JAMDA

journal homepage: www.jamda.com

Original Study

Hemodynamic Mechanisms Underlying Initial Orthostatic Hypotension, Delayed Recovery and Orthostatic Hypotension

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Keywords:
Systemic vascular resistance
cardiac output
orthostatic blood pressure
orthostatic hypotension
initial orthostatic hypotension
delayed blood pressure recovery

A B S T R A C T

Objectives: Continuous noninvasive blood pressure (BP) measurement enables us to observe rapid changes in BP and to study underlying hemodynamic mechanisms. This study aimed to gain insight into the pathophysiological mechanisms underlying short-term orthostatic BP recovery patterns in a real-world clinical setting with (pre)syncope patients.
Setting and Participants: In a prospective cohort study, the active lying-to-standing test was performed in suspected (pre)syncope patients in the emergency department with continuous noninvasive finger arterial BP measurement.
Measures: Changes in systolic BP, cardiac output (CO), and systemic vascular resistance (SVR) were studied in normal BP recovery, initial orthostatic hypotension, delayed BP recovery, and sustained orthostatic hypotension.
Results: In normal recovery (n = 47), ΔBP at nadir was −24 (23) mmHg, with a CO change of +10 (21%) and SVR of −23 (21%). In initial orthostatic hypotension (n = 7) ΔBP at nadir was −49 (17) mmHg and CO and SVR change was −5 (46%) and −29 (58%), respectively. Delayed recovery (n = 12) differed significantly from normal recovery 30 seconds after standing, with a ΔBP of −32 (19) vs 1 (16) mmHg, respectively. Delayed recovery was associated with a significant difference in SVR changes compared to normal recovery, −17 (26%) vs +4 (20%), respectively. There was no difference in CO changes. In sustained orthostatic hypotension (n = 16), ΔBP at 180 seconds after standing was −39 (21) mmHg, with changes in CO of −16 (31%) and SVR of −9 (20%).
Conclusions/Implications: Hemodynamic patterns following active standing are heterogeneous and differ across orthostatic BP recovery patterns, suggesting that volume status, medication use, and autonomic dysfunction should all be taken into account when evaluating these patients. Moreover, results suggest that a delayed BP recovery is associated with an impaired increase in SVR in a significant proportion of individuals, implying that physicians treating older adults with hypertension should consider the possible negative effect of intensive hypertension treatment on initial orthostatic blood pressure control.

Evaluation of blood pressure (BP) changes on standing is an important diagnostic measure in patients with complaints of orthostatic intolerance, (pre)syncope, or suspected autonomic dysfunction.[1] Symptoms on or during standing can be a debilitating condition, one that can be difficult to evaluate accurately and difficult to treat. Noninvasive measurement of continuous finger arterial pressure enables assessment of rapid changes in BP. Using this technology, a spectrum of orthostatic BP recovery patterns within 180 seconds of standing has recently been defined, that is, normal BP recovery, initial orthostatic hypotension, delayed BP recovery, and sustained orthostatic hypotension.[2–5] Initial orthostatic hypotension is common in teenagers and young adults.[3] Delayed BP recovery and sustained

The authors declare no conflicts of interest.

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https://doi.org/10.1016/j.jamda.2018.05.031
1525-8610/

orthostatic hypotension are increasingly prevalent in the older population, ranging between 11.3% and 43.1% in delayed BP recovery and 4.2% and 18.5% in sustained orthostatic hypotension in 50- to 80-year-olds.[4] Sustained orthostatic hypotension is associated with increased cardiovascular morbidity and mortality, and recent studies suggest a similar association for delayed BP recovery, pointing toward subclinical impaired physiology.[6,7] However, limited data are available regarding the hemodynamic changes underlying this spectrum of orthostatic BP recovery patterns.[8–11] Moreover, most studies have been performed in controlled laboratory settings with selected groups of healthy subjects or patients with neurodegenerative diseases.[8,9] A better understanding of the hemodynamic mechanisms of initial orthostatic hypotension, delayed BP recovery, and sustained orthostatic hypotension is an important issue given new guidelines on the treatment of hypertension in older adults.[12] Intensive treatment of hypertension could do harm in older adults by leading to falls and syncope as a result of hypotension and cerebral hypoperfusion on standing.[13,14] The aim of the present investigation was therefore to gain insight into the hemodynamic mechanisms underlying the spectrum of short-term orthostatic BP recovery patterns in (pre) syncope patients in a clinical setting.

