Association Between Different Measures of Blood Pressure and Coronary Artery Calcium in Postmenopausal Women

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Abstract—The aim of this study was to determine the magnitude and significance of the associations among coronary artery calcium (CAC) and systolic blood pressure, diastolic blood pressure, pulse pressure, and mean arterial pressure. Women 50 to 59 years of age at baseline in the Women’s Health Initiative clinical trial of conjugated equine estrogen underwent computed tomography scanning of the chest after the end of the trial. Blood pressures were measured twice with the participant in the seated position using a conventional mercury sphygmomanometer. The study included 1064 women with a mean age of 55.1 (2.8) years. The prevalence of a CAC score >0, ≥10, and >100 was 47%, 39%, and 19%, respectively. There was a linear association between the log-odds of any CAC and systolic blood pressure, whereas there was a curvilinear and inverse association with diastolic blood pressure. For any value of diastolic blood pressure, the probability of CAC increased with higher levels of systolic blood pressure, whereas for any given value of systolic blood pressure, the probability of any CAC decreased with higher levels of diastolic blood pressure. Also, a pulse pressure ≥55 mm Hg was associated with a higher odds (1.95; 95% CI, 1.24 to 3.06) for having any CAC, whereas individuals with isolated systolic hypertension had a 73% higher odds for CAC >0 (95% CI, 1.03 to 2.90; P=0.04). In postmenopausal women, higher levels of pulse pressure and systolic blood pressure were strong determinants of CAC, whereas diastolic blood pressure was inversely related. (Hypertension. 2008;52:833-840.)

Key Words: calcium • coronary • pulse pressure • women • coronary artery disease • atherosclerosis • postmenopausal

In a regulated process similar to skeletal bone formation,1 calcium is deposited in atherosclerotic plaques.2 With the advent of computed tomography (CT), these calcified atheromatous plaques can be detected throughout the vasculature.3 Moreover, because of decreases in the acquisition time required to obtain the images, these calcium deposits can also be visualized in the coronary arteries.4 The extent of calcified coronary atherosclerotic plaques is highly correlated with both the total atheromatous plaque burden5 and the percentage of stenosis6 in that vascular bed as well as being a strong and independent predictor of incident coronary heart disease (CHD) events in both men and women.7,8

Coronary artery calcium (CAC) is increasingly advocated as a component of individual cardiovascular disease (CVD) risk stratification procedures.9 Accordingly, knowledge of the differential associations between risk factors for CAC and CHD is clinically relevant. Previous studies have found significant associations among several CVD risk factors (age, male sex, cigarette smoking, diabetes, and family history) of CHD and the presence and extent of CAC,10,11 whereas the associations for different cholesterol fractions are more modest.12 Notably, hypertension has been shown to be strongly associated with the presence of CAC.13 However, previous reports have not typically explored the association with individual measures of blood pressure. Therefore, this study examined the associations among 4 different measures of blood pressure (systolic, diastolic, pulse pressure, and mean arterial pressure) and CAC.

Methods

Subjects
Subjects for the current study were a subset of women who were 50 to 59 years of age at baseline in the Women’s Health Initiative (WHI) clinical trial of conjugated equine estrogen (CEE) who underwent a one-time CT scan of the chest after the end of the trial to determine CAC. Detailed descriptions of the WHI study design and baseline characteristics of participants in the WHI CEE trial have been published previously.14 Briefly, CEE participants were postmenopausal women who were 50 to 79 years of age at randomization and had a history of hysterectomy before enrollment in the WHI. Study participants were randomized to receive CEE (0.625 mg per...
day of Premarin; Wyeth Pharmaceuticals) or a matching placebo. Methods for data collection, management, and quality assurance have been published previously.\textsuperscript{15}

The Women’s Health Initiative Coronary Artery Calcium Study (WHI-CACS) obtained coronary calcium measurements using cardiac CT for WHI CEE participants who were 50 to 59 years of age at the time of randomization into the CEE trial. The Human Subjects Review Committee at each participating institution approved the WHI study protocols. In accordance with institutional guidelines, all subjects provided written informed consent.

Data Collection

At the baseline WHI clinic visit, CEE trial participants provided data on a wide range of factors. The presence of high cholesterol or diabetes was identified by self-reported use of a medication for that condition. Smoking was categorized as current, former, or none. Ethnicity was determined by self-report with the following categories: non-Hispanic white, African-American/black (non-Hispanic), Hispanic, Asian/Pacific Islander, American Indian/Alaska Native, or unknown (women who indicated “other” ethnicity or did not answer the question). Education and income were ascertained by self-report from a range of options. Use of postmenopausal hormone therapy before WHI CEE trial enrollment was ascertained via an interview.

