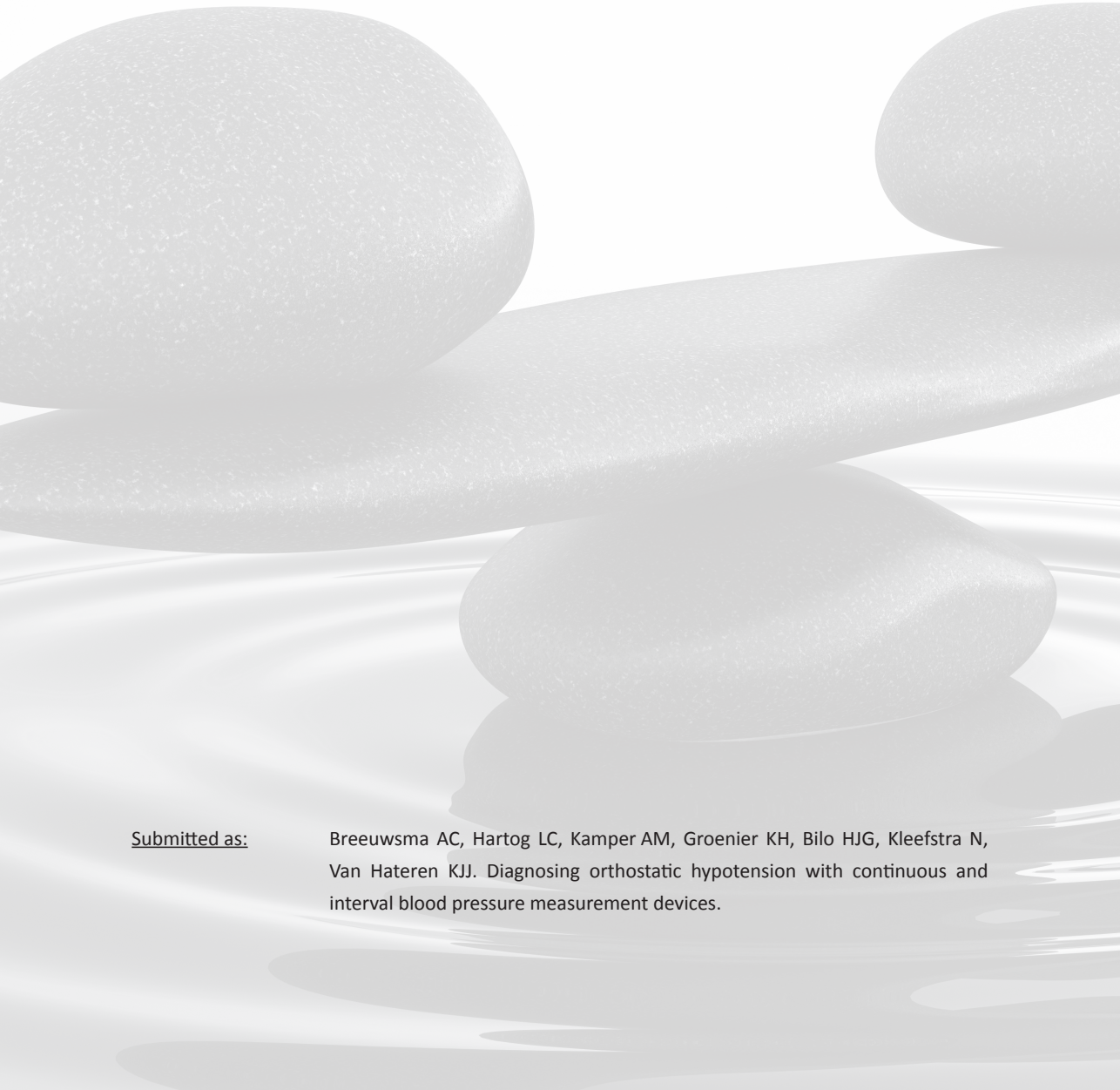
CHAPTER 3

Diagnosing orthostatic hypotension with continuous and interval blood pressure measurement devices



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ABSTRACT

Background: Orthostatic hypotension (OH) is defined as a drop in systolic blood pressure (SBP) of ≥20 mmHg and/or a drop in diastolic blood pressure (DBP) of ≥10 mm Hg within 3 minutes of standing. The international guidelines recommend diagnosing OH with a continuous blood pressure (BP) measurement device, although in daily practice interval BP measurement devices are used more often. We aimed to investigate the difference in observed prevalence of OH between an interval and a continuous BP measurement device.

