The prevalence and pathological correlates of orthostatic hypotension and its subtypes when measured using beat-to-beat technology in a sample of older adults living in the community

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Abstract

Background: beat-to-beat technology is increasingly used for investigating orthostatic intolerance (OI) but the prevalence of orthostatic hypotension (OH) diagnosed with this technology is unclear.

Objectives: (i) to use beat-to-beat technology to define the prevalence of OH, (ii) to investigate the pathological correlates of OH, (iii) to report the diversity of postural BP responses.

Methods: cross-sectional study of adults ≥65 years. BP responses to a 3-min head-up tilt were analysed.

Results: of 326 participants, 203(62.3%) were females. The median (IQR) age was 73 (70–78). One hundred and ninety-one (58.6%) met standard (20 mmHg systolic/10 mmHg diastolic) criteria for OH. The prevalence was higher in females (60.1% F versus 56.1% M); 47% were arteriolar subtype, 33% were venular, 9% were mixed and 11.0% could not be classified. Morphological analysis identified 102 subjects with ‘small drop, overshoot’, 131 with ‘medium drop, slow recovery’ and 31 with ‘large drop, nonrecovery’. Those with OH had a lower BMI (P = 0.02), a higher resting heart rate (P = 0.005), were more likely to take a psychotropic (P = 0.02), have vertigo (P = 0.004) and report OI (P = 0.02). The 95th centile for the duration of systolic BP (SYSBP) decay >20 mmHg was 175 s and the slope of systolic BP decay was 4.75 mmHg/s. The 5th centile for percentage recovery of SYSBP was 81.4%.

Conclusion: (i) beat-to-beat methods identify a higher prevalence of OH than sphygmomanometry, (ii) the pathological correlates of OH diagnosed in this manner are similar to those described for sphygmomanometry, (iii) there is a diverse pattern of orthostatic BP decay that could be used in future research to predict adverse outcomes in OH.

Keywords: orthostatic hypotension, prevalence, Finometer, older people

Introduction

In the 16 years that have passed since the first definition of orthostatic hypotension (OH) [1], the technology for its identification has progressed considerably. Beat-to-beat photoplethysmography is now used increasingly for the assessment of orthostatic intolerance (OI). This technology is capable of demonstrating elaborate responses to a change in posture [2]. There have been calls for its use in preference to sphygmomanometry in future research on OH [3].
While there have been numerous epidemiological studies documenting the prevalence of OH in a variety of older populations [4], the majority have used sphygmomanometers. Among these studies are a number of works that have identified pathological correlates of OH [5, 6].

Two studies have reported the prevalence of OH using beat-to-beat technology. The first [7] sampled subjects attending a Geriatric day centre and reported an OH prevalence of 72% in fallers and 50% in non-fallers. The second [8] reported a prevalence of 94% in community-dwelling elders. Neither investigated whether the usual correlates of OH identified by studies such as the Atherosclerosis Risk In Communities (ARIC) [5] and Malmö Preventive Project (MPP) [6] could be found for OH diagnosed using beat-to-beat technology.

It is our objective to report, using beat-to-beat technology, the prevalence of OH in community-dwelling elders and document whether the pathological correlates of OH identified in the aforementioned studies also exist for OH diagnosed using photoplethysmography.

Methods

Study design

This is a substudy of the Health Inequalities and Ageing in the Community Evaluation (HIACe) study which was an evaluation of health status in older community-dwelling adults. Recruitment extended from May 2007 to February 2009. Ethical approval was granted by the local Research Ethics Committee.

Work focused on four sectors of a medium-sized city in Ireland. Census sampling of subjects ≥65 was used in two smaller sectors while random selection of subjects ≥ 65 was used in the two larger sectors. Subjects were visited by a field-researcher who collected information on demographics and completed the short-form 36 (SF-36) [9]. All participants were invited to attend our day hospital. Apart from moderate-severe dementia, there were no exclusion criteria.

Diagnosis of orthostatic hypotension

Tests were performed in a darkened climate-controlled room following a minimum of 2 h fasting. Following 5-min rest in the supine position, patients underwent head-up tilting (HUT) to 70°. This was sustained for a period of 3 min with beat-to-beat BP monitoring provided by a Finometer (TNO Systems, Amsterdam) [10]. We asked patients to describe symptoms experienced during the test. Individuals were deemed symptomatic if they described one of the symptoms of OH listed by Freeman [11].

