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Original Article

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Comparison of the Assessment of Orthostatic Hypotension Using Peripheral and Central Blood Pressure Measurements

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Abstract

Background: Orthostatic hypotension (OH) is associated with falls and cardiovascular events. There is growing evidence that central blood pressure (CBP) is better than peripheral blood pressure (PBP) in predicting adverse outcomes. The objectives of this study were to assess 1) the prevalence of OH identified using PBP and CBP and the levels of agreement, 2) the respective associations between OH and falls and cardiovascular comorbidities, by PBP and CBP, and 3) the association of OH with arterial wall stiffness markers (augmentation pressure (AP) and augmentation index (AI)).

Methods: An observational case-control study of subjects aged 50 years and above was conducted at the University of Alberta Hospital inpatient wards and outpatient clinics. This study used a non-invasive technology called SphygmoCor to assess changes in CBP between lying, 1, 3 and 6 min of standing. AP and AI, which are markers of arterial wall stiffness, were also measured in this study. Dementia, significant psychological problems, and isolation precautions were exclusion criteria. Both PBP and CBP were measured with arm cuffs in lying and standing positions. OH was diagnosed using consensus criteria.

Results: Of the 71 participants recruited, mean age was 72.3 ±10.3 years, 52% were males, 32% had a history of falls and 72% had hypertension. OH occurred within 1, 3 or 6 min of standing (transient OH) in 31% by PBP and 27% by CBP (kappa = 0.56). OH persisted for all 6 min (persistent OH) in 16% by both PBP and CBP (kappa = 0.68). A significant relationship was observed between transient OH by CBP and baseline hypertension (P = 0.05) and dyslipidemia (P = 0.02). There was a significant difference in the mean AP between subjects with and without central persistent OH (P = 0.02), but not between subjects with and without peripheral persistent OH. The mean AI was not significantly different between subjects with or without central or peripheral persistent OH and between subjects with and without peripheral or central transient OH.

Conclusion: Prevalence of OH was similar between PBP and CBP. However, there was only moderate agreement with OH identified by PBP and CBP indicating some inconsistencies across the sample in identifying OH.

Keywords: Orthostatic hypotension; Central blood pressure; Peripheral blood pressure; Aortic stiffness

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Introduction

An accurate measurement of blood pressure (BP) and postural changes is essential to plan therapy in the elderly. Automated oscillometric devices are available and are widely used for home blood pressure monitoring (HBPM), 24-h ambulatory blood pressure monitoring and in-office monitoring. Recent innovations enable these devices to measure central blood pressure (CBP) non-invasively. In many individuals, peripheral blood pressure (PBP) measured over the brachial artery differs from aortic CBP measured through novel non-invasive techniques. Although brachial PBP has long been used clinically as the standard method of blood pressure measurement, there is growing evidence to suggest that CBP has incremental ability over PBP in predicting target organ damage and cardiovascular (CV) events [1].

Orthostatic or postural hypotension (OH/PH) is a common, under-recognized disabling condition [2]. In this condition, subjects experience a systolic blood pressure (SBP) drop of 20 mm Hg or more, or a diastolic blood pressure (DBP) drop of 10 mm Hg or more, with or without an increase in heart or pulse rate, with or without symptoms, and within 3 min after standing [3]. If this BP drop occurs at 6 min, it is called delayed OH/PH [4]. OH/PH is associated with an increased incidence of morbidities (falls, CV issues and cognitive decline) and mortality [5]. However, there is some uncertainty over the diagnostic criteria using CBP for OH/PH in patients with and without hypertension. Our hypothesis is CBP will be good in measuring OH and predicting its relevant outcomes. The objectives of this study were 1) to assess the prevalence of OH/PH using PBP and CBP, 2) to assess whether the respective association between OH/ PH and falls, OH/PH and CV

Table 1. Baseline Characteristics of Hypertensive and Normotensive Groups

Variables	Hypertensive[a] (n = 51), mean (SD) or no. (%)	Normotensive (n = 20), mean (SD) or no. (%)
Female	26 (51.0%)	8 (40.0%)
Age (years)	72.6 (11.0)	71.7 (8.5)
BMI (kg/m^2)	27.7 (6.0)	26.8 (4.3)
History of orthostatic hypotension	1 (2.0%)	0 (0.0%)
History of falls	14 (27.5%)	9 (45.0%)
Current alcohol use	13 (25.5%)	9 (45.0%)
Current or past smoker	30 (58.8%)	2 (10.0%)
Coronary artery disease	9 (17.6%)	2 (10.0%)
Stroke†	9 (17.6%)	0 (0.0%)
Heart failure	4 (7.8%)	0 (0.0%)
Type II diabetes	15 (29.4%)	2 (10.0%)
Dyslipidemia	22 (43.1%)	4 (20.0%)
Peripheral vascular disease	3 (5.9%)	1 (5.0%)
Chronic kidney disease	2 (3.9%)	1 (5.0%)
Symptoms of orthostatic hypotension	6 (11.8%)	3 (15.0%)
Use of medications associated with orthostatic hypotension†	49 (96.1%)	10 (50.0%)

