High Prevalence but Uncertain Clinical Significance of Orthostatic Hypotension Without Symptoms

Running title: Miller et al.; Orthostatic Hypotension Uncertain Significance

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Orthostatic hypotension (OH) is common in adults, and when accompanied by symptoms (dizziness, light-headedness, or fainting) carries an increased risk of falls, fractures, and mortality.\textsuperscript{1} Symptoms are attributed to transiently reduced cerebral perfusion. The underlying causes of OH are numerous and include dehydration, “autonomic dysfunction”, and medications that affect vascular compliance or responsiveness to autonomic reflexes.\textsuperscript{2} Risk factors for OH in population-based studies include age, hypertension, hypertension treatment, diabetes, and sedative/hypnotic medication use.\textsuperscript{3}

In order to standardize the assessment and diagnosis of OH, the American Autonomic Society and American Association of Neurology defines OH as a decrease in systolic blood pressure (BP) of $\geq 20$ mmHg or diastolic BP of $\geq 10$ mmHg within 3 minutes of standing.\textsuperscript{2} Recently, the availability of continuous BP monitoring during provocative testing (going from seated to standing) has provided opportunities to further characterize patterns of OH which may have prognostic value and/or pathophysiologic relevance. While there is now a consensus on the definitions of OH and its variants, few studies have assessed the prevalence of OH and its variants in the general population. This lack of data likely reflects the absence of a simple assessment tool, which is necessary in population-based studies.

In this issue of Circulation, Finucane and colleagues present results of a population-based, nationally representative survey on the prevalence of OH in adults in Ireland.\textsuperscript{4} The investigators use a novel continuous monitor (Finometer) for waveform analysis of beat-to-beat BP measurements during provocative testing. For this test, participants were supine for 10 minutes, at which time they stood for 2 minutes while the monitor recorded BP continuously. At two minutes, participants were also asked to report symptoms of “orthostatic intolerance”. In this paper, OH was defined as a decrease in systolic BP of $\geq 20$ mm Hg or diastolic BP of $\geq 10$
mmHg at 2 minutes of standing, in contrast to the standard 3 minute test. The authors also report two variants of OH. The variant, initial orthostatic hypotension (IOH), was defined as a drop in systolic BP of ≥40 mmHg or diastolic BP of ≥20 mmHg within 15 seconds of standing accompanied by symptoms (e.g. dizziness or light-headedness). The variant, impaired blood pressure stabilization, was based on the time-course of BP monitoring and was defined by a lack of returning to baseline BP after 40 seconds.

Table 1 summarizes principal findings of the survey. With increasing decade of life, the prevalence of OH increased as well, from 4.2% in 50-59 year olds to 18.5% in those ≥80 years. IOH was highly prevalent (~35%) and did not vary by age. The prevalence of impaired blood pressure stabilization, defined as a lack of return to baseline BP at 40 seconds upon standing, increased with each decade, and affected > 40% of those ≥80 years.

The relevance of these findings to clinical management of patients with OH is uncertain, given the lack of prospective data on outcomes and the overriding clinical importance of whether or not there were concurrent symptoms. It is well-recognized that most patients with OH are asymptomatic. Typically, reports of OH symptoms (e.g. mild and fleeting light-headedness, feeling dizziness or felling faint, or after a report of syncope) will prompt a clinical evaluation. OH associated with orthostatic symptoms is most relevant to initiating further diagnostic evaluations and in making treatment decisions. However, there are no guidelines on clinical decision-making in those with OH but without symptoms.

Measurement of OH in asymptomatic patients is presumably done for the purpose of identifying persons who are at high risk for falling. However, the relationship of OH with subsequent falls has been inconsistent in observational studies. In a large cohort of community-dwelling adults in Boston, OH was not associated with a greater risk of falls overall,
except in a subgroup of those with uncontrolled hypertension. Poor vision, balance and gait problems, vertigo, muscle atrophy, co-morbid conditions, and medication use might be more important risk factors for falls than OH.

Identification of OH in patients who are symptom free may create diagnostic and therapeutic dilemmas. Detection of OH in the clinic with the continuous monitoring device would add much data, but would further complicate BP management. For example, a clinician may be reluctant to escalate antihypertensive drug treatment in an asymptomatic patient with OH, even if the patient has not achieved BP control. Large epidemiological studies have shown that anti-hypertensive medications are associated with increased risk of serious fall injuries, and some question the value of aggressive blood pressure lowering in the elderly. The high prevalence of OH in the elderly and perceived risk of falls led, in part, to the new JNC VIII recommendation which raised the systolic BP treatment threshold from \( <140 \text{ mmHg} \) to \( <150 \text{ mmHg} \). On the other hand, there is substantial concern that the new JNC VIII recommendation might increase the risk of stroke. Further, there is much debate on whether withdrawing antihypertensive medications on the basis of OH is justified, especially in the absence of symptoms.