Prior to HUT, sitting BP was measured following 3-min rest. Thereafter, patients were asked to stand up and had their BP measured within 30 s. A semi-automatic sphygmomanometer was used (Omron 705IT).

Analysis of beat-to-beat outputs was performed using Beatscope v1.1. Measurements were made using raw data and then repeated with 5-s averaging [7]. OH was defined as a reduction in BP from baseline of 20 mmHg systolic or 10 mmHg diastolic within 3 min of tilting. If the subject could not tolerate HUT for 3 min, the lowest BP achieved was recorded.

Pattern analysis of Finometer outputs

Raw data were used for calculating the following parameters (Figure 1). Nadir BP measurements were recorded as the average of the lowest three consecutive cardiac cycles.

- Time spent within criterion BP; the time elapsing between the onset of BP decay (>20 mmHg systolic or >10 mmHg diastolic) and its subsequent recovery to ‘normal’ (i.e. <20 mmHg below baseline for systolic or <10 mmHg diastolic);
- Slope of BP decay;
- Percentage recovery of BP.

Modelflow measurements of total peripheral resistance (TPR) and cardiac output (CO) were used to divide OH into three physiological subtypes. Deegan et al. defined an arteriolar subtype characterised by a predominant drop in TPR, a venular subtype characterised by a predominant drop in CO and a mixed subtype that was characterised by drops in both (AVM) [12].

We used the K-means cluster analysis feature of PASW-20.0 to assign cases to groups based on the clustering...
variables Delta SBP and final percentage recovery of SBP. Romero-Ortuno et al. [8] described three clusters of OH and proposed that these may be useful in predicting falls and frailty. The first cluster was characterised by a medium drop in blood pressure and slow recovery towards baseline BP, the second by a small drop in BP and an overshoot of BP during recovery and the final by a large drop in BP without significant recovery towards baseline.

**Blood pressure and heart rate measurement**

Twenty four-hour ambulatory monitoring of BP was performed using SpaceLabs devices with 30-min measurement intervals during the day and 60-min intervals overnight. Hypertension was defined as a mean BP in excess of 135/85 mmHg, self-reported hypertension or the use of an anti-hypertensive agent.

Resting heart rate was measured using R–R interval calculation during the final minute of the supine period pre-HUT.

**Further investigations**

Participants were asked to fast from 8 p.m. on the night before attending for phlebotomy. Blood tests were performed in accredited laboratories. Echocardiography was performed on an Agilent Sonos 4500 by a cardiac technician.

**Further data collection**

Information on co-morbidity and medications was collected. Psychotropic agents were defined as benzodiazepine and non-benzodiazepine hypnotics, typical and atypical antipsychotics or any antidepressant agent.

**Statistical methods**

PASW-20.0 was used for statistical analysis. Parametric t-tests were employed for comparison of normal variables and the Mann–Whitney U test was used for skew data. Categorical variables were compared using Pearson’s Chi-square test.

Following initial unadjusted analysis, a Forward stepwise Binary Logistic Regression model was constructed (using the Wald statistic). The dependent variable was OH diagnosed using raw data. Explanatory variables were those identified from univariate analysis to be significantly different between groups. The significance level for all tests was 5%.

**Identification of a subgroup without adverse sequelae of OH**

The major adverse consequences of OH are an increased risk of vascular morbidity and an increased risk of cerebral hypoperfusion and falls.

Individuals without a history of vascular disease denying a fall in the preceding 12 months were identified as a group of subjects who had not suffered adverse effects of OH. We analysed the distribution of patterns of BP decay in these individuals. Values below the 5th centile or above the 95th centile were considered abnormal [13, 14].

**Prevalence and pathological correlates of OH**

**Results**

**Basic demographics**

Five hundred and fifty-two subjects completed the field survey. Of these, 160 declined medical assessment. A further 42 declined HUT. Of 350 individuals undergoing HUT, 24 Finometer outputs were of insufficient quality for subsequent analysis. The remaining 326 were analysed in full.