Methods: A cross-sectional observational study. BP was measured with both an interval and a continuous BP measurement device during postural change from supine to the standing position. The differences in prevalence were tested with the McNemar test._Positive and negative proportions of agreement were calculated to observe the agreement of diagnosing OH between the two devices.

Results: A total of 104 patients with a mean age of 69 years were included. The prevalence of OH was 35.6% (95% CI: 26.4-44.8) with the interval BP measurement and 45.2% (95% CI: 35.6-54.8) with the continuous BP measurement device (p-value for the difference = .121). The positive proportion of agreement was 59.5% and the negative proportion of agreement was 72.5%.

Conclusions: Although the prevalence of OH was not significantly different between the continuous and the interval BP measurement devices, the positive and negative proportions of agreement were low. We conclude that continuous BP measurement cannot be substituted by an interval BP measurement to diagnose OH.

INTRODUCTION

Orthostatic hypotension (OH) is a clinical condition frequently affecting the elderly population and its prevalence rises with age [1, 2]. The prevalence varies from 7% to 55% in the elderly population [2-6].

OH is defined as a drop in systolic blood pressure (SBP) of at least 20 mmHg and/or a drop in diastolic blood pressure (DBP) of at least 10 mmHg within 3 minutes (min) of standing after 5 min of rest in supine position [7, 8]. Guidelines recommend to diagnose OH with continuous instead of interval blood pressure (BP) measurement devices [8], although the study of Romero-Ortuno suggested a lack of specificity for diagnosing OH [9]. On the contrary, automated sphygmomanometers are commonly used for this purpose in daily practice, but they underreport OH, compared to continuous measurement, due to the delay in time [10, 11]. Due to these different results, concerns are raised against the threshold in the diagnostic criteria and it is hard to apply the criteria on different BP measurement devices in clinical practice.

This study aimed to investigate the difference in the prevalence of OH when OH is measured using two BP measurement devices (continuous versus interval) during postural change from supine to standing position in patients of at least 50 years, and to investigate to what extend the results of these methods agree with each other. We hypothesized that the prevalence of OH with the continuous BP measurements would be higher compared to the interval BP measurements.

MATERIAL AND METHODS

Study population

For this cross-sectional study, the inclusion and study period was from January to February 2016. Patients > 50 years of age combined with a medical history of cardiovascular disease (CVD), diabetes mellitus (DM), and/or hypertension with an appointment at the outpatient clinic of internal medicine (Isala hospital, Zwolle, the Netherlands) were included. Patients with a contraindication of BP measurements in one arm, inability to stand without assistance, known peripheral vessel disease in one or both arms, needing a large (≥42 cm) or small (≤28 cm) cuff, and incapability of giving consent were excluded. A non-blinded randomization procedure was performed for the side of the specific BP measurement device (Figure 1).

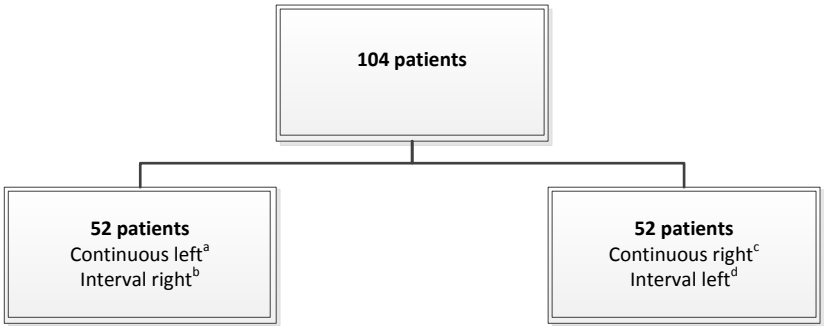

Figure 1. Randomization. [a]: Continuous BP measurement device on the left arm. [b]: Interval BP measurement device on the right arm. [c]: Continuous BP measurement device on the right arm. [d]: Interval BP measurement device on the left arm.

