assess TSI independent of the MAP response. Adjusting for orthostatic MAP in this manner is conceptually similar to asking the question "What if these two groups had the same MAP response on standing, how would their TSI recover?".

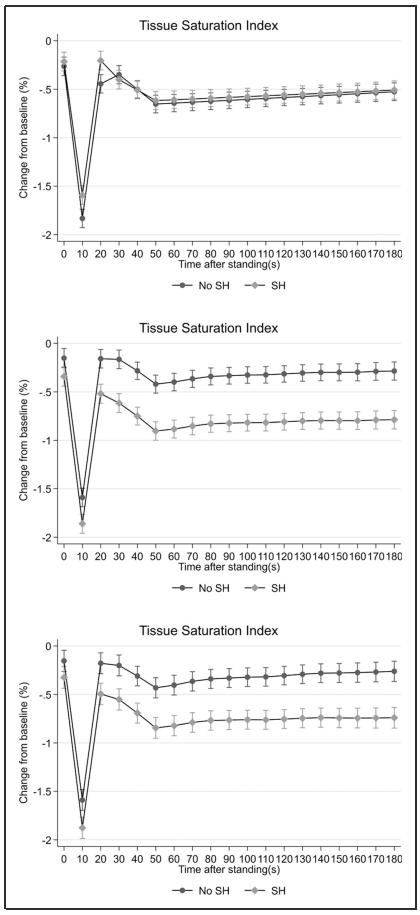
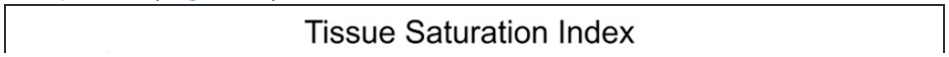


Figure 3. Conditional means and 95% CIs for change in tissue saturation index from baseline by supine hypertension (SH) estimated from mixed-effects models. Models are adjusted for age, sex, education, and height (top), additionally adjusted for beat-to-beat mean arterial pressure (middle), and additionally adjusted for smoking history, alcohol excess, stand transition time, depressive symptoms, antidepressant medications, antihypertensive medications, benzodiazepines, antipsychotics, diabetes, number of cardiovascular conditions, cancer, kidney disease, body mass index, timed-up-and-go time, change in beat-to-beat cardiac output, seated systolic blood pressure, and pulse wave velocity (bottom). As baseline is calculated as an average of readings 60 to 30 s before standing, it may not always be at 0.

After 3 minutes of standing, a deficit of −0.83% (95% CI, −0.93 to −0.74) remained in those with SH. This relationship persisted in the fully adjusted model (Figure 3, bottom). Examining the TSI response by SH severity, those with the most severe levels of SH had the largest initial drop. Overall, there is some evidence of a gradient by severity of SH, particularly in the earlier stages of the response (Figure 4).



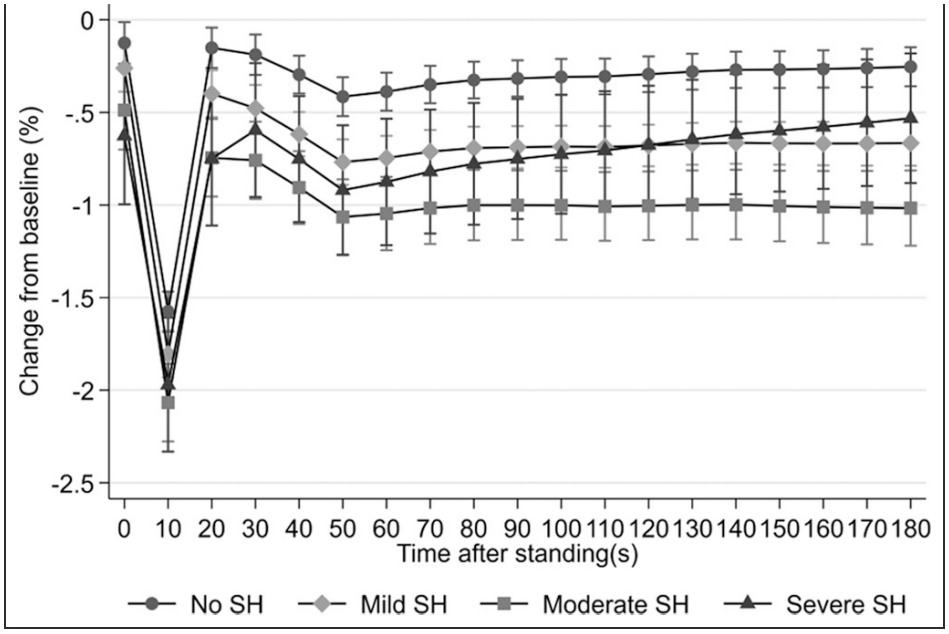


Figure 4. Conditional means and 95% CIs for change in tissue saturation index from baseline adjusted for age, sex, education, height, beat-to-beat mean arterial pressure, smoking history, alcohol excess, stand transition time, depressive symptoms, antidepressant medications, antihypertensive medications, benzodiazepines, antipsychotics, diabetes, number of cardiovascular conditions, cancer, kidney disease, body mass index, timed-up-and-go time, change in beat-to-beat cardiac output, seated systolic blood pressure, and pulse wave velocity by severity of supine hypertension (SH) estimated from mixed-effects models. As baseline is calculated as an average of readings 60 to 30 s before standing, it may not always be at 0.

