Prognosis of Diastolic and Systolic Orthostatic Hypotension in Older Persons

Heikki Luukinen, MD; Keijo Koski, MD; Pekka Laippala, PhD; Sirkka-Liisa Kivelä, MD

Background: Orthostatic hypotension (OH) predicts mortality in hypertensive persons with diabetes mellitus, but no increase in mortality has been found among random samples of home-dwelling persons with OH. We examined the risks of nonvascular and vascular deaths according to different definitions of OH among home-dwelling elderly persons.

Subjects and Methods: The study population consisted of all persons aged 70 years or older living in 5 rural municipalities (N = 969), of whom 853 (86%) participated. Orthostatic hypotension was defined as a systolic blood pressure (BP) drop of 20 mm Hg or more or a diastolic BP drop of 10 mm Hg or more 1 minute or 3 minutes after standing up. Nonvascular and vascular deaths during the follow-up period were recorded. Data on diseases, symptoms, medications, the results of clinical examinations and tests, functional ability, and health behavior were collected at the beginning of the follow-up period.

Results: Of the sample, 30% had OH: the prevalence of systolic OH 1 minute and 3 minutes after standing up was 22% and 19%, respectively; that of diastolic OH 1 minute and 3 minutes after standing up was 6% for each. No differences in the occurrence of nonvascular deaths were found according to any of these definitions. By Cox multivariate regression analysis, the hazard ratio of vascular death associated with a diastolic BP reduction of 1 mm Hg 1 minute after standing up was 1.02 (P = .03), adjusted for systolic BP postural changes at 1 and 3 minutes and a diastolic BP change at 3 minutes. Adjusted for other significant factors associated with vascular death, the hazard ratio for vascular death associated with diastolic OH 1 minute after standing up was 2.04 (95% confidence interval, 1.01-4.15). The corresponding hazard ratio for systolic OH 3 minutes after standing up was 1.69 (95% confidence interval, 1.02-2.80). Using a cutoff point of 7 mm Hg or greater for a diastolic BP change 1 minute after standing up, the hazard ratio for vascular death was highest: 2.20 (95% confidence interval, 1.23-3.93). By logistic regression analysis, the baseline associates of diastolic OH 1 minute after standing up were dizziness when turning the neck (odds ratio [OR], 2.44), the use of a calcium antagonist (OR, 2.31), the use of a diuretic medication (OR, 2.29), a high systolic BP (OR, 2.23), and a low body mass index (OR, 2.26). The baseline associates of systolic OH 3 minutes after standing up were male sex (OR, 1.52), diabetes mellitus (OR, 1.92), a high systolic BP (OR, 2.91), and a low body mass index (OR, 1.68).

Conclusions: The presence of diastolic OH 1 minute and systolic OH 3 minutes after standing up predict vascular death in older persons. They differ from each other in their prevalence and in several associates, suggesting different pathophysiologic backgrounds. Clinicians should prescribe vasodilating and volume-depleting medications with caution for elderly persons with diastolic OH 1 minute after standing up. Appropriate treatment of hypotension might be the best means to manage the different types of OH with poor vascular prognoses.

Arch Intern Med. 1999;159:273-280

Orthostatic hypotension develops if the compensatory mechanisms fail to resist the approximately 500-mL reduction of blood coming to the heart as a person stands up from a lying position. When cardiac output decreases, baroreceptors located in the heart, aorta, and carotid artery are stimulated to increase the heart rate and cause peripheral vasoconstriction to maintain the blood pressure (BP).1 Orthostatic hypotension is a common clinical finding in older persons, with a prevalence of 6% to 30%, depending on the characteristics of the target population and the definition of the disorder. According to the results of some epidemiologic studies, orthostatic hypotension is associated with advanced age, whereas others have found no association.