[a]Obtained from medical records. †P < 0.05.

comorbidities, is stronger by CBP or PBP, and 3) to assess the association of OH with arterial wall stiffness markers (augmentation pressure (AP) and augmentation index (AI)), as the alteration of the reflection pressure wave due to arterial wall stiffness could be one of the underlying mechanisms of OH in the central artery.

Methodology

An observational case-control study was conducted over a 3-month period at the University of Alberta Hospital in Edmonton, Canada and included a convenience sample of 71 normotensive and hypertensive subjects from both inpatient wards and outpatient clinics. Each patient provided informed written consent. Inclusion criteria were age of 50 years or greater with a diagnosis of hypertension (or controls without hypertension) who were willing to participate in the study and were able to stand with or without a walking aid. Subjects who did not speak English, had a history of dementia, blindness, anxiety or significant psychological problems including schizophrenia, substance abuse, pain, medically unstable, terminal illness, who were on infection precautions or not able to consent for the study were excluded.

BP measurements were taken using a SphygmoCor device. Estimated CBP indices included central SBP, central DBP and pulse pressure. AI and AP, which are arterial wall stiffness parameters, were also measured. PBP was measured with regular BP cuffs over the brachial artery, in both supine and standing positions. First, PBP was measured in the supine position twice after 10 min of rest. Following this, PBP was measured at 1, 3 and 6 min of standing, twice for each interval. After the completion of PBP measurements, the CBP measurements were taken. Using the non-invasive SphygmoCor system, CBP was measured twice in the supine position, twice on intervals of 1, 3, and 6 min of standing, and the average of these two readings were taken. The calibrated SphygmorCor system began by measuring PBP, then switched to measure CBP, using the aortic pressure waveform estimated by a validated transfer function [6]. CBP indices, AP and AI, were also generated from this waveform. For the purpose of this study, transient OH was defined as a drop in BP meeting OH criteria (listed above) in the standing position at 1 or 3 or 6 min. Persistent OH was defined as a drop in BP at all the three time points 1, 3 and 6 min.

Demographic variables (age and sex), vascular risk factors (type 2 diabetes, hypertension, dyslipidemia, smoking, coronary artery disease, heart failure, cerebrovascular disease, peripheral vascular disease, and renal failure), history of dementia, depression and other mental illnesses, history of falls, and current medications were collected. Comorbidities were delineated from self-report and review of medical records. The presence of OH/PH related symptoms was also collected.

The outcomes of this study were 1) the prevalence of OH/PH by CBP and PBP measurements, 2) the association between comorbidities and OH/PH, 3) the agreement between OH/PH by CBP and PBP measurements, and 4) the association between transient OH and persistent OH with CV outcomes and falls.

Ethics approval was obtained from the University of Alberta Health Research Ethics Board and operations/adminis-

Table 2. Prevalence and Agreement of Orthostatic Hypotension (OH) by Peripheral and Central Blood Pressures and by Types of Orthostatic Hypotension[a]

Types of OH	Peripheral blood pressure (n = 71), no. (%)	Central blood pressure (n = 71), no. (%)	Agreement (kappa[b])
Early OH	12 (16.9%)	17 (23.9%)	0.70
OH	19 (26.8%)	12 (16.9%)	0.72
Delayed OH	18 (25.4%)	14 (19.7%)	0.44
Transient OH	22 (31.0%)	19 (26.8%)	0.56
Persistent OH	11 (15.5%)	11 (15.5%)	0.68

[a]Early OH: at 1 min of standing; OH: at 3 min of standing; delayed OH: at 6 min of standing; transient OH: at 1 or 3 or 6 min of standing; persistent OH: seen at 1, 3, and 6 min of standing. [b]Fleiss's guidelines (Fleiss et al, 2003) characterize kappa > 0.75 as excellent, 0.40 - 0.75 as good, < 0.40 as poor.

trative approval was obtained from Alberta Health Services.