Blood pressure was measured at baseline and then at each clinic visit until the end of the CEE trial. After a 5-minute rest, blood pressures were measured twice with the participant in the seated position using a conventional mercury sphygmomanometer and appropriately sized cuffs. Systolic blood pressure (SBP) was defined as the pressure level at which the first of ≥2 regular Korotkoff sounds were heard. Diastolic blood pressure (DBP) was defined as pressure level of the last of these rhythmic sounds. Hypertension was defined as an SBP ≥140, a DBP ≥90, or use of a blood pressure-lowering medication. Prehypertension was defined as an SBP ≥120 but <140 or a DBP ≥80 but <90. Pulse pressure (PP) was calculated as the difference between the SBP and DBP, whereas mean arterial pressure (MAP) was defined as DBP + 1/3 (SBP − DBP). For these analyses, we evaluated the associations between CAC and both baselines and the last available blood pressure measurement, as well as the difference between the 2 values.

Coronary Artery Calcified Plaque Measurements

Women in the CEE trial who were 50 to 59 years of age at time of randomization to CEE or placebo at 28 WHI clinical centers (n = 1742) were mailed invitations to participate in WHI-CACS. Exclusion criteria were a last measured or reported weight of ≥300 pounds (because of technical and equipment-related restrictions), participant request for no further contact or clinic visits, or participant lost to follow-up or deceased since randomization (30.4% of participants were excluded for ≥1 of these reasons). A total of 1079 women (61.6% of those eligible at the 28 clinical centers) provided informed consent and received cardiac CT exams by electron beam or multidetector–row CT = 1.3 years after the CEE trial ended. A standardized protocol was developed based on previous multicenter experience with cardiac CT.\textsuperscript{16} Phantom scan and test images were obtained from each CT system to verify technical parameters and system performance. Analyses of the measurements were performed by certified staff at the central reading center at Wake Forest University who were masked to participants’ treatment assignment. The Agatston score was calculated on a computer workstation (TeraRecon Inc) by experienced image analysts using established parameters (lesion size of >1 mm\textsuperscript{2}, adjustment for slice thickness, and threshold of 130 Hounsfield units).\textsuperscript{17}

Women with a history of coronary revascularization before randomization were excluded from the analysis (n = 12). The reading protocol specified exclusion of coronary stents, pacemakers, metallic clips, and other surgical remnants from the analysis process. Three women with incomplete scans were excluded. The final data set included 1064 participants without previous revascularization and with nonmissing CAC scores.

Statistical Analyses

The primary outcome variable was a CAC score >0, whereas CAC severity (CAC = 0, 0 < CAC ≤ 100, or CAC > 100) was treated as a secondary outcome. The 6 primary exposure variables of interest were SBP, DBP, PP, MAP, blood pressure medication use, and hypertension status. Baseline characteristics were compared between participants with a CAC score of 0 versus >zero. Differences between the groups were assessed using \( \chi^2 \) tests for categorical variables, \( t \) tests for normally distributed continuous variables, and Wilcoxon tests for non-normally distributed continuous variables.

For the main analysis, logistic regression models were used to evaluate the association between the primary exposure variables and presence of any CAC. For the secondary analysis, nominal polychotomous logistic regression models were used to evaluate the association between the primary exposure variables and the severity of CAC. Separate tests were used to determine whether primary exposure variables were associated with different levels of CAC, and a test of heterogeneity (p-het) was performed to see whether these associations differed by severity of CAC. To control for potential confounding, we adjusted for age, race/ethnicity, diabetes, dyslipidemia, smoking, body mass index (BMI), family history of CHD, education, income, and CEE assignment. A 2-sided \( P \) value < 0.05 was considered statistically significant. The main statistical analyses were performed using SAS version 9.1 (SAS Institute Inc). Graphs of generalized additive models and goodness of fit were assessed with R version 2.6.

Results

Baseline Characteristics

There were 1064 subjects available for this study. The mean age at WHI randomization (baseline) was 55.1 (2.8) years and 64.8 (2.9) years at CAC ascertainment. WHI-CACS women had an average of 7.4 years of participation in the CEE trial and an average interval of 1.3 years from trial end to scanning. The prevalence of a coronary calcium score >0 was 47%, whereas the prevalence of a CAC score ≥10 and >100 was 39% and 19%, respectively. Those with any CAC had significantly higher age at enrollment in the WHI (Table 1). With adjustment for this variable, those with any CAC had significantly higher BMI, waist circumference, hip circumference, waist-to-hip ratio, and pack-years of smoking but lower reported physical activity. The CAC >0 group also had higher prevalences of current smoking, cholesterol medication use, and medical treatment for diabetes. Conversely, those with any CAC had a lower prevalence of achieving a college degree or a gross annual income >$35 000.

Of those who reported taking a medication for blood pressure control, 12% were taking an angiotensin-converting enzyme inhibitor, 1% an angiotensin receptor blocker, 13% a \( \beta \)-blocker, 15% a calcium channel blocker, 22% a diuretic, 7% a combination medication, and 30% >1 blood pressure medication. Those with a CAC score >0 had a higher use of angiotensin-converting enzyme inhibitors (8.4% versus 3.8%), calcium channel blockers (8.4% versus 6.8%), and multiple blood pressure medications (17.9% versus 12.6%), whereas the rates for angiotensin receptor blockers (0.0% versus 1.1%), \( \beta \)-blockers (6.5% versus 6.1%), diuretics (11.0% versus 11.0%), and combination medications (3.4% versus 3.0%) were similar.

