Should Primary Care Patients Be Screened for Orthostatic Hypotension?

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BACKGROUND. Primary care physicians test for orthostatic hypotension to find risk factors they can modify. By doing so, they may prevent adverse outcomes related to falls and ischemic organ injury due to hypoperfusion. Varied recommendations have been made regarding which patients to test, measurement methods, and the definition of a clinically significant postural decline in blood pressure.

METHODS. We identified research articles relating to orthostatic hypotension by doing a literature review. Eleven articles were selected on the basis of quality of research methods and applicability to primary care practice from which prevalence, associated factors, and outcomes related to orthostatic hypotension were reported.

RESULTS. The prevalence of orthostatic hypotension varied from 13% to 30.3% in elderly patients. Hypertension was the most consistently associated diagnosis. Two of 3 studies did not find an association between orthostatic hypotension and mortality, and the third found that association only in patients with diabetes and hypertension.

CONCLUSIONS. The information available does not support postural blood pressure testing as a screening device among patients attending primary care practices. However, there is evidence to support the testing of high-risk subgroups of patients. Answers to the proposed research questions will clarify how testing for orthostatic hypotension can be most effectively applied in primary care.

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CLINICAL QUESTION Should primary care patients be screened for orthostatic hypotension?

Clinicians seeking the cause of a fall, syncopal episode, or complaint of lightheadedness commonly test for postural or orthostatic hypotension. It may also be sought as an indicator of a patient's adverse response to a medication or as a reflection of circulatory system volume loss. Elderly patients with hypertension are more vulnerable to acute postural hypotension, since their cerebral blood flow at rest is closer to the threshold for cerebral ischemia.[1] Particular patient subsets, such as patients with diabetes and those with other causes of autonomic neuropathy, are especially susceptible to chronic postural hypotension.[2] Medications that lower blood pressure are used to treat cardiovascular and other chronic illnesses, and the clinician often must increase the dose of such a medication until the patient develops side effects, making orthostatic hypotension more likely.[3] A fall or near fall may be a major consequence of orthostatic hypotension.[4] Either may cause the person to be less active because of injury or fear of falling, leading to debilitation and further functional decline. Hypotension may also cause underperfusion of organs, resulting in ischemic injuries, such as strokes,[5,6] particularly if there is compromised vascular supply or failure of autoregulation. The short-term significance of orthostatic hypotension for a particular patient is usually evident, but long-term adverse outcomes for affected patients are more difficult to predict.

Screening to detect orthostatic hypotension might allow the clinician to make therapeutic changes to prevent these associated problems. Screening (also called case finding) is used here as commonly defined in primary care practice, where a test is applied to patients who are well or complaining of apparently unrelated symptoms. Diagnostic testing, however, occurs when the patient has known risk factors, complaints, findings, or established diagnoses that have been associated with the condition for which the patient is being tested. Although advanced age and hypertension, with their associated morbidities and medications, are known risk factors for orthostatic hypotension, these patients make up large subpopulations in primary care practices, and testing them will be considered screening for the purposes of this review.

Reference Standard Issues

The types of reference standards a postural drop in blood pressure might be compared with to determine significance are: (1) direct measures of blood pressure, such as intra-arterial measurements; (2) concomitant measures of cardiac and cerebral perfusion; and (3) associations with long-term outcomes. Each of these has methodological problems for studies of ambulatory populations. Invasive methods are not appropriate for asymptomatic patients, and measures of cerebral perfusion, such as ocular

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plethysmography and radionuclear scans, are difficult to apply in various positions.[7] Studies have shown poor correlation between blood pressure changes and cerebral perfusion, probably due to patients' varying ability to autoregulate blood flow.[8] Outcomes, such as falls, myocardial infarctions, strokes, and overall mortality, have been used to determine the significance of the finding of orthostatic hypotension, but this assumes that a measurement on one occasion will be representative of future blood pressure responses.