Age-associated physiological changes, an elevated BP, volume depletion, medication that impairs the homeostasis of the circulation, immobility, and autonomic insufficiency may lead to orthostatic hypotension. According to the results of epidemiologic studies, a low body mass index (BMI) high BP, Parkinson disease, stroke, transient ischemic attacks, a past myocardial infarction, and...
SUBJECTS AND METHODS

SUBJECTS

This study is part of a large population-based study project, the primary aim of which has been to examine risk factors and the effects of the prevention of falls in elderly persons. The population sample was determined accordingly. The subjects consisted of all home-dwelling persons aged 70 years or older who lived in 5 rural municipalities in northern Finland on September 1, 1991 (N = 969). A total of 833 persons (86%) participated in the examinations, which were carried out by research nurses, and orthostatic testing on standing at 1 minute and 3 minutes was successfully carried out in 792 (82%). The characteristics of the study population are described in Table 1.

MEASUREMENTS

Weight was measured with the subject in light clothing without shoes (0.1-kg accuracy), and height (centimeters) was measured with the subject standing or approximated. The BMI (weight in kilograms divided by the square of height in meters) was calculated from these values.

electrocardiographic abnormalities are examples of disorders that are associated with orthostatic hypotension. The risk of death is increased among hypertensive persons with diabetes mellitus who have orthostatic hypotension, but no increase in risk has been found among random samples of older persons with orthostatic hypotension. This suggests that the prognostic significance of orthostatic hypotension is more important in frail populations with many diseases than among home-dwelling persons.

It has been suggested that the prognostic significance of orthostatic hypotension may differ according to whether the diastolic or systolic orthostatic BP drop is being measured. The possible variation in prognosis related to the time between standing up and the measurement of orthostatic hypotension has not been evaluated. Different cutoff points in the definition of diastolic and systolic orthostatic hypotension have been used, but possible differences in survival prognosis according to the different cutoff points are unknown.

We examined the survival prognoses of nonvascular and vascular diseases in elderly persons having orthostatic hypotension according to different definitions, supplementing the analyses with different cutoff points in orthostatic hypotension that appeared to be important. To examine the underlying mechanisms behind a poor survival prognosis, the associations between clinical factors and orthostatic hypotension were also studied.
BP AND ORTHOSTATIC TESTING

Blood pressure was measured by a trained nurse after 5 minutes' rest with the subject supine, using a mercury manometer with a 12.5 x 40-cm cuff and a stethoscope with a bell. The right arm of the participant was used for measurement, unless it was injured. The similarity of the BP readings obtained by the 2 nurses who carried out these examinations was confirmed in pretests performed with a 2-limb stethoscope. The heart rate was recorded for 30 seconds after a rest. The orthostatic test consisted of pulse counts at 30 seconds and 2 minutes 30 seconds and BP measurements at 1 minute and 3 minutes after standing up.

ASSOCIATIONS BETWEEN SELF-RATED AND CLINICAL MEASURES

The validity of self-rated measures was evaluated by examining the associations between measures obtained from the clinical examinations and the self-reported measures representing similar characteristics. Congestive heart failure was associated with strain dyspnea (P<.001) and with rest dyspnea (P = .008) and coronary heart disease with chest pain (P<.001). The use of diuretic medication was associated with dizziness (P = .004) and dryness of the mouth (P<.001), each symptom occurring at least every other day. The heart rate rise 30 seconds after standing up in subjects experiencing dizzy symptoms when turning the neck was lower (mean, 8.6) than that found in others (11.0) (P = .008).

DEFINITIONS OF ORTHOSTATIC HYPOTENSION

Orthostatic hypotension was defined as a drop of 20 mm Hg or more in the systolic BP or a drop of 10 mm Hg or more in the diastolic BP either 1 minute or 3 minutes after standing up from a lying position. Systolic orthostatic hypotension (OH-S) was defined as a drop of 20 mm Hg or more in the systolic BP 1 minute (OH-S1) or 3 minutes (OH-S3) after standing up from a lying position. Diastolic orthostatic hypotension (OH-D) was defined as a drop of 10 mm Hg or more in diastolic BP 1 minute (OH-D1) or 3 minutes (OH-D3) after standing up from a lying position.

TIMES AND CAUSES OF DEATH DURING THE FOLLOW-UP PERIOD

Death certificates were obtained from the Central Statistical Office of Finland to record the times and the main causes of death in the cohort from the day of orthostatic testing to the end of the follow-up period. Vascular deaths were defined as diagnoses 390 to 4599 in International Classification of Diseases, Ninth Revision.