Table 2 shows the comparison of blood pressure measures stratified by CAC status. With adjustment for age, those who had any CAC had significantly higher levels of baseline SBP, last available SBP, PP, and MAP, but not DBP, at either
baseline or the last available measurement. There was also a significant difference in the distribution of hypertension, prehypertension, and normal blood pressure between those who had any CAC compared with those with no CAC. There were no significant differences in the temporal changes in SBP or DBP by CAC status.

The Figure shows the odds of having a CAC score >0 by: (1) DBP; (2) SBP; (3) PP; and (4) MAP. With adjustment for age, race, diabetes, dyslipidemia, smoking, BMI, family history of CHD, education, income, antihypertensive drug use, and DBP, there was a linear association between the log-odds of any CAC and SBP (p-linear=0.99). Conversely, with the same adjustment (but replacing SBP with DBP), the association between the odds of any CAC and DBP was nonlinear (p-linear=0.03) and instead was quadratic (p-quad=0.50). Specifically, at higher levels of DBP, the odds for any CAC decreased and actually became <1.0. There was a linear association (p-linear=0.70) between PP and the odds of any CAC that was similar in magnitude as that for SBP. There was no discernable association between MAP and the odds for any CAC (p-lin=0.11).

For any value of DBP, the probability of CAC increased with higher levels of SBP. Conversely, for any given value of SBP, the probability of any CAC decreased with higher levels of DBP. We therefore explored the multivariable associations among different levels of baseline and last available SBP and DBP, as well as PP, MAP, and a diagnosis of hypertension and prehypertension (Table 3). After adjustment for age, race/ethnicity, diabetes, dyslipidemia, smoking, BMI, family history of CHD, CEE treatment assignment, education, in-
come, antihypertensive drug use, and DBP, SBP at both time points was positively associated with an increased risk of CAC. Conversely, there was a significant inverse trend between both baseline and last available DBP and the odds of CAC. With adjustment for the same risk factors (except DBP), PP was positively associated with an increased risk of CAC. These results suggest that individuals with isolated systolic hypertension (ISH) may be at higher odds for the presence of coronary artery disease. Indeed, compared with those with a normal blood pressure (SBP <140 and a DBP <90), those with ISH had a 73% higher odds for CAC (95% CI, 1.03 to 2.90; \( P = 0.04 \)) independent of other risk factors and blood pressure medication status. Finally, in fully adjusted models, there were no significant associations among

<table>
<thead>
<tr>
<th>Blood Pressure Variable</th>
<th>CAC&gt;0</th>
<th>CAC=0</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline SBP, mm Hg†</td>
<td>127 (16.3)</td>
<td>122.7 (14.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Last SBP, mm Hg†</td>
<td>125.3 (15.6)</td>
<td>121.2 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP difference, last−baseline‡</td>
<td>3.5 (15.4)</td>
<td>2 (13.4)</td>
<td>0.21</td>
</tr>
<tr>
<td>Among those not on antihypertensive medications, mm Hg†</td>
<td>-5.4 (20)</td>
<td>-6.3 (16.5)</td>
<td>0.65</td>
</tr>
<tr>
<td>Among those on an antihypertensive medication, mm Hg†</td>
<td>-7.9 (10.7)</td>
<td>-7.7 (10.5)</td>
<td>0.95</td>
</tr>
<tr>
<td>Baseline DBP, mm Hg†</td>
<td>77.9 (8.7)</td>
<td>77.7 (8.9)</td>
<td>0.72</td>
</tr>
<tr>
<td>Last DBP, mm Hg†</td>
<td>72.3 (9.3)</td>
<td>73.3 (9.1)</td>
<td>0.13</td>
</tr>
<tr>
<td>DBP difference, last−baseline‡</td>
<td>-2.2 (10)</td>
<td>-2 (8.8)</td>
<td>0.94</td>
</tr>
<tr>
<td>Among those not on antihypertensive medications, mm Hg†</td>
<td>-7.9 (10.7)</td>
<td>-7.7 (10.5)</td>
<td>0.95</td>
</tr>
<tr>
<td>Among those on an antihypertensive medication, mm Hg†</td>
<td>-2.2 (10)</td>
<td>-2 (8.8)</td>
<td>0.94</td>
</tr>
<tr>
<td>Days from last blood pressure to CAC scan†</td>
<td>539.1 (241.4)</td>
<td>531.7 (228.2)</td>
<td>0.19</td>
</tr>
<tr>
<td>PP, mm Hg†</td>
<td>49.1 (13)</td>
<td>45 (10.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP, mm Hg†</td>
<td>94.2 (10)</td>
<td>92.7 (10)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension status‡</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normotensive‡</td>
<td>24.8 (124)</td>
<td>32.6 (184)</td>
<td></td>
</tr>
<tr>
<td>Prehypertensive‡</td>
<td>31.9 (159)</td>
<td>36.3 (205)</td>
<td></td>
</tr>
<tr>
<td>Hypertensive‡</td>
<td>43.3 (216)</td>
<td>31.2 (176)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age.
†Mean (SD); percