Systemic Hypertension: An Over View Of Various Cardiovascular Risk Factors And Multiple Treatments

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Abstract
Systemic hypertension is a major risk factor for cardiovascular disease and is present in 69% of patients with a first myocardial infarction, in 77% of patients with a first stroke, in 74% of patients with chronic heart failure, and in 60% of patients with peripheral arterial disease. Double-blind, randomized, placebo-controlled trials have found that antihypertensive drug therapy reduces cardiovascular events in patients aged younger than 80 years and in patients aged 80 years and older in the Hypertension in the Very Elderly Trial. Although the optimal blood pressure treatment goal has not been determined, existing epidemiologic and clinical trial data suggest that a reasonable therapeutic blood pressure goal should be <140/90 mm Hg in patients younger than 80 years and a systolic blood pressure of 140-145 mm Hg if tolerated in patients aged 80 years and older. Non-pharmacologic lifestyle measures should be encouraged both to prevent development of hypertension and as adjunctive therapy in patients with hypertension. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, and diuretics have all reduced cardiovascular events in randomized trials. The choice of specific drugs depends on efficacy, tolerability, presence of specific comorbidities, and cost.

Keywords: hypertension, diuretics, beta blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers

Introduction
The age-adjusted prevalence of systemic hypertension in the United States is 64% of older men and 78% of older women according to the American Heart Association (AHA) Statistics Committee and Stroke Statistics Committee [1]. Patients with hypertension should be evaluated for other cardiovascular risk factors including smoking, dyslipidemia, diabetes mellitus, age older than 55 years for men and 65 years for women, body mass index ≥30 kg/m², physical inactivity, microalbuminuria, an estimated glomerular filtration rate <60 ml/min/1.73 m², and for a family history of premature cardiovascular disease (younger than 55 years in fathers or brothers and younger than 65 years in mothers or sisters) [2]. Patients with hypertension should also be evaluated for target organ damage and cardiovascular disease including left ventricular hypertrophy, prior myocardial infarction, angina pectoris, prior coronary revascularization, congestive heart failure, stroke or transient ischemic attack, peripheral arterial disease, nephropathy, and retinopathy [2].

The higher the systolic or diastolic blood pressure, the higher the risk of cardiovascular morbidity and mortality [3]. Increased systolic blood pressure and pulse pressure are stronger risk factors for cardiovascular morbidity and mortality in older persons than is increased diastolic blood pressure [4-6]. An increased pulse pressure found in older persons with isolated systolic hypertension indicates decreased vascular compliance in the large arteries and is even a better marker of risk than is systolic or diastolic blood pressure [4-6].

Effect of antihypertensive therapy in reducing cardiovascular events
Numerous prospective, double-blind, randomized, placebo-controlled studies have shown that antihypertensive drug therapy reduces the development of new coronary events, stroke, and CHF [2,7,27-38]. Older patients with hypertension if treated appropriately will have a greater absolute reduction in cardiovascular events such as major coronary events, stroke, CHF, and renal insufficiency and a greater reduction in dementia [39] than in younger patients. Therapy with antihypertensive drugs reduces the incidence of all strokes 38% in women, by 34% in men, by 36% in older persons, and by 34% in persons older than 80 years [14]. The overall data suggest that the decrease of stroke in older persons with hypertension is related more to a reduction in blood pressure than to the type of antihypertensive drugs used [14].

Use of antihypertensive drug therapy
A meta-analysis of 147 randomized trials including 464,000 patients with hypertension showed that except for the extra protective effect of beta blockers given after myocardial infarction and a minor additional effect of calcium channel blockers in preventing stroke, use of beta blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), diuretics, and calcium channel blockers cause a similar reduction in coronary events and stroke for a given decrease in blood pressure [56,57]. The proportionate decrease in cardiovascular events was the same or similar regardless of pretreatment blood pressure and the presence or absence of cardiovascular events [56,57]. Atenolol should not be used [58-60]. Beta blockers such as carvedilol, nebivolol, and bisoprolol are preferred [60]. Centrally acting agents, such as clonidine, reserpine, and guanethidine, should not be used as monotherapy because they have been associated with a high incidence of significant side effects, including sedation, depression, and constipation.