Data collection

Demographic characteristics, a full medical history including a history of CVD, DM, hypertension, polyneuropathy, Parkinson's disease, pacemaker implantation, falls in the previous year, and medication use were collected. History of CVD was defined as a history of angina pectoris, myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, stroke, and/or transient ischemic attack.

The BP measurement procedure was performed by a trained medical student. BP was measured using an interval and continuous BP measurement device simultaneously during postural change from supine to standing position. Interval BP was measured with an automated sphygmomanometer, the validated A&D UA-767 plus [12]. Interval BP was measured twice in supine position after 5 minutes of rest, and twice at 1 min and twice at 3 min after postural change to standing position, resulting in a total of 6 measurements. Continuous BP was measured with the Finometer Pro (Finapres Medical Systems BV), a continuous non-invasive beat-to-beat BP measurement device, which has been validated compared to invasive BP recordings [12, 13]. Finger circumference was measured to apply the proper sized finger cuff of the Finometer Pro [14]. Height differences were corrected by a height nulling procedure, by supporting both arms at heart level in supine and standing position, and by repeatedly checking the position of both arms [14, 15]. By using the return-to-flow (RTF) calibration system, the measured BP in the finger was reconstructed to the upper arm BP [14]. The presence or absence of characteristic symptoms of OH during postural change (dizziness, light-headedness, and blurred vision) was reported and defined as orthostatic complaints. BP measurement data of the Finometer Pro were exported with the BeatScope software (Finapres Medical Systems BV). Baseline mean supine SBP and DBP were calculated over the last minute prior to postural change. After postural change, lowest SBP and DBP were calculated for several timeframes (15-44s, 45-74s, 75-104s, 105-134s, 135-164s, 165-194s, and 195-224s). The first 14 s of the measurements were excluded. To

compare the prevalence of OH between the interval and the continuous BP measurement device, only the data of the continuous BP measurement device from the four timeframes around 1 and 3 minutes after postural change (45-74s, 75-104s, 165-194s, and 195-224s) were used. Records with poor quality signals (e.g. artefacts) were excluded by visual inspection of the graphics in the BeatScope output files.
OH was defined as a drop in SBP of at least 20 mmHg or a drop in DBP of at least 10 mmHg within 3 min after postural change [7].

Statistical analysis
Mean and standard deviation (SD) were used to present normally distributed continuous variables, and median and interquartile range (IQR) were used for non-normally distributed continuous variables. Proportions were used to present categorical variables. Normality tests were performed by inspection of the Q-Q plots and histograms.
The difference in prevalence of OH according to the BP measurement device was analysed with a two-sided McNemar test. The positive and the negative proportions of agreement were calculated [16]. The positive proportion of agreement is the number of both postural changes that diagnosed OH divided by the total number of OH diagnosed for each of the postural changes. The negative proportion of agreement is the number of both postural changes that excluded OH divided by the total number of excluded OH for each of the postural changes. Both positive and negative proportions of agreement were reported as percentages.
P-values below .05 were considered to be statistically significant. Statistical analyses were performed using the SPSS software (version 23; IBM, Armonk, New York, USA).

Ethical approval and clinical trial registration
The present study was registered at www.trialregister.nl (NTR5525) and was approved by the medical ethics committee (number 15.06.95). This study was performed in accordance with the declaration of Helsinki. Written informed consent was obtained during the scheduled medical appointment. The data was recorded and analysed anonymously. The 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) statement was used to describe this observational cohort study [17].

RESULTS

In the present study, 104 patients (59 men, 45 women) were included (Figure 2). Baseline characteristics of the study population are presented in Table 1. Baseline characteristics of patients with the Finometer on the left arm and patients with the Finometer on the right arm were presented in Appendix Table A1.