This assumption is probably not justifiable. For example, in one study of 40 elderly patients visiting an outpatient clinic with postural symptoms and given a diagnosis of orthostatic hypotension, only 67% continued to have orthostatic hypotension on a second visit.[9] In another study, a decrease of 20 mm Hg in systolic pressure was found in 13.8% of 3858 elderly Italian patients and on repeated measurements 7 days later in 12.6%; however, the criteria were met at both visits in only 36.3% of those with systolic orthostatic hypotension on either visit.[10] These studies demonstrate that the prevalence of postural hypotension varies from day to day, and reproducibility in particular patients is modest. Studies that use such cross-sectional measurements of postural blood pressure changes and associate them with subsequent morbidity and mortality are susceptible to the effects of historical biases and regression to the mean.

Definition of Orthostatic Hypotension and Methods of Measurement

The most common definition of a significant orthostatic drop has been a decrease in systolic blood pressure of 20 mm Hg or more when the subject moves to a more upright posture. Some studies[10,11] include a diastolic drop in blood pressure of greater than 10 mm Hg in the definition. Most have tested patients moving from the supine to the standing position, and measured standing blood pressure between 1 and 5 minutes after attaining standing posture. The length of time that subjects remained supine or sitting before standing varied. A recent study measuring decline in systolic pressure in 430 older subjects going from sitting to standing found an orthostatic hypotension prevalence of 18.9%, if only 1 sitting and 1 standing measurement were used. However, if the sitting blood pressure was taken 3 times and the mean of the second and third pressures was compared with the standing pressure, the prevalence of orthostatic hypotension was only 4.9%. These authors concluded that an alerting response affects the first pressure and can result in an overestimation of orthostatic hypotension prevalence.[12] Testing soon after standing is supported by the study by Williams and colleagues[13] that found that 83% of 39 geriatric inpatients had the maximum drop in blood pressure within the first minute after tilting upright. Patients with suggestive symptoms, however, have also been found who did not meet criteria for orthostatic hypotension until after they had been standing 13 to 30 minutes.[14] A joint consensus of the American Autonomic Society and the American Academy of Neurology committee[15] defined orthostatic hypotension as a reduction in systolic blood pressure of 20 mm Hg or diastolic blood pressure of 10 mm Hg within 3 minutes of standing. All studies that we refer to used a postural drop in systolic blood pressure of at least 20 mm Hg as the criterion for orthostatic hypotension.

METHODS

Literature Search

Initially, the MEDLINE database for 1966 and later was searched using "hypotension, orthostatic" as the main Medical Subject Headings (MESH) search term, limited to English language publications and clinical trials. The same search was repeated to find related review articles. Then bibliographies of those reviews and recent primary care textbook chapters were inspected to find additional pertinent studies. Articles related to orthostatic hypotension were also sought in the following secondary-literature databases: *Evidenced-Based Medicine*, the POEMs (Patient-Oriented Evidence that Matters) section of *The Journal of Family Practice*, and The *Cochrane Library*.

TABLE 1

Study Selection Criteria

Category	Requirement
Design	Prospective or cross-sectional
Subject number	≥90
Subject source	Primary care clinic or community
Subject enrollment	Random or consecutive
Methods	Well described and applicable to a family practice setting
Comparison with standing blood pressure	Preceding lying or sitting blood pressure
Measurements or associations	Orthostatic hypotension prevalence, or cross-sectional associations, or long-term outcomes

The search was then expanded into the nursing literature and also into clinical trials related to the MESH terms "hypotension," "accidental falls," "hip fractures," "myocardial infarction," and "stroke," and the text term "tilt test."

Analysis of Articles

Research articles were critically analyzed to determine the quality of the research methods, analyses, and conclusions using the criteria developed at McMaster University.[16] Sixty reports of clinical studies were initially evaluated. Of these, only 2 were randomized control trials, both using multifactorial interventions that included recommendations to treat orthostatic hypotension if detected.[17,18] There were 3 other prospective studies. No study was done in a family practice setting, but 2 were done in primary care clinics and 10 used community-dwelling subjects. No relevant reviews were found in the secondary databases.