Methods

Patient Selection

This study was conducted in the emergency department of a tertiary teaching hospital between January and August 2014. All consecutive patients older than 18 years attending the emergency department Monday to Friday (8 AM to 6 PM) and suspected of (pre) syncope were included. Syncope was defined as a transient loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.[1] Presyncope was defined as the feeling of almost losing consciousness with similar prodromal symptoms as in syncope. Patients were excluded if they were not able to stand for 5 minutes, were hemodynamically instable (supine systolic BP $<$ 90 mmHg), were in need of immediate treatment, or if a cognitive disorder impaired informed consent. Continuous noninvasive orthostatic BP measurements were performed by 2 trained researchers, approximately 1 to 2 hours after arrival at the emergency department. Patient data were derived from the medical records. The attending physicians in the emergency department work according to the syncope guideline of the European Society of Cardiology.[1] The study complied with the Declaration of Helsinki; the protocol was approved by the Medical Ethics Committee and verbal informed consent was obtained from all patients.

Protocol

For continuous measurements, Nexfin (BMEYE, Edwards Life-Sciences, Irvine, CA), a noninvasive continuous finger arterial pressure (FinAP) measurement device, was used. From the finger waveform, heart beats are detected and systolic BP, diastolic BP, mean BP, and pulse rate are derived in a beat-to-beat mode. FinAP measurement has been validated extensively as a reliable method to track orthostatic changes in BP.[15,16] Recent studies suggest that reconstructed BP levels lie between invasively measured BP and auscultatory pressures, with FinAP measurements remaining accurate at low pressures.[16]

At the start of the measurement, patients rested supine on a medical examination table. The FinAP wrist-worn unit and an appropriately sized finger cuff were affixed to the patient. The measurement hand was placed at heart level, with the height correction unit that compensates for hydrostatic pressure enabled. This height correction unit was zeroed and the automatic Physiocal was activated, according to the manufacturer's manual. Patients were instructed to be silent during the entire measurement and to avoid any movements. After 5 to 10 minutes of supine rest, patients were instructed to stand up as quickly as possible, preferably within 3 seconds. Older adults received assistance if needed. Just before standing up, the Physiocal was disabled and after 60 seconds it was reactivated. The FinAP measurement was stopped after 5 minutes of standing. Subsequently, patients were asked if they had experienced any symptoms like lightheadedness or seeing black spots during standing.

Definitions of Short-Term (180 Seconds) Orthostatic BP Recovery Patterns

The orthostatic BP recovery patterns were defined according to recent work.[4,5] Normal BP recovery was defined as recovery of systolic BP to baseline values, not exceeding a decrease of more than 20 mmHg at 30 seconds of standing. Initial orthostatic hypotension was defined as a transient decrease of $>$40 mmHg in systolic BP within 15 seconds of active standing, with complete BP recovery within 30 seconds of standing. Delayed BP recovery was defined as delayed recovery of systolic BP to baseline values of more than 20 mmHg at 30 seconds of standing, but not meeting the criteria of sustained orthostatic hypotension. Sustained orthostatic hypotension was defined as a sustained decrease in systolic BP of $\geq$20 mmHg between 60 and 180 seconds of standing. With the presence of supine hypertension (supine systolic BP $\geq$ 160 mmHg), a reduction of $\geq$30 mmHg was used. This latter criterion was not applied to the definition of delayed BP recovery.

Hemodynamic Analysis

The continuous BP measurements with Nexfin were stored on the hard disc of Nexfin for offline analysis. Using Frame Inspector (BMEYE, Amsterdam, The Netherlands), the recordings were converted to Excel files for beat-to-beat analysis. These files were used for offline inspection of the quality of the recordings, artifacts, and proper position of markers and identification of the BP recovery patterns. Artifacts were detected by visual inspection and were then either removed or linearly interpolated. The marker indicating active standing up was added during the active lying-to-standing test, but the position was re-evaluated following offline inspection. Based on changes in height correction unit, BP, and heart rate, the moment of standing up was adjusted where appropriate.

For hemodynamic analysis, the measured signal was digitally sampled at 200 Hz before storing it on the disk. Mean arterial pressure was calculated from the integral of the arterial pressure wave over 1 beat divided by the corresponding beat interval. Heart rate was computed as the inverse of the interbeat interval and expressed as beats per minute. Beat-to-beat left ventricular stroke volume expressed in milliliters was calculated by Nexfin-CO trek (BMEYE BV, The Netherlands) by dividing the area under the systolic portion of the arterial pressure curve by the aortic input impedance, similar to the method of Wesseling et al.[17] Cardiac output, expressed in liters/minute, was the product of stroke volume and heart rate. Total SVR, expressed in millimeters of mercury seconds per milliliter (mmHg s/ml), was calculated by dividing the mean arterial pressure by the computed CO. In conditions with regular heartbeats, determination of CO by noninvasive continuous FinAP measurement with Nexfin has been validated in different settings and is not different from thermodilution CO from invasive measurement.[18] Thereafter, measurements with atrial fibrillation, irregular heart beats, and too many artifacts were excluded because CO estimates are not validated in these conditions. By applying these selection criteria, we improved the reliability of the analysis of CO and SVR changes.

Resting supine values for CO and SVR were set at 100% (baseline), and changes were expressed in percentages from supine control.