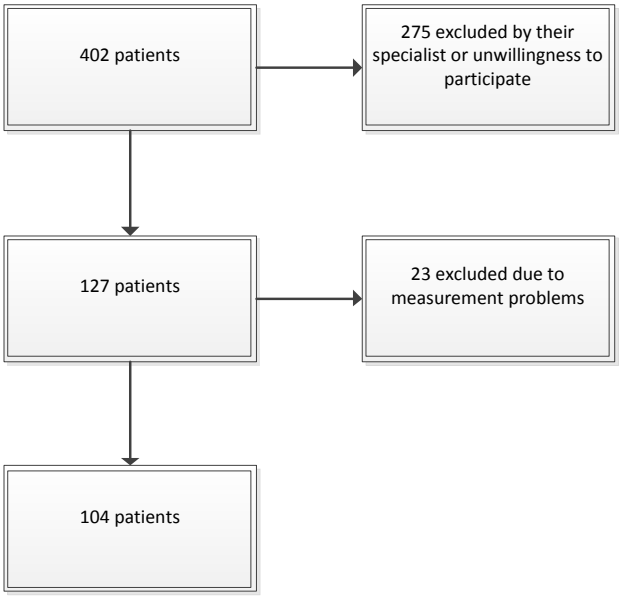

Figure 2. Patient selection.

No significant difference in the prevalence of OH was observed between the interval BP and continuous BP measurement devices. The prevalence of OH with the interval BP measurement device was 35.6% (95% CI: 26.4-44.8) compared to 45.2% (95% CI: 35.6-54.8) when measured with the continuous BP measurement device. The positive percentage of agreement was 59.5% and the negative percentage of agreement was 72.5%. Orthostatic complaints were reported by 22.1% (95% CI: 14.1-30.1) of the study population.

The prevalence of OH increased to 66.3% (95% CI: 57.2-75.4) when all seven timeframes of the continuous BP measurement device were included, which is significantly higher compared to the prevalence with the interval BP measurement device (p-value <.001). In this case the positive percentage of agreement was 52.9% and the negative percentage of agreement was 54.7%.

Table 1. Baseline characteristics.

	Patients (n=104)
Characteristics	
Age (years)	68.8 (8.5)[a]
Female	45 (43)
BMI (kg/m^2)	27.0 (24.7-31.7)[b]
Drinking and/or eating before measurements	63 (61)
Medical History	
Hypertension	82 (79)
DM	64 (62)
History of CVD	38 (37)
Polyneuropathy	33 (32)
Parkinson's disease	0 (0)
Pacemaker implantation	8 (8)
History of falls	31 (30)
Medication	
Anti-hypertensive medication	86 (83)
Anti-arrhythmic medication	6 (6)
Nitrates	13 (13)
Oral glucose lowering therapy	32 (31)
Insulin	52 (50)
Psychiatric medication	13 (13)
Anti-parkinsonian medication	1 (1)
Measurements continuous BP	
Lying SBP (mmHg)	150.3 (137.3-162.9)[b]
Lying DBP (mmHg)	76.7 (9.2)[a]
Lying HR (beats/min)	67.6 (60.4-73.8)[b]
Lying CO (L/min)	6.21 (1.96)[a]
Measurements interval BP	
Lying SBP (mmHg)	132.3 (124.0-152.8)[b]
Lying DBP (mmHg)	75.8 (67.1-82.4)[b]
Lying HR (beats/min)	65.5 (9.4)[a]

Values are presented as n (%), unless indicated otherwise. [a]: Mean (±SD). [b]: Median (IQR). [c]: % [95% Confidence Interval (CI)].

DISCUSSION

No significant difference in the prevalence of OH was observed between the continuous and the interval BP measurement device, 45.2% versus 35.6% respectively. The percentage of positive proportion of agreement was 59.5% and the percentage of negative proportion of agreement was 72.5%, which is considered to be poor.

When all timeframes of the continuous BP measurement device were included, it lead to a 21% absolute increase in the prevalence of OH compared to the interval BP measurement device and even lower proportions of agreement.