STATISTICAL ANALYSES

Survival distributions were calculated using the Kaplan-Meier estimator, and the test was based on the Cox-Mantel procedure. Proportional hazards models were used to analyze survival times, and the results are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). Cross-tabulations were used to assess the associates of orthostatic hypotension. Continuous variables were compared by using the Student t test. Risk factors for orthostatic hypotension were analyzed by using logistic regression analyses, the results of which were summarized by odds ratios (ORs) and 95% CIs. Computation was carried out using commercially available software (BMDP Statistical Software Inc, Los Angeles, Calif) on a SUN/UNIX mainframe computer (Sun Microsystems, Inc, Palo Alto, Calif).

minutes, 0.795. All correlations were statistically significant at P<.001.

Sixty-seven persons (8%) died of nonvascular causes and 102 (13%) of vascular causes, with 623 persons (79%) surviving during the follow-up of about 4 years. The mean (SD) survival times before a nonvascular death among those with OH-S1, OH-S3, OH-D1, and OH-D3 and the persons without orthostatic hypotension were 841 (400), 838 (462), 576 (424), 1215 (0), and 846 (466) days, respectively. The corresponding survival times before a vascular death were 804 (410), 751 (361), 825 (436), 625 (321), and 803 (473) days. The survival times before nonvascular and vascular deaths did not differ statistically between the persons with orthostatic hypotension and those without (Student t tests, P>.05).

ASSOCIATIONS BETWEEN ORTHOSTATIC HYPOTENSION AND NONVASCULAR AND VASCULAR DEATHS

The diastolic BP drop 1 minute after standing up was significantly greater among those who died of vascular causes (mean [SD], -2.2 [10.0] mm Hg) compared with the survivors (-4.8 [10.1] mm Hg) (t1 = 3.08, P = .002). Other diastolic or systolic postural BP changes measured either 1 minute or 3 minutes after standing up did not differ statistically (P>.05) between those who died of nonvascular or vascular causes and the survivors. Cox regression analyses were performed in a stepwise manner by including all the systolic and diastolic BP changes measured 1 and 3 minutes after standing up to test the possible independence of association with nonvascular or vascular death. No terms emerged in the model to predict nonvascular death. A diastolic BP change 1 minute after standing up was associated with vascular death, the HR associated with a diastolic BP fall of 1 mm Hg being 1.02 (P = .03; data not shown).

Cox regression analyses of nonvascular death were performed in connection with the different definitions of orthostatic hypotension. The HRs (95% CIs) for death associated with OH-S1, OH-D1, OH-S3, and OH-D3 were 1.08 (0.59-1.97), 1.74 (0.69-4.38), 1.20 (0.65-2.22), and 0.26 (0.04-1.88), respectively, compared with persons without orthostatic hypotension (data not shown).

Increased vascular mortality was found in the persons with OH-D1 (HR, 2.72; 95% CI, 1.46-5.05) and those with OH-S3 (HR, 1.84; 95% CI, 1.17-2.87) compared with persons without orthostatic hypotension (Table 2).
Table 1. Characteristics of the Study Population (N = 792)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>76.0 (4.9)</td>
</tr>
<tr>
<td>Men</td>
<td>300 (38)</td>
</tr>
<tr>
<td>Dependence in at least 1 daily activity</td>
<td>245 (31)</td>
</tr>
<tr>
<td>Self-rated health‡</td>
<td>86% (14%)</td>
</tr>
<tr>
<td>Good</td>
<td>172 (22)</td>
</tr>
<tr>
<td>Average</td>
<td>451 (57)</td>
</tr>
<tr>
<td>Poor</td>
<td>167 (21)</td>
</tr>
<tr>
<td>Low cognition (MMSE score, ≥23)</td>
<td>310 (39)</td>
</tr>
<tr>
<td>Use of psychotropic medicine</td>
<td>244 (31)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>158 (20)</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>9 (1)</td>
</tr>
<tr>
<td>Diagnosis of congestive heart failure</td>
<td>268 (34)</td>
</tr>
<tr>
<td>Diagnosis of coronary heart disease</td>
<td>169 (21)</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>28.4 (5.0)</td>
</tr>
<tr>
<td>Systolic BP, mean (SD), mm Hg</td>
<td>157.5 (25.2)</td>
</tr>
<tr>
<td>Diastolic BP, mean (SD), mm Hg</td>
<td>80.7 (11.9)</td>
</tr>
</tbody>
</table>

*MMSE indicates Mini-Mental State Examination; BP, blood pressure.
†Except where noted, the values are number (percentage).
‡Numbers do not total 792 because of missing data.