Trials of aggressive vs standard BP goals provide some reassurance that lower BP, while increasing OH symptoms, does not increase risk of falls or fractures. In the ACCORD trial, a large randomized trial of intensive goal (systolic BP \( <120 \text{ mmHg} \)) vs standard BP goal (systolic BP \( <140 \text{ mmHg} \)) in patients with Type 2 diabetes, the intensive BP goal was not associated with an increased risk of falls or fractures at one year follow-up. In the SANDS trial, there were greater reports of dizziness (35 vs 17%), but not falls, in the aggressive compared to the standard BP goal groups. In the SPS3 trial, which randomized adults following lacunar infarction, a lower
BP target was associated with a trend towards an increased risk of orthostatic syncope, but a lower trend for recurrent stroke. For milder symptoms such as dizziness, which can often be managed by behavior modification, e.g. sitting on the side of the bed before standing, the risk of falling in those with OH may be far less than the risk of a CVD event that may occur after stopping antihypertensive therapy or liberalizing BP treatment goals.

A critical factor in decision-making on medication titration is patient preference. In a cross-sectional survey of cognitively intact adults with hypertension who were at risk for falls, 50% reported a preference for maintaining better BP control, with the potential of reducing CVD risk, while the other 50% had a preference for reducing OH symptoms from a lower dose or withdrawal of medication. The percentage of participants who prioritized CVD risk reduction was less in those with lower education, lower income, and those in poorer health.

The study Finucane et al. has several limitations that should be considered. First, it was a cross-sectional study. Establishing the relationship of OH (and its variants) with CVD or falls risk will require prospective studies. It is premature, based on the available cross-sectional data, to advocate for routine OH testing without such research. Second, the population from which the normative data was derived is homogeneous in race/ethnicity. The patterns of OH described here may not be relevant to populations with different dietary patterns, sodium intake, medication use, or with different CVD risk profiles. Third, it is important to distinguish ‘usual’ from ‘normal’ prevalence of OH. The data reported in this paper reflect a population with a high prevalence of hypertension and a high risk of vascular disease, i.e. usual rates. With efforts to promote cardiovascular health and prevent hypertension, rates of OH might fall and reflect ‘normal’ prevalence in a less diseased population. Fourth, the authors did not assess risk factors with OH (and its variants) and did not provide any information on how, when or what questions
were used to assess OH symptoms during the testing. Fifth, the duration of the provocative test, 2 minutes, was less than the 3 minutes recommended by professional organizations. Lastly, the investigators used the Finometer. This device uses a finger BP cuff, with return flow calibration and height correction algorithms; it was judged to provide “reliable BP values” (with an estimated grade of A/B by British Hypertension Society Standards). However, independent testing of the Finometer as an accurate measure of BP by international standards is unavailable. Whether this device could be incorporated into routine care would also need to be assessed.

In conclusion, the authors document a high prevalence of age-associated OH in a representative sample of adults from Ireland. The continuous beat-to-beat monitoring provided by the Finometer device during the seated-to-standing change highlights the high prevalence of OH in the population, and in particular in the elderly. However, the clinical relevance of these findings must be established before routine testing in asymptomatic patients can be recommended.

Conflict of Interest Disclosures: None.

References:


**Table 1.** Prevalence of Orthostatic Hypotension and variants of Hypotension in adults in the Irish Longitudinal Study on Ageing.

<table>
<thead>
<tr>
<th>Orthostatic Hypotension (%)*</th>
<th>Age in Years</th>
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<tbody>
<tr>
<td></td>
<td>50-59</td>
</tr>
<tr>
<td>Initial orthostatic hypotension (%)†</td>
<td>35.0</td>
</tr>
<tr>
<td>Impaired blood pressure stabilization (%)‡</td>
<td>9.1</td>
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</tbody>
</table>

* Orthostatic Hypotension (OH)" was defined as a decrease in systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mmHg at 2 minutes of standing
† “Initial orthostatic hypotension (IOH)” is defined as a drop in SBP ≥ 40 mmHg or DBP ≥20 mmHg within 15 seconds of standing accompanied by symptoms (e.g., dizziness or light-headedness)
‡ “Impaired blood pressure stabilization at 40 seconds” is defined by a lack of returning to baseline BP after 40 seconds
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