Most patients with hypertension will need 2 or more antihypertensive drugs to control their blood pressure [2,7]. If the blood pressure is more than 20/10 mm Hg above the goal blood pressure, drug therapy should be initiated with 2 antihypertensive drugs [2,7].

Methods
MESA is a prospective cohort study designed to investigate the prevalence and progression of subclinical cardiovascular disease in a population-based sample. Details of the study design have been published elsewhere. There were 6,814 participants in MESA ages 45–84 from four ethnic groups, White, African American, Hispanic, and Chinese. Recruitment took place from July 2000 to August 2002 at six US field centers (Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St. Paul, Minnesota). All participants were free of known cardiovascular disease at the time of enrollment. The institutional review boards at all participating institutions approved the study, and all participants provided informed consent.
Age interactions were tested in the adjusted regression analyses and considered significant at \( p < 0.05 \). Age was stratified as older as or younger than 65 years to compare to previous elderly cohort analysis.\(^{14}\) Because there were a small number of younger participants with advanced hypertension, Stages I and II were combined for these analyses. If interactions were significant we presented the stratified results.

We excluded participants with treated hypertension (n = 2,533), as done in previous blood pressure studies in MESA.\(^{14}\) Because the effect of blood pressure medication on AVC and the amount of misclassification as a result of treatment on blood pressure is unknown. A sensitivity analysis including treated hypertension patients in the analysis was conducted but did not change inferences. All statistical analysis were performed with SPSS 16.0.1 software for Windows (SPSS Inc, Chicago, Illinois) and S-Plus (release 8.0, Insightful Inc, Seattle, WA).

Results

There were 4,275 participants without treated hypertension in this analysis, 2,783 were <65 years old. Differences were present in AVC risk factors between those with and without hypertension (Table 1). Hypertensive participants were more often older, diabetic, had a higher BMI, and more likely to be African-American. Overall, 407 participants had AVC, for a prevalence of 9.5% in this cohort. This AVC prevalence is lower than in previous reports from the MESA cohort,\(^{7,14}\) due to the exclusion of participants with treated hypertension who had a prevalence of AVC of 20%.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n=2206)</th>
<th>Pre-HTN (n=1304)</th>
<th>Stage I (n=566)</th>
<th>Stage II (n=199)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVC Prevalence</td>
<td>139 (6%)</td>
<td>144 (11%)</td>
<td>93 (17%)</td>
<td>31 (16%)</td>
</tr>
<tr>
<td>AVC Score(^{1})</td>
<td>45 (17.144)</td>
<td>54 (18.115)</td>
<td>73 (15.209)</td>
<td>69 (17.246)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 (9)</td>
<td>62 (10)</td>
<td>65 (10)</td>
<td>68 (9)</td>
</tr>
<tr>
<td>Female</td>
<td>1215(55%)</td>
<td>600 (46%)</td>
<td>279 (49%)</td>
<td>118 (59%)</td>
</tr>
<tr>
<td>White</td>
<td>960 (44%)</td>
<td>515 (40%)</td>
<td>215 (38%)</td>
<td>63 (32%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>325 (15%)</td>
<td>153 (12%)</td>
<td>71 (13%)</td>
<td>23 (12%)</td>
</tr>
<tr>
<td>Black</td>
<td>402 (18%)</td>
<td>320 (25%)</td>
<td>148 (26%)</td>
<td>70 (35%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>519 (24%)</td>
<td>316 (24%)</td>
<td>131 (23%)</td>
<td>43 (22%)</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>1079 (49%)</td>
<td>662 (51%)</td>
<td>297 (53%)</td>
<td>98 (50%)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m2)</td>
<td>26.8 (5.0)</td>
<td>28.4 (5.1)</td>
<td>28.0 (5.3)</td>
<td>29.2 (6.0)</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>93 (14)</td>
<td>99 (13)</td>
<td>98 (14)</td>
<td>101 (15)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>140 (6%)</td>
<td>124 (10%)</td>
<td>69 (12%)</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>98 (26)</td>
<td>104 (33)</td>
<td>104 (28)</td>
<td>106 (27)</td>
</tr>
<tr>
<td>Low-density lipoprotein (mg/dL)</td>
<td>119 (32)</td>
<td>121 (31)</td>
<td>121 (30)</td>
<td>123 (32)</td>
</tr>
<tr>
<td>High-density lipoprotein (mg/dL)</td>
<td>52 (15)</td>
<td>51 (15)</td>
<td>52 (15)</td>
<td>52 (15)</td>
</tr>
<tr>
<td>Triglycerides(^{6}) (mg/dL)</td>
<td>103 (72, 148)</td>
<td>115 [77, 165]</td>
<td>119 [82, 168]</td>
<td>116 [85, 165]</td>
</tr>
<tr>
<td>Lipid Lowering Meds</td>
<td>206 (9%)</td>
<td>141 (11%)</td>
<td>70 (12%)</td>
<td>18 (9%)</td>
</tr>
</tbody>
</table>