Table 2. Crude and Adjusted Hazard Ratios (HRs) for Mortality in Cox Regression Analyses Using Different Definitions of Orthostatic Hypotension Among Elderly People

<table>
<thead>
<tr>
<th>Definition*</th>
<th>Death Rate/100 Person-Years</th>
<th>Crude</th>
<th>Adjusted†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP 1 min after standing up</td>
<td>4.8</td>
<td>1.55 (0.99-2.42)</td>
<td>1.47 (0.88-2.45)</td>
</tr>
<tr>
<td>Diastolic BP 1 min after standing up</td>
<td>8.4</td>
<td>2.72 (1.46-5.05)</td>
<td>2.04 (1.01-4.15)</td>
</tr>
<tr>
<td>Systolic BP 3 min after standing up</td>
<td>5.7</td>
<td>1.84 (1.17-2.87)</td>
<td>1.69 (1.02-2.80)</td>
</tr>
<tr>
<td>Diastolic BP 3 min after standing up</td>
<td>3.5</td>
<td>1.12 (0.49-2.59)</td>
<td>0.86 (0.33-2.23)</td>
</tr>
</tbody>
</table>

*BP indicates blood pressure.
†Adjusted for age (≥80 years), sex, low (<mean − 1 SD) orthostatic (0.5 minute) heart rate rise, rest dyspnea occurring at least every other day, diabetes mellitus, stroke, low cognitive status (Mini-Mental State Examination score, ≤23), diagnosis of congestive heart failure, lost vibration sense, high (>mean + 1 SD) systolic BP, the use of more than 4 kinds of medication, low (<mean − 1 SD) peak expiratory flow, and low (<mean − 1 SD) body mass index.

Survival analyses with stratified values of diastolic BP drops (<0, 0-9, or ≥10 mm Hg) showed that 90%, 83%, and 73%, respectively, survived. Those with a diastolic BP drop of 0 to 9 mm Hg (n = 216) had a poorer prognosis than those with a drop of less than 0 mm Hg (n = 330) (Cox-Mantel, 6.1; P = .001), but no statistical difference was found between the 0-to-9-mm-Hg and 10-mm-Hg-or-greater changes (Cox-Mantel, 2.9; P = .09) (Figure 1). According to systolic BP drops (<0, 0-19, and ≥20 mm Hg), the corresponding proportions were 89%, 90%, and 81%, respectively. The survival prognosis was poorer in those with a systolic BP drop of 20 mm Hg or greater (n = 148) than in those with a drop of 0 to 10 mm Hg (n = 345) (Cox-Mantel, 7.1; P = .008), but no difference existed between the 0-to-19-mm-Hg and less-than-0-mm-Hg changes. Hence, comparison was made between the group with a drop in the systolic BP of 20 mm Hg or greater and the 2 groups with a better survival prognosis combined (Cox-Mantel, 6.2; P = .01) (Figure 2).

Cross-tabulations showed vascular death to be associated (P < .05) with advanced age (≥80 years), diabetes mellitus, stroke, a diagnosis of congestive heart failure, low cognitive status (Mini-Mental State Examination score, ≤23), high (>mean + 1 SD) systolic BP, an absent sense of vibration, low (<mean − 1 SD) BMI, low (<mean − 1 SD) peak expiratory flow, the use of more than 4 kinds of medication, and rest dyspnea occurring at least every other day. In addition to these variables, male sex (P = .14) and low (<mean − 1 SD) heart rate rise 30 seconds after standing up (P = .07) were entered in the Cox regression models to analyze the predictors of vascular mortality.