Statistical analysis

Descriptive statistics were reported for all demographic and clinical parameters. The prevalence of OH/PH was described for the study sample. Baseline patient characteristics and clinical outcomes were reported according to the presence and absence of hypertension. Percentages were used to describe discrete variables, and medians with 25th and 75th percentiles were used to describe continuous variables. Differences in the means of continuous variables were tested by Student's *t*-tests or Mann-Whitney U tests. Differences in proportions were tested by Chi-square or Fisher's exact tests. Multiple logistic regression analysis was conducted to examine the association between the dichotomized morbidities and OH/PH using CBP and PBP after controlling for potential confounders. Age was dichotomized into ≤ 65 years and > 65 years. Statistical analysis was performed using STATA. A P-value of < 0.05 was considered as statistically significant.

Results

Among the 71 participants, the mean age was 72.3 ± 10.3 years, 52% were males, 32% had a history of falls and 72% had hypertension (Table 1). Of these with hypertension, 12 subjects (6%) exhibited symptomatic OH during the assessment. There was a statistically significant association between symptoms and age group (P = 0.01) but not with sex. No significant association between OH and the number of drugs used or causative drug use was found.

Using the consensus statement on the definition of OH, OH was identified at 1, 3 or 6 min of standing (transient OH) in 31% by PBP and 27% by CBP with a moderate agreement (kappa = 0.56) and across all durations (persistent OH) in 16% by both PBP and CBP with a stronger agreement (kappa = 0.68) (Table 2).

A significant relationship was observed between transient OH as measured by CBP and having hypertension (P = 0.05) and dyslipidemia (P = 0.02), but the association was not significant with other CV risk factors. There was a significant difference in the mean AP between subjects with and without central persistent OH (P = 0.02), but not between subjects with and without peripheral persistent OH. The mean AI was not significantly different between subjects with or without central or peripheral persistent OH and between subjects with and without peripheral or central transient OH. In this study, transient OH was associated with past falls (P = 0.02), but not with persistent OH (P = 0.48) (Tables 3 and 4).

Discussion

It has been appreciated that there may be significant differences between CBP and PBP. A number of studies showed measurement of the BP in aorta or CBP was related to major CV events [7, 8]. Indirect reading of CBP can be measured non-invasively by SphygomoCor system. One study showed that orthostatic symptoms are better reflected by CBP as measured non-invasively in the carotids. When carotid and brachial BPs were measured simultaneously using cuff-oscillometric and tonometric methods, the orthostatic decline in BP was more prominent in the carotid artery. In that study, while nine subjects were diagnosed with OH via the brachial BP, 21 subjects were diagnosed by carotid BP (P < 0.001), and these results indicated that evaluation of OH by brachial BP may underestimate OH [9]. These study results indicated that the evaluation of orthostatic changes with CBP may be better. However, in our study, CBP can similarly identify OH like PBP, and there was moderate agreement between transient OH at any time (kappa = 0.56) and with persistent OH (kappa = 0.68). Alteration of the reflection pressure wave could be one of the underlying mechanisms of OH in the central artery. We also saw in this study a significant association with AP only with central persistent OH, but not with other indices. OH/PH can increase the risk for multiple conditions, such as falls, which continue to be a major problem in healthcare causing extended hospital days, fractures, head injuries, and even death. By diagnosing OH/PH accurately, falls can be prevented by following non-pharmacological OH/PH precautions and modifying relevant risk factors [10]. Some prospective studies did not show an association between OH and falls [11, 12]. But in this study transient OH was associated with past falls but not seen with persistent OH, and this could be related to the small sample size of this study.

Table 3. Relationship Between Transient Orthostatic Hypotension (OH)[a], Cardiovascular and Fall-Related Outcomes by Peripheral and Central Blood Pressures