Previous studies reported a prevalence of OH ranging from 6% to 18% in community-dwelling elderly and 37% to 50% in nursing homes, as measured with interval BP measurement devices [4, 11, 18-21]. The observed prevalence of OH with the automated sphygmomanometer in the present study lies within the range of these studies. On the other hand, Romero-Ortuno presented a prevalence of OH of 94% in community-dwelling elderly measured with a continuous BP measurement device [9] which is twice the prevalence described in the present study. Concerns about using continuous BP measurement devices for diagnosing OH are previously reported [9, 22, 23]. A lack of specificity is suggested and the clinical interpretation and relevance is questioned [9, 22, 23]. In response to the increasing use of these devices the updated consensus added the word 'sustained' to the criteria in 2011 [24]. However, the duration of sustained is not defined [25], which makes it difficult to apply these criteria. Therefore, diagnosing OH with a continuous BP measurement device combined with the current diagnostic criteria might not be reliable and could lead to diagnose clinically irrelevant OH.

The present study observed no significant difference in the prevalence of OH between the continuous and the interval BP measurement device when the same amount of measurements was compared. However, in clinical practice the continuous BP measurement device provides more than four measurements and the present study observed a significant higher prevalence of OH with the continuous BP measurement device when all seven timeframes were used. This implies that clinicians, who use the continuous BP measurement device, would diagnose OH more often than clinicians who use the interval BP measurement device. Due to the lack of a golden standard, no sensitivity and specificity tests were performed. However, the positive and negative proportions of agreement were poor, 59.5% and 72.5%, respectively. A positive proportion of agreement of 59.5% indicates that only a little more than half of the subjects diagnosed with OH, are diagnosed with OH with both devices.

Strengths and limitations

The present study had several strengths. All measurements were performed and evaluated by the same individual to overcome inter-observer bias. All patients were non-blinded randomized for both the sequence of the postural changes and the side of the BP measurements.

Generalizability is limited to elderly patients visiting the internal outpatient clinic. Due to the fact that the patients included in this study had to be able to stand for five minutes without assistance, the study group was slightly biased compared to the population visiting the internal outpatient clinic, and the results are, of course, only useful in patients who are able to stand. Other limitations are the small study sample and the fact that the curves in BeatScope were judged by only one individual.

CONCLUSION

Although no significant difference in the prevalence of OH was observed between the continuous and the interval BP measurement devices, the positive and negative proportions of agreement were low. We conclude that continuous and interval BP measurements cannot be replaced by each other for establishing OH.

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SUPPLEMENTAL DATA

Appendix Table A1. Differences in baseline characteristics divided by the side of the continuous BP measurement device.

	Finometer on the left arm	Finometer on the right arm
Characteristics		
Age (years)	69.0 (64.3-74.0)[a]	69.0 (60.3-76.8)[a]
Female	25 (48)	20 (39)
BMI (kg/m^2)	26.6 (23.8-32.0)[a]	27.3 (24.7-31.6)[a]
Drinking and/or eating	33 (64)	30 (58)
Medical History		
Hypertension	42 (80)	40 (77)
DM	31 (60)	33 (64)
History of CVD	18 (35)	20 (39)
Polyneuropathy	17 (33)	16 (31)
Pacemaker implantation	4 (8)	4 (8)
History of falls	18 (35)	13 (25)
Medication		
Anti-hypertensive medication	44 (85)	42 (81)
Anti-arrhythmic medication	1 (2)	5 (10)
Nitrates	6 (12)	7 (14)
Oral glucose lowering therapy	14 (27)	18 (35)
Insulin	25 (48)	27 (52)
Psychiatric medication	5 (10)	8 (15)
Baseline SBP (mmHg)	136.5 (125.0-159.0)	132.0 (120.1-153.4)
Baseline DBP (mmHg)	74.3 (67.5-83.0)	77.0 (67.0-84.5)
Baseline HR (beats/min)	65.5 (58.0-70.5)	63.5 (58.1-71.4)

Values are presented as n (%), unless indicated otherwise. [a]: Median (p25-75).