Among those with OH-D1 and in the persons without orthostatic hypotension, OH-D1 (HR, 2.04; 95% CI, 1.01-4.15), male sex (HR, 2.19; 95% CI, 1.24-3.87), the occurrence of rest dyspnea (HR, 2.05; 95% CI, 1.11-3.79), diabetes mellitus (HR, 2.42; 95% CI, 1.38-4.23), a high systolic BP (HR, 2.26; 95% CI, 1.30-3.93), and low peak expiratory flow (HR, 1.98; 95% CI, 1.02-3.83) were significantly associated with high vascular mortality. The significant contribution of OH-D1 to vascular death did not change after adjustment for Parkinson disease and the use of psychotropic medication.

Among those with OH-S3 and in the persons without orthostatic hypotension, OH-S3 (HR, 1.69; 95% CI, 1.02-2.80), male sex (HR, 1.78; 95% CI, 1.08-2.92), diabetes mellitus (HR, 1.84; 95% CI, 1.08-3.12), low cognitive status (HR, 2.17; 95% CI, 1.32-3.57), stroke (HR, 5.84; 95% CI, 1.68-20.25), a high systolic BP (HR, 1.66; 95% CI, 1.02-2.71), and low BMI (HR, 1.90; 95% CI, 1.17-3.11) were significantly associated with high vascular mortality. Adjustment for Parkinson disease and the use of psychotropic medication did not alter the result.

The orthostatic diastolic BP drop at 1 minute was further stratified using various cutoff limits to look for the best predictor of vascular death. The highest rela-
tive risk for vascular death was found using a cutoff point of 7 mm Hg or higher. The corresponding adjusted HR for vascular death was 2.20 (95% CI, 1.23-3.93). The HR associated with a cutoff of 0 mm Hg or greater was 1.60 (95% CI, 1.05-2.45).

ASSOCIATES OF ORTHOSTATIC HYPOTENSION

According to bivariate analyses, OH-D1 was associated (P<.05) with diagnoses of hypertension and congestive heart failure; diabetes mellitus; stroke; low (<mean – 1 SD) BMI; high (>mean + 1 SD) systolic and diastolic BPs; dizziness at least every other day; dryness of the mouth at least every other day; dizziness when turning the neck; the use of a high (>4) number of kinds of medication; and the use of psychotropic, calcium antagonist, and diuretic medication. Among the continuous variables (Table 3), the systolic BP was higher, the orthostatic heart rate rise at 30 seconds was lower, and the number of kinds of medication was higher in the persons with orthostatic hypotension than those without the disorder. A breakdown by sex showed that a heart rate rise at 30 seconds after standing up was significantly associated with OH-D1 in men (5.5 vs 11.5 beats per minute; P=.03) but not in women (8.1 vs 10.7 beats per minute; P=.11). The number of kinds of medication was higher in both men (P=.009) and women (P=.03) with OH-D1, but no other significant corresponding differences after gender breakdown were found.

Systolic orthostatic hypotension 3 minutes after standing was significantly associated with diabetes mellitus, a diagnosis of hypertension, high (>mean + 1 SD) systolic and diastolic BPs, and low (<mean – 1 SD) BMI. Among the continuous variables, systolic and diastolic BPs were higher and BMI was lower in persons with orthostatic hypotension than in those without (Table 3). In men, systolic and diastolic BPs were higher (P<.001 for both) in persons with OH-S3 than in those without orthostatic hypotension. Women with orthostatic hypotension had higher systolic BPs (P<.001) and lower BMIs (P=.003) than did women without the disorder. All the other corresponding differences after gender breakdown were nonsignificant (P>.05).

Stepwise logistic regression analyses were carried out by using the statistically significantly associated dichotomized variables as covariates, with only 1 variable among those of similar characteristics being used. The use of diuretic medication was, therefore, analyzed instead of dryness of the mouth. Because it was a consequence rather than a predictor of orthostatic hypotension, dizziness was not used as a covariate. Stroke was not included because it had occurred in only 5 persons. Dizziness when turning the neck, the use of calcium antagonists, the use of diuretic medication, and high systolic BPs emerged as being significantly associated, whereas a low BMI was not significantly associated with OH-D1. According to the results of stepwise logistic regression analysis, the significant associates of OH-S3 were male sex, a high systolic BP, and diabetes mellitus, and the association with a low BMI was not significant (Table 4).

Table 3. Characteristics of Persons Without Orthostatic Hypotension (OH-N) Compared With Those With Diastolic (OH-D1) and Systolic (OH-S3) Orthostatic Hypotension, by Clinical Continuous Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>OH-N (n = 552)</th>
<th>OH-D1 (n = 45)</th>
<th>OH-S3 (n = 148)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>75.9 (4.8)</td>
<td>76.7 (5.3)</td>
<td>76.2 (5.2)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>154 (24.3)</td>
<td>163 (30.1)†</td>
<td>169 (25.5)‡</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>79.9 (11.1)</td>
<td>82.6 (13.8)</td>
<td>83.6 (10.5)‡</td>
</tr>
<tr>
<td>Orthostatic heart rate rise in 30 s, beats per minute</td>
<td>10.9 (8.2)</td>
<td>7.2 (7.1)§</td>
<td>9.7 (8.3)‡</td>
</tr>
<tr>
<td>Orthostatic heart rate rise in 2 min</td>
<td>9.0 (8.8)</td>
<td>8.7 (7.5)</td>
<td>9.1 (8.2)</td>
</tr>
<tr>
<td>30 s, beats per minute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of kinds of medication</td>
<td>4.7 (3.4)</td>
<td>6.6 (3.6)§</td>
<td>4.7 (3.5)</td>
</tr>
<tr>
<td>Peak expiratory flow, kPa</td>
<td>286 (111)</td>
<td>265 (101)</td>
<td>291 (110)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.8 (5.2)</td>
<td>27.6 (4.7)</td>
<td>27.5 (4.6)§</td>
</tr>
</tbody>
</table>

*Data are given as mean (SD). BP indicates blood pressure.
†P<.05, Student t test.
‡P<.001, Student t test.
§P<.01, Student t test.

Table 4. Associates of Diastolic Orthostatic Hypotension (OH-D1) and Systolic Orthostatic Hypotension (OH-S3) by Logistic Regression Analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>SE</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>OH-D1</td>
<td>Dizziness when turning neck</td>
<td>0.89</td>
<td>0.39</td>
<td>2.44</td>
</tr>
<tr>
<td></td>
<td>Use of calcium antagonist</td>
<td>0.84</td>
<td>0.36</td>
<td>2.31</td>
</tr>
<tr>
<td></td>
<td>Use of diuretic medication</td>
<td>0.83</td>
<td>0.35</td>
<td>2.29</td>
</tr>
<tr>
<td></td>
<td>High systolic blood pressure*</td>
<td>0.80</td>
<td>0.41</td>
<td>2.23</td>
</tr>
<tr>
<td></td>
<td>Low body mass index*</td>
<td>0.82</td>
<td>0.44</td>
<td>2.26</td>
</tr>
<tr>
<td>OH-S3</td>
<td>Male sex</td>
<td>0.42</td>
<td>0.20</td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>0.65</td>
<td>0.23</td>
<td>1.92</td>
</tr>
<tr>
<td></td>
<td>High systolic blood pressure*</td>
<td>1.07</td>
<td>0.23</td>
<td>2.91</td>
</tr>
<tr>
<td></td>
<td>Low body mass index*</td>
<td>0.32</td>
<td>0.27</td>
<td>1.68</td>
</tr>
</tbody>
</table>

*Cutoff point 1 SD beyond mean.
According to the results of bivariate analyses, in persons with OH-D3, only a postural heart rate rise at 30 seconds was lower (7.3 [SD, 7.9]) than in persons without orthostatic hypotension (10.9 [SD, 8.2]) (P = .004). A low (<mean − 1 SD) BMI was more common among those with OH-D3 than in persons without orthostatic hypotension (P = .02). Other corresponding differences in the tested variables were not significant (P > .05).

In the persons with OH-S1, as with those with OH-S3, systolic (P < .001) and diastolic (P < .001) BPs were higher, the BMI was lower (P = .004), and diabetes mellitus (P = .04) was more common than in persons without orthostatic hypotension. In addition, stroke (P = .01) occurred more commonly in persons with OH-S1.

COMMENT

The main new finding in this study was that diastolic orthostatic hypotension measured 1 minute after standing up and systolic orthostatic hypotension measured 3 minutes after standing up predicted a high vascular mortality in elderly home-dwelling persons who were able to stand during the test.