Sensitivity Tests

Those with SH exhibited a greater increase in cardiac output upon standing but stabilized at lower levels than those without SH (Figure S1, top). There was no difference in maximum increase of heart rate upon standing between the groups; however, those with SH stabilized at lower levels than those without SH (Figure S1, bottom).

Adjusting for change in cardiac output (Figure S2) or heart rate (Figure S3) did not alter the TSI response compared with previous models (Figure 3).

DISCUSSION

This study demonstrated that in a large cohort of community-dwelling older adults, SH was associated with a larger drop and impaired recovery of cerebral oxygenation upon standing when standardized to orthostatic MAP. This suggests that CA is impaired and less efficient in those with SH. These effects persisted after adjusting for important covariates including age, cardiovascular conditions, and medications, as well as heart rate and change in cardiac output. TSI stabilized more quickly in those without SH or with mild SH than those in moderate/severe categories of SH.

In agreement with previous studies, we have shown that the orthostatic BP response is influenced by baseline BP levels,[31] that the magnitude of the drop is related to baseline supine BP,[32,33] and that the slowest/most impaired BP recovery is in those with the highest baseline BP.[17]

This is the first study to describe the cerebrovascular response to orthostasis and CA

efficacy in those with SH. SH may share underlying mechanisms with essential hypertension. Previous studies have reported mixed results as to whether essential hypertension impairs CA efficacy.[34–37] In chronic hypertension, the cerebral autoregulatory curve is moved to the right. Thus, tolerance to hypotension is impaired.[3] Some people with OH have an expanded autoregulatory range and, therefore, can tolerate large changes in BP.[38] However, it is generally observed in those with neurogenic OH, as evidenced by severe autonomic dysfunction. Lassen first proposed a pressure-passive relationship within the cerebral autoregulatory range of ≈60 to 150 mmHg MAP.[39] However, later studies indicate a smaller plateau[3] and even suggest that CBF and oxygenation are not independent of BP changes.[40]

Future Problems

Poor regulation of cerebral oxygenation upon standing may increase symptoms of orthostatic intolerance, falls, or syncope in the short term, all affecting quality of life. Chronic hypotensive burden may lead to functional and structural brain changes such as increased WMH and cognitive impairment and may also be a risk for hypoperfusion of other end organs. A recent study by Palma et al[16] examined longitudinal changes in those with SH. The study reported associations with WMH in SH. However, there were no differences in cognition as measured by MOCA scores, although the study was not designed/powered to detect cognitive changes. An earlier TILDA study reported poor cognitive performance in those who had both OH and SH, compared with those who had OH only,[15] as well as cognitive decline over a 4-year period in those with SH-OH.[8] This current study suggests that those with SH may have deficits in cerebral regulation, which in turn may be a pathway for cognitive impairment. Future work should explore these links.

Possible Mechanisms

The SH group had a significantly higher PWV (10.0 versus 10.9 m/s), indicating increased arterial stiffness. In chronic hypertension, arterial stiffness increases, thus increased pulsatility in the vessels[41] leads to remodeling of the vasculature and long-term changes in brain structure and function such as WMH. Evidence of remodeling in SH in the Palma study demonstrates association with increased left ventricular hypertrophy as well as WMH. In this study, we included PWV as a covariate in our fully controlled models, but this did not explain the differences in the TSI response in those with SH. We also included TUG—an indicator of sarcopenia[42] and thus muscle pump function—as a covariate. Although the SH group had a slower TUG, this did not explain the differences we observed in the TSI response. Likewise, the heart rate response or change in cardiac output did not account for the differences we observed. In fact, the increase in cardiac output was greater in those with SH, suggesting that it may be a sufficient response, although stabilization in the recovery phase was at a lower level.

METHODOLOGICAL CONSIDERATIONS

CA and CA efficiency are typically assessed by calculation of indexes that are standardized to BP. For example, Mol et al[30] defined CA as the drop in oxygenated hemoglobin divided by MAP within 60 s of postural change. However, assessment of CA based on such ratios represents a loss of information, with a reduction to a single quantitative value that does not capture the

rapid, transient, or more subtle patterns of impairment in the response. Here, we balanced the use of continuous data and the practicalities of statistical comparisons by utilizing mixed-effects models to examine multiple time points over the full time course of the response. This method also allowed us to standardize the TSI response to BP and adjust for multiple covariates of interest.