The criteria shown in Table 1 were used to select the best studies on which to base conclusions for primary care physicians. The randomized controlled trials were included, although they did not meet all of the criteria. Eleven selected studies were then critically reviewed by an investigator who was blinded to the authors, study site, and journal in which they were published. This secondary analysis confirmed that the study met the selection criteria and further critiqued test methodologies for reliability, validity, and utility for clinicians.

RESULTS

Prevalence in Community-Dwelling Populations

Table 2 shows those studies that report prevalence of orthostatic hypotension, using the populations most representative of those seen in primary care. Of the studies using elderly subjects, the highest prevalence (30.3%)

TABLE 2

Prevalence of Orthostatic Hypotension in People Living in the Community

Study	N	Age, years	Population/ Selection	Significant BP Drop Definition	Prevalence of OH, %	Comments
Tilvis et al[11] (1996)	569	75+	Finns living in community of Helsinki/Random	≥20 mm Hg systolic or ≥10 mm Hg diastolic after 1 min standing	30.3	Tested between 8 and 10 AM, prevalence 26.6% in "healthy aged." Criteria met in 7.5%
Raiha et al[23] (1995)	347	65+	Finns living in community of Turku/Random	≥20 mm Hg systolic at 3 min after standing	28.0	Stratified by age and sex
MacLennon et al[19] (1980)	186	65+	English general practice patients/ Nonrandom	≥20 mm Hg systolic at 2 min after standing	22	Majority of subjects were hypertensive
Rutan[24] (1992)	4931	65+	US community dwellers/Random	≥20 mm Hg systolic or ≥10 mm Hg diastolic after 3 min standing	16.2	Prevalence was 18.2% if those with OH symptoms on testing were included
Alli et al[10] (1992)	3858	65+	Italian general practice patients/ Random	≥20 mm Hg systolic after standing	13.8	Prevalence was 14.1% on repeat testing 1 week later, but found in only 36.3% at both visits
Robertson et al[20] (1998)	398	65+	US internal medicine outpatient clinic/ Nonrandom	≥20 mm Hg systolic 5 min after standing	13	Also studied those with ≥10 mm Hg diastolic drop
Harris et al[21] (1991)	8000	25-74	US community dwellers, nondiabetic/ Random	≥20 mm Hg systolic at 1 min after standing	10	

BP denotes blood pressure; OH, orthostatic hypotension.

TABLE 3

Orthostatic Hypotension Associations and Outcomes

Study	Cross-Sectional Associations	Outcomes Associated	Outcomes Not Associated	Comments
Tilvis et al[11] (1996)	Supine systolic		Mortality pressure	
Raiha et al[23] (1995)	Hypertension		Mortality	
MacLennon et al[19] (1980)	Supine systolic pressure			
Rutan[24] et al (1992)	Difficulty walking, frequent falls, history of MI, history of TIA			
Alli et al[10] (1992)	None on multivariate analysis			
Robertson et al[20] (1998)	Supine systolic pressure			Supine systolic pressure and COPD were associated with a 20-mm drop in diastolic pressure
Harris et al[21] (1991)	Supine systolic pressure			Subjects aged 25-74 years. Diabetics excluded and analysis reported for subjects not on antihypertensive medication
Davis et al[22] (1987)	Diabetes mellitus, stroke history, use of antihypertensive medications (without considering relative weight)	Diabetic hypertensives had increased mortality	Mortality in nondiabetic patients	OH defined as 20-mm difference in average of 2 sitting BPs subtracted from standing BP

MI denotes myocardial infarction; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; OH, orthostatic hypotension; BP, blood pressure.

was in the study by Tilvis and coworkers.[11] However, those subjects were all older than 75 years, a significant drop in systolic or diastolic blood pressure was considered positive for orthostatic hypotension, and testing was done by nurses between 8 AM and 10 AM. Orthostatic hypotension among 186 elderly patents registered in 2 group general practices in England was found to have a prevalence of 22% overall: 26% in men and 20% in women aged 65 to 74 years, and 24% in men and 15% in women for those older than 75 years.[19] Thirteen percent of elderly patients attending an internal medicine clinic had orthostatic hypotension.[20] Thus, the prevalence in older people living in the community ranged from approximately 13% to 30%, with some of the variation apparently attributable to differences in age, selection criteria, and measurement methods.