In agreement with the results of a previous study,3 we did not find significant associations between orthostatic hypotension and death from nonvascular disease. Orthostatic hypotension was not associated with reduced physical or mental abilities, which may explain why in the present study orthostatic hypotension was not significantly associated with the occurrence of death from nonvascular disease.

According to the results of a previous study, systolic orthostatic hypotension increases the mortality risk among hypertensive persons with diabetes mellitus.10 In another study,3 although an association between diastolic orthostatic hypotension and vascular death was found in a sample of community-dwelling elderly persons, this association disappeared with a multivariate analysis.3 The participation rate in that study was considerably lower than in the present study. Those who did not participate in our study did not differ from those who did in age and significant demographic, health, and functional characteristics.12-15 However, the excluded persons who could not stand during the orthostatic test were older (mean, 78.5 years) and leaner (mean BMI, 25.8), and more of them had had stroke (15%) and parkinsonism (15%) than the participants. These exclusions actually decreased our power to find significant associations between death and orthostatic hypotension.

Incorrect death certificate data might have biased our results concerning the relationship between orthostatic hypotension and death. The death certificate data were based on clinical diagnoses made by health center and hospital physicians for 14% and 65% of subjects, respectively, and autopsies yielded 21% of the data. The validity of data concerning the main causes of death has been examined in the present university hospital area by Stenhack,21 who found that almost one fourth of the diseases designated as causes of death were clinically unsuspected, and almost 15% of clinical causes of death were not confirmed at autopsy. Brain infarctions carry a validity problem of this kind, but cardiovascular diseases are better validated. For vascular death causes, the main problem concerns distinguishing cerebrovascular from cardiovascular diagnoses.21 Our results concerning total survival prognosis for vascular disease are not likely to be biased by incorrect mortality data.

Cardiac and cerebrovascular disease might explain the increased vascular mortality found because myocardial infarctions, electrocardiographic abnormalities, transient ischemic attacks, and carotid stenosis are associated with orthostatic hypotension.7 Blood flow in the left coronary artery occurs during diastole.22 Hence, coronary circulation in persons with diastolic orthostatic hypotension may be reduced, and this may lead to a poor survival prognosis. The men with OH-D1 in the present study had a reduced heart rate rise after standing up. In addition to a lowering effect on postural BP, a baroreflex-mediated reduced postural heart rate rise may be a marker of a serious heart disease, which is associated with a reduced parasympathetic response to exercise.23

The associates of OH-D1 represent disturbances in function of the baroreflex and factors that may affect cardiac filling, consequently leading to a diminished stroke volume as a person stands up. A high BP may impair both of these by impairing baroreceptor sensitivity and by reducing cardiac compliance.24 Dizzy symptoms when turning the neck while rising from a lying position may be a marker of a hypersensitive carotid sinus,25 which may provoke bradycardia and an inability to maintain BP after standing up. Cerebral nervous system disorders, such as stroke, may lead to defective afferent baroreceptor input, which predisposes affected persons to orthostatic hypotension.1 The use of medications that may impair arterial vasoconstriction and reduce the blood volume may diminish the stroke volume and lead to orthostatic hypotension. Shonnon et al26 found advanced age to include a risk of orthostatic hypotension as a result of significant diuretic-induced weight loss and natriuresis.

The associates of OH-S3 represent sympathetic failure or other factors that impair peripheral vasoconstriction.27-30 Male sex as an associate of OH-S3 may be a marker of advanced vascular sclerosis, which increases the probability of orthostatic hypotension. Peripheral sympathetic system failure or atherosclerosis may explain the association found between OH-S3 and diabetes mellitus. A vagal failure is often found in diabetic persons, which itself could be an explanation for a poor survival prognosis for cardiac disease.31 Survival times according to the type of orthostatic hypotension did not clearly differ in the present study, however, giving no support to the assumption that the prevalence of sudden death from arrhythmia is overrepresented in persons with OH-D1 and those with OH-S3.