Of 326 participants, 203 (62.3%) were females. The median [inter-quartile range (IQR)] age was 73 (70–78) years. The median Barthel score was 20 (20–20) and MMSE was 30 (30–30). Thirty-three (10%) subjects reported a fall in the preceding 12 months.

**Participants compared with non-participants**

We compared those who completed HUT (n = 326) to those who did not (n = 226). Participants had a median age of 73 years (70–78) compared with 75 years (70–81) in the non-participant group (P = 0.003) and were more likely to be female (62.3 versus 57.1%) (P = 0.179). Participants had a higher median SF-36 Physical Health Score of 50.7 (41.5–56.1) versus 47.1 (33.4–54.0) in non-participants (P = 0.002). The SF-36 Mental Health Score was lower in participants with a median of 56.5 (47.8–59.6) compared with 57.6 (53.2–60.2) in non-participants (P = 0.055).

**Prevalence of OH**

Using raw data, 191 (58.6%) subjects met the criteria for OH. The prevalence was higher in females (60.1%) than in males (56.1%). Of 191, 89 (47%) were of arteriolar subtype, 63 (33%) were venular, 18 (9%) were mixed and 21 (11.0%) could not be classified [12].

When 5-s averaging was applied to the data, OH was identified in 169 (51.8%) individuals.

Morphological analysis of the 326 studies identified 102 (31%) subjects with ‘small drop, overshoot’, 131 (40%) with ‘medium drop, slow recovery’ and 31 (9%) with ‘large drop, nonrecovery’ [8].

Sit-stand testing with sphygmomanometer identified OH in 17.3%.

**Duration of hypotension**

The median duration of systolic BP reductions >20 mmHg was 23 s (12–66 s). The corresponding value for diastolic BP reductions >10 mmHg was 17 s (10–44 s). Specifying a minimum duration of hypotension of 60 s would reduce the prevalence of OH to 23.3%, a minimum duration of 120 s would bring it to 13.5% and a minimum duration of 180 s to 9.0%.

**Univariate comparison of OH to non-OH groups**

Table 1 summarises the unadjusted comparison of individuals with OH to those without. Those with OH had a lower
median BMI, a significantly higher mean resting heart rate, were significantly more likely to be taking a psychotropic agent and to have vertigo. They were not more likely to have hypertension.

Multivariate comparison of OH to non-OH individuals

In multivariate analysis, each b.p.m. increase in heart rate was found to be predictive of OH (OR: 1.037, 95% CI: 1.008–1.066).

Pattern analysis of beat-to-beat BP recordings

Table 2 summarises the distribution of each of the orthostatic BP patterns in the subgroup without adverse sequelae of OH (n = 223).

Discussion

Using beat-to-beat technology, we identified OH in 59% of community-dwelling adults ≥65 years. This compares to a prevalence of 17.3% in our group when sphygmomanometer monitoring was used. The prevalence of OH diagnosed with Finometer monitoring is far greater than the 5–30% reported by previous epidemiological studies using sphygmomanometers [4]. The prevalence reported in our cohort is similar to the earliest study using beat-to-beat technology [7], but is lower than the recent prevalence of 94% reported by Romero-Ortuno et al. [8].

The univariate correlates of OH in our cohort are similar to those described elsewhere. In agreement with the findings of MPP [6], we have demonstrated patients with OH to have a higher resting heart rate. The observed association with psychotropic agents has been demonstrated before [15] as has the association with a lower BMI [16]. The recognition of vertigo as an associate of OH is interesting in the context of work linking vestibular function to the autonomic regulation of BP [17, 18].

We have not seen some of the other correlates of OH. This may be explained by the small sample size of our study when compared with bigger studies such as ARIC and MPP.
This is supported by trends within the univariate analysis that mirror, without reaching statistical significance, the findings of other epidemiological work. For example, individuals with OH in our cohort tended to have lower vitamin B12 and D were more likely to be ‘non-dippers’ and had a higher prevalence of HTN.