Less evidence is available for wider-age samples. In the National Health and Nutrition Examination Survey II study of 8000 people in the United States who were aged 25 to 74 years and did not have diabetes, 6.6% had a decrease in blood pressure of 20 mm Hg going from supine to seated. The prevalence increased with age, but this appeared to be partially explained by the associated increase in systolic blood pressure.[21]

Cross-Sectional Associations and Long-Term Outcomes

Table 3 lists cross-sectional associations and long-term outcomes that were reported in the selected studies. In the Hypertension Detection and Follow-up Program study of community dwelling people with hypertension aged 30 to 69 years, those with orthostatic hypotension had a higher prevalence of diabetes mellitus, history of stroke, and use of antihypertensive drugs. These associations disappeared when relative body weight was added to the model. In the same study, patients with hypertension, diabetes

mellitus, and orthostatic hypotension had the highest 5-year mortality rate.[22] Logistic regression analysis of results for a sample of 398 outpatients showed only supine blood pressure to be significantly associated with systolic orthostatic hypotension, while that and chronic obstructive pulmonary disease were associated with a 20-mm decrease in diastolic pressure.[20] Factors not associated with systolic orthostatic hypotension in each of these studies were: (1) body mass index and serum levels of glucose, insulin, cholesterol, triglycerides, albumin, and intact parathyroid hormone[11]; (2) sex, body mass index, disability, diabetes, hypertension, arteriosclerotic cardiovascular disease, congestive heart failure, cerebral artery disease, emphysema, nitrates, diuretics, beta-blockers, or ambulatory electrocardiogram monitoring[23]; (3) beat-to-beat variation and vibration sense[19]; (4) systolic hypertension, electrocardiogram abnormality, carotid artery stenosis or history of stroke, angina pectoris, or diabetes mellitus[24]; (5) sex, age, heart rate, congestive heart failure, diabetes, varicose veins, Parkinson's disease, diuretics, adrenergic antagonists, antipsychotics, beta-agonists, and alpha-adrenergic blockers[10]; (6) hypertension and chronic obstructive pulmonary disease[20]; (7) age[21]; and (8) age, sex, race, diabetes, hematocrit, smoking, or relative weight.[22]

Three nonintervention studies prospectively examined outcomes. In a 4-year follow-up of postural hypotension and postural dizziness in the Helsinki Aging Study, neither had prognostic significance for mortality.[11] A 10-year study of community-dwelling Finns older than 65 years showed no correlation between orthostatic hypotension and mortality on multivariate analysis.[23] In the Hypertension Detection and Follow-up Program study, factoring in body weight removed the association between systolic orthostatic hypotension and mortality, except in people with diabetes.

Interventions

Nonpharmacologic interventions recommended for reduction of orthostatic falls in patients' blood pressures include increasing dietary salt intake, wearing compressive stockings, elevating the head of the bed, and hand clenching or ankle pumps before standing.[18] Pharmacologic treatments include changing or decreasing the dose of medications with hypotensive effects. If orthostatic hypotension persists, fludrocortisone, sympathomimetic amines, erythropoietin, nonsteroidal anti-inflammatory drugs, somatostatin analogs, and other vasoactive medications have been effective in some cases.[25] Perhaps best studied has been midodrine hydrochloride, which was shown to be effective in a recent double-blinded crossover trial.[26]

Treatment of orthostatic hypotension has been included as part of multifactorial interventions in 2 randomized trials on elderly people who have fallen. In the first, done in a home for the aged (average age 88), 77 of the 160 people who had fallen were found to have orthostatic hypotension. It was thought to be the main cause of falls in 15.6% of these people, and a contributing cause in another 26%. After the intervention, no significant decrease in falls or mortality was demonstrable, but there were significantly more hospitalizations in the control group.[17] In the second prevention trial, 301 community-dwelling people older than 70 with at least 1 risk factor for falls were followed up for 1 year after risk reduction recommendations were made for the 153 who were randomly selected for interventions. At the initial assessment, orthostatic hypotension was present in 46% of the intervention group and 39% of the control patients. At reassessment, the prevalence of orthostatic hypotension decreased in both groups to 34% and 30% respectively, which was not significantly different from initial levels. The effect of the combined interventions, however, was significantly fewer falls (35% vs 47%).[18]

DISCUSSION

Orthostatic hypotension, as commonly defined, is prevalent in elderly community-dwelling populations; effective interventions are available; and potential consequences are important. However, the results of the prospective studies are mixed in their confirmation of associations with these adverse effects, and at least 2 studies have not shown an association between postural hypotension and increased mortality. Of the 2 randomized controlled studies[17,18] that recommended treatment of orthostatic hypotension as part of a multifactorial intervention in people who have fallen, one showed a decrease in hospitalizations and the other a decrease in falls, but the relative contribution of reduction in orthostatic hypotension was not clearly delineated in either.

Primary care office screening among continuity patients might produce more effective interventions, since responses to medication changes and other interventions may be more quickly assessed. Until confirmatory intervention studies are done in primary care settings, routine testing for orthostatic hypotension cannot be recommended. However, clinicians should have a high index of suspicion for its presence in older patients being treated for cardiovascular disease, mental illness, or diabetes, particularly after adding or increasing doses of medications with hypotensive effects.

IMPLICATIONS FOR FURTHER RESEARCH

Family physicians regularly see postural hypotension in association with adverse outcomes, such as syncope and falls, and their patients seem to benefit from interventions to prevent its occurrence. Published studies are inconclusive regarding associations between orthostatic hypotension and effective interventions. Definitive evidence will require further studies in the type of primary care settings where susceptible people most often receive medical evaluation and treatment.

Until clinically useful methods to determine cerebral perfusion are devised, measurement of peripheral blood

pressure will remain our most closely related measurement. Determining the most efficient methods of measuring postural changes in blood pressure in the busy office practice is the priority. Pertinent questions include: Should the testing be done by the nurse before the office visit to minimize white-coat hypertension effects? Is a measurement of the change from sitting to standing sufficiently sensitive? Do morning measurements increase sensitivity? Do repeated measures and allowance of equilibration time between position changes improve specificity? Would determination of the relative drop in blood pressure with postural change be a better predictor of adverse outcomes than the absolute pressure drop? Does knowledge of a patient's blood pressure trend at repeated visits help determine the significance of orthostatic hypotension? Does 24-hour blood pressure monitoring or intermittent blood pressure measurement over several days give better information about postural blood pressure responses than measurements made in the office? The practical utility of these findings must be considered, since protocols requiring repeated measures, delays between measurements, or expensive monitoring equipment are unlikely to be used during routine office visits.

After these questions have been answered, prospective studies can re-examine the definition of orthostatic hypotension and determine if there are associations with concurrent risk factors and long-term outcomes. A large intervention study in primary care practices could then determine whether testing for and treating orthostatic hypotension is beneficial in the management of at-risk primary care patients.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Primary care office screening of asymptomatic patients to detect orthostatic hypotension is not supported by present data. In higher-risk subgroups, such as people with hypertension or diabetes, the elderly, and patients on medications with hypotensive effects, clinicians are advised to ask about postural symptoms suggesting cerebral hypoperfusion. If suggestive symptoms are elicited, or if the clinician finds postural hypotension to a degree he or she considers significant, treatment changes may decrease the risk of injuries due to inadequate brain perfusion.

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