Variables	Transient OH			
	Peripheral blood pressure, mean (SD) or no. (%)		Central blood pressure, mean (SD) or no. (%)	
	No (n = 49)	Yes (n = 22)	No (n = 52)	Yes (n = 19)
Central AP (%)	14.9 (9.0)	18.0 (9.3)	14.8 (9.0)	18.7 (9.0)
Central AI (%)	29.3 (11.7)	30.2 (11.0)	28.8 (11.3)	31.8 (11.9)
Symptoms of OH	21 (42.9%)	9 (40.9%)	25 (48.1%)	5 (26.3%)
History of OH	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (5.3%)
History of falls	18 (36.7%)	5 (22.7%)	21 (40.4%)	2 (10.5%)
Hypertension	33 (67.3%)	18 (81.8%)	34 (65.4%)	17 (89.5%)†
Coronary artery disease	8 (16.3%)	3 (13.6%)	8 (15.4%)	3 (15.8%)
Stroke	7 (14.3%)	2 (9.1%)	6 (11.5%)	3 (15.8%)
Heart failure	3 (6.1%)	1 (4.5%)	2 (3.8%)	2 (10.5%)
Type II diabetes	11 (22.4%)	6 (27.3%)	13 (25.0%)	4 (21.1%)
Dyslipidemia	15 (30.6%)	11 (50.0%)	15 (28.8%)	11 (57.9%)†
Peripheral vascular disease	4 (8.2%)	0 (0.0%)	2 (3.8%)	2 (10.5%)
CKD	1 (2.0%)	2 (9.1%)	1 (1.9%)	2 (10.5%)

a. Orthostatic hypotension as measured and present at 1 or 3 or 6 min of standing. †P < 0.05.

One of the strengths of this study is that this is the first cohort study to measure OH using CBP. In this study, we have analyzed transient OH, persistent OH, as well as early and delayed OH. Limitations of this study include its cross-sectional nature, which shows only association and not causation, and the small sample size. Additionally, the selection of the 20 mm Hg/10 mm Hg drop as the threshold for defining OH for CBP based on the consensus criteria for PBP measurement may still not be an optimal cut-off for CBP.

Clinical significance

The traditional diagnostic criteria for OH/PH with PBP do not

Table 4. Relationship Between Persistent Orthostatic Hypotension (OH)[a], Cardiovascular and Fall-Related Outcomes by Peripheral and Central Blood Pressures

Variables	Persistent OH			
	Peripheral blood pressure, mean (SD) or no. (%)		Central blood pressure, mean (SD) or no. (%)	
	No (n = 60)	Yes (n = 11)	No (n = 60)	Yes (n = 11)
Central AP (%)	15.2 (9.2)	19.5 (7.9)	14.8 (8.6)	22.2 (9.9)†
Central AI (%)	28.8 (11.3)	34.2 (11.7)	29.3 (11.7)	31.6 (10.0)
Symptoms of OH	25 (41.7%)	5 (45.5%)	25 (41.7%)	5 (45.5%)
History of OH	0 (0.0%)	1 (9.1%)	0 (0.0%)	1 (9.1%)
History of falls	21 (35.0%)	2 (18.2%)	21 (35.0%)	2 (18.2%)
Hypertension	41 (68.3%)	10 (90.9%)	41 (68.3%)	10 (90.9%)
Coronary artery disease	9 (15.0%)	2 (18.2%)	10 (16.7%)	1 (9.1%)
Stroke	7 (11.7%)	2 (18.2%)	8 (13.3%)	1 (9.1%)
Heart failure	4 (6.7%)	0 (0.0%)	3 (5.0%)	1 (9.1%)
Type II diabetes	14 (23.3%)	3 (27.3%)	14 (23.3%)	3 (27.3%)
Dyslipidemia	18 (30.0%)	8 (72.7%)†	19 (31.7%)	7 (63.6%)
Peripheral vascular disease	4 (6.7%)	0 (0.0%)	4 (6.7%)	0 (0.0%)
CKD	2 (3.3%)	1 (9.1%)	1 (1.7%)	2 (18.2%)

[a]Orthostatic hypotension as measured and present at 1, 3, and 6 min of standing. †P < 0.05.

cause symptoms or adverse outcomes in all subjects (asymptomatic OH). This study assessed whether identifying the OH/PH using CBP, would have important implications for future diagnosis and management of OH/PH in patients. But this study showed that CBP can similarly identify OH like PBP. Future studies with a large sample size are needed to define appropriate cut-offs and also to validate central OH in clinical practice.

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Conflict of Interest

None.

Author Contributions

Kannayiram Alagiakrishnan: study design, planning, implementation, leading the study group and writing the manuscript. Raj Padwal and Peter Hamilton: study design, planning, helping with recruitment process, involvement in the preparation of the manuscript and medical supervision of study subjects if necessary. Ambikaipakan Senthilselvan: statistical analysis and presentation of results in the manuscript. Ruojin Bu (summer student): collecting the data from recruited subjects, entering the data in spreadsheet and participation in the preparation of manuscript.

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