Data are presented as mean(\(SD\)) for continuous variables, number(%) for categorical variables.

\(^{1}\)JNC-7 categories: Normal (SBP < 120 mmHg and DBP < 80 mmHg), Pre-HTN (SBP 120–139 mmHg or DBP 80–89 mmHg), Stage I (SBP 140–159 mmHg or DBP 90–99 mmHg), Stage II (SBP ≥160 mmHg or DBP ≥ 100 mmHg).\(^{6}\) Median [IQR]

Discussion

This study confirms that hypertension is associated with AVC as measured by CT, and demonstrates that hypertension severity, defined by either JNC-7 hypertension stage or continuous BP, is associated with increased risk for prevalent AVC. This study also demonstrates an important age interaction, specifically that the association of hypertension with prevalent AVC is greatest in those age <65 years. We did not find any associations with hypertension and severity of AVC.

The finding of an association between hypertension and AVC is consistent with the results of previous studies.\(^{17,19–22,24,25}\) Most previous analyses have used only the presence of hypertension in evaluating the associations with AVC as measured by echocardiography. In the reports by Lindroos and Boon, the ORs for AVC in the presence of hypertension, were 1.74 and 2.38 respectively. However, both studies used a more severe definition of hypertension, with a systolic blood pressure >160 mmHg or diastolic >90 mmHg\(^{16}\) or 95 mmHg\(^{22}\). Also in contrast to the present study, in which hypertension was defined by JNC-7 stages, other previous population study cohorts including, the Cardiovascular Health Study (CHS) and the Stroke Prevention: Assessment of Risk in a Community (SPARC) study, defined hypertension by either self-report or antihypertensive medication use. In CHS, the reported OR was 1.23 (95% CI: 1.1 – 1.4) and in SPARC the OR was 1.93 (95% CI: 1.12 – 3.32). In addition, none of these prior studies was able to demonstrate an association of BP as a continuous variable with aortic sclerosis. These previous studies did not exclude those with treated hypertension, which may have biased the results of their BP-based analyses.

Conclusion

This study extends the results of previous studies by demonstrating that the association of hypertension with AVC is strongest in those less than age 65 years. While hypertension remains an important cardiovascular risk factor in the elderly,\(^{23}\) the effect of hypertension is attenuated in older populations.\(^{29}\) Similarly, the impact of lipoprotein-associated risk on AVC has been shown to be attenuated with age.\(^{30}\) If these findings are confirmed in future prospective studies, then targeting traditional risk factors, specifically dyslipidemia and hypertension, may be most effective in those less than age 65 years.

References