Persons with autonomic nervous system failure have reduced brain-level mean arterial BPs and low mean flow velocities in middle cerebral arteries during head-up tilt.32 This may link both systolic and diastolic orthostatic hypotension to fatal strokes.
Our results suggest that the definitions of orthostatic hypotension differ from each other as regards their clinical relevance and associated factors. Although all correlations between the diastolic and systolic postural BP changes were significant, these correlations, with the exception of the early and the late systolic changes, were surprisingly weak. In line with this, a diminished postural heart rate rise and low BMI were the only common associates as regards early and late diastolic postural BP reduction. The high risk of death from vascular disease associated with a low diastolic BP is reduced soon after the effect of exercise related to postural stress. At rest, coronary circulation may not be compromised by a low diastolic BP. The similar associated factors and the high correlation found between the early and late systolic postural BP reductions suggest that in both disorders, there is peripheral vascular damage. This may determine the permanent nature and the worse survival prognosis related to late rather than early postural BP reduction.

We estimated the clinical measurements to have been taken accurately and consistently between the 2 research groups and the correlations between the self-reported and clinical measures were modest. The measures were derived from multiple sources, and the researchers were unaware of the test results made by others. Some facts in the study design warrant attention. Recording by the physicians of the use of medication was carried out about 3 months from the orthostatic test. Although the orthostatic tests were not performed by the duty nurses, in some persons with symptomatic orthostatic hypotension, the medication of the participant may have been changed before the clinical examinations. Symptoms associated with orthostatic testing were not asked about. This prevented examining the relationships between death and postural dizziness, the importance of which has been stressed by some research groups. We cannot ensure the intra-individual reproducibility of orthostatic test results, which has been found to be low in institutionalized persons and lower for systolic than diastolic BP measurements. The time of day, of meals, and activities relative to the time of orthostatic testing may have placed our participants in different situations, which might have contributed to the orthostatic test results. We may have missed some persons who in other daily circumstances would have presented a hypotensive test result.

As also found in the present study among home-dwelling subjects, diastolic orthostatic hypotension defined in the traditional manner is a less common finding in community-dwelling elderly adults than systolic orthostatic hypotension. A diastolic BP drop 1 minute after standing up appeared to be a sensitive measure of vascular survival prognosis. The traditional cutoff point used in the definition, 10 mm Hg or greater, is obviously too high for optimal use in the prediction of vascular disease prognosis among elderly persons because the strongest predictive cutoff value was found to be 7 mm Hg or greater, and an association with death from vascular disease still existed when using a cutoff value of 0 mm Hg or higher. New data are needed on the associations between different cutoff points of diastolic orthostatic hypotension and cardiac and cerebrovascular events. Likewise, the contribution of OH-S3 to both cardiovascular and cerebrovascular events should be examined.

Conclusion

Our results strongly encourage clinicians to perform orthostatic tests on their older patients. Changes in heart rate when a person stands up and changes in both the diastolic reading 1 minute and the systolic reading 3 minutes after standing up should be observed. As previously indicated for orthostatic hypotension, vasodilating and volume-depleting medications should be prescribed with caution to persons with OH-D1. These patients should be well hydrated, and they would benefit by avoiding rapid changes of posture and by sitting on the side of the bed on first arising. The treatment of hypertension is obviously the best single factor in improving postural BP regulation. A randomized clinical trial has shown that mild diuretic therapy improves the prognosis of patients with and without diabetes with isolated systolic hypertension. Successful treatment of hypertension may enhance baroreceptor sensitivity, increase vascular compliance, and reduce the threshold for cerebral autoregulation.

Accepted for publication April 20, 1998.

This study was supported by the Finnish Ministry of Social Welfare and Health, the Academy of Finland, the Uulu Arho Foundation, Helsinki, and the Tampere University Hospital, Tampere, Finland, and Oulu University Hospital (Oulu, Finland) Medical Research Funds.

We thank the study persons and the staff of the health centers in the participating municipalities for their support in this study. We also thank the applications system analyst, Paavo Soini, for managing the data.

Reprints: Heikki Luukinen, MD, Unit of General Practice, Oulu University Hospital, Aapistie 1, FIN-90220, Oulu, Finland (e-mail: hluukine@sun3.oulu.fi).

References

9. Tilvis RS, Hakala SM, Valvanne J, Erkinjuntti T. Postural hypotension and dizzi-