Clinical Implications

We found a remaining difference of almost 1% in TSI after 3 minutes in those with SH. Differences of this magnitude have previously been shown to be associated with clinical outcomes such as depression.[43] Bachus et al[44] also found drops in cerebral oxygenation of ≈5% (range, −2% to −10%) relating to syncope in tilt-table tests. Together, these suggest small differences in cerebral oxygenation are clinically relevant.

Treating those with SH is challenging when it is accompanied by OH, and clinical recommendations are to prioritize nonpharmacological management when possible.[1] Previous work reported that a large drop in BP and nonrecovery was associated with the use of β-blockers in particular, and antidepressants, as well as being a predictor of orthostatic intolerance.[17,45] Treatment interventions such as salt-retaining fludrocortisone used to treat OH may exasperate or even cause SH.

There is some concern that lowering BP may lead to lower cerebral blood flow and oxygenation. There is evidence from smaller studies that the cerebral autoregulatory curve is restored after treatment for hypertension and cerebral hemodynamics remain intact after lowering BP.[46] A recent study of treated chronic hypertensive patients shows that some CA measures derived from transcranial Doppler and NIRS recordings (transfer function estimates of coherence, gain, phase, and transit times) were comparable to controls.[47] However, duration of hypertension may also be a factor, and cerebrovascular resistance was increased in this cohort. Studies from the SPRINT (Systolic Blood Pressure Intervention Trial) show no increase in falls or OH prevalence after intensive lowering BP.[48] For some people, stability of BP may reduce OH. A recent SPRINT study also reported that OH was not associated with an increased risk of falls, syncope, or CVD events, even in the intensive treatment group.[49] This suggests antihypertensive treatment improves OH and the BP response, which may in turn influence the TSI response. To better understand the implications for treatment of OH and CA, it will be necessary to examine all of these components in trials and derive more precise phenotyping to guide treatments.

Current hypertension guidelines refer to seated and standing measurements for monitoring BP. However, our study highlights the importance of screening for SH, particularly in older adults, which may have additional diagnostic value in managing OH and identifying those at risk for falls. This is even more important as BP can appear lower when sitting.[50] Also, a previous study comparing seated office BP, supine BP, and ambulatory BP (n=280) reported that supine BP had greater sensitivity and specificity for diagnosing hypertension than seated BP,[51] although 24-hour ambulatory BP monitoring is a reasonable approach for capturing SH.[52]

Strengths and Limitations

Strengths of this study include the large sample size consisting of community-dwelling older adults and the comprehensive data on health behaviors, comorbidities, medication use, and demographics, which allowed for adjustment of potential confounders. Another strength is the

noninvasive continuous assessment of both peripheral BP and cerebral oxygenation. Limitations include the cross-sectional nature of the study. Blood hemoglobin and CO_2 were not measured due to practical limitations in such a large cohort. CO_2 vasoreactivity is reduced in individuals with hypertension.[53] A small reduction in CO_2 is also expected with postural change[54] contributing to a reduction in cerebral flow, evident in controls and orthostatic intolerant patients.[55] However, the relationship is complex, and cerebral CO_2 reactivity alone does not account for this drop.[56] While collection of NIRS data may be subject to interoperator, bias all TILDA health assessment data are collected by a team of rigorously trained nurses who follow a detailed protocol, minimizing such biases. Due to practicalities, participants were not asked to fast or refrain from caffeine, smoking, alcohol, or medications before the health assessment; however, this is more representative of daily living.

Conclusions

In this large population study, we determined that cerebral oxygenation and CA is impaired in those with SH, and this impairment is graded by severity of SH. The implications are that in older patients, consideration should be given to measuring SH and screening for OH. Therapeutic studies are needed to better understand the relationship between cerebral oxygenation, medications, supine BP, and OH.

Perspectives

Current routine clinical BP assessment relies on seated BP readings, but there may be benefit to screening for SH, particularly for older adults who may be at risk for OH and falls.

ARTICLE INFORMATION

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For Sources of Funding and Disclosures, see page 218.

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Disclosures

None.

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Novelty and Significance

What Is New?

- Those with supine hypertension demonstrated an impaired blood pressure response and slower recovery in response to orthostasis, graded by severity of supine hypertension.
- Those with supine hypertension displayed deficits in maintaining cerebral oxygenation after standing, when the response was standardized to mean arterial blood pressure.
- Our results suggest cerebral autoregulation is impaired in those with supine hypertension.

What Is Relevant?

- Impaired stabilization is relevant in the context of managing hypertension, as well as orthostatic hypotension, and identifying those at risk for falls.
- Currently supine hypertension is not routinely screened for in the clinic.

Summary

There is evidence of impaired cerebral oxygenation and cerebral autoregulation in this large cohort of older adults. Future clinical studies are needed to investigate the relationship between cerebral oxygenation, supine blood pressure, medications, and orthostatic hypotension.