Beat-to-beat technology has the ability to identify short-duration orthostatic BP decay. The prevalence of OH reduces as we extend the duration of hypotension required. It is difficult to appoint a ‘cut-off’ as there are no clear indications from the literature as to which drops in BP are most relevant. ARIC measured BP 2 min following orthostasis [5]. MPP measured it at 1 min [6]. This might suggest that prolonged hypotension is required for the prediction of vascular risk. Neither of these studies, however, attempted to measure short-duration changes. There is evidence that the endothelium is involved in the BP response to a change in posture [19]. Orthostatic BP decay resulting from defective endothelial responses is likely to be short-lived due to rapid baroreceptor compensation. Short-duration BP decay may therefore be significant.

Another adverse consequence of OH is recurrent cerebral hypoperfusion [11, 20]. There is little guidance within the literature regarding the duration of hypotension likely to cause hypoperfusion. Recent work suggests that hypotension resolving within 30 s is unlikely to result in symptoms [21]. This is contradicted, however, by the symptoms experienced by individuals with initial OH which, by definition, recover within 30 s [22].

It is clear that an arbitrary time ‘cut-off’ is not likely to help us predict adverse outcomes in OH. There is growing recognition that established diagnostic criteria for OH may not be applicable to beat-to-beat technology [7, 23, 24]. It is for this reason that there has been movement away from using the duration of hypotension and absolute change in BP to define OH but instead to the pattern of BP response to orthostasis.

Our OH cohort does not demonstrate any obvious increased burden of vascular disease despite this being a well-recognised correlate of OH. Doubtless, there is among their number a subgroup that is at increased vascular risk [5, 6]. The task of future researchers is to identify the beat-to-beat pattern of BP decay in this subgroup predictive of future adverse outcomes. Investigators have already published physiological [12] and morphological [8] classifications that they propose will be of use in this context. We have reported their prevalence above. Studies report conflicting accounts of Modellflow accuracy. The authors of the physiological AVM classification system rely on Modellflow and acknowledge this limitation [12]. Their classification remains to be validated as a useful predictor of adverse outcomes in OH. Our paper is the first to describe the relative prevalence of the AVM subtypes and will be of use to researchers investigating the validity of this classification system.

Other investigators focus on the pattern of BP decay [25] and BP recovery [8, 20]. Table 2 identifies the mean ± 2 SD values for parameters of BP decay and recovery. This will help investigators to identify ‘abnormal’ patterns of BP response to tilt testing.

Our use of a tilt table may explain the lower prevalence of OH compared with the 94% reported by Romero-Ortuno. The standard orthostatic stressor used for the diagnosis of OH is debated. Some favour HUT [10, 26] while others argue that an active stand is preferable [27]. The greater physiological stress associated with active stand [22] may lead to greater sensitivity, but the question remains which of these stressors will be more specific. It might be that orthostatic BP decay occurring in the context of more gentle orthostatic stress (e.g. HUT) is more likely to be pathological than that occurring as a result of more aggressive orthostatic stress (e.g. Active Stand).

One limitation of this study is that observations are based on a single measure of orthostatic BP decay. This is shared by most epidemiological studies of OH [5, 6]. It is not known what the intra-individual variability in the pattern of BP decay would be in older people with repeated tilt testing. We controlled for this by standardising environmental conditions and timing of HUT.

The study is subject to some selection bias. Non-participants were older and had slightly lower levels of physical health. This may strengthen our study since it demonstrates a high prevalence of OH in a particularly healthy cohort.

Following the recent publication of the MPP [6] there has been a call for the use of beat-to-beat technology for more accurate characterisation of OH in future longitudinal studies [3]. Our study identifies some of the difficulties that will be encountered by researchers answering this call. Investigators will need to clarify the relevance of short-duration BP changes, identify pathological patterns of BP decay, determine the correct orthostatic stressor to combine with beat-to-beat measurement techniques and assess the intra-participant variability in beat-to-beat BP decay with repeated testing. Beat-to-beat technology is, without question, a powerful tool but we are only in the early stages of understanding how to use it to predict future adverse outcomes in OH.

Key points

- Beat-to-beat monitoring of orthostatic BP responses, when compared with studies using sphygmomanometers, reveals a higher prevalence of OH.
- OH identified in this manner has many of the correlates of OH identified using sphygmomanometers in large epidemiological studies but is not associated with a greater burden of vascular disease.
- Future research efforts must focus on identifying subtypes of beat-to-beat recorded orthostatic BP decay that will be predictive of adverse outcomes.

Conflicts of interest

None declared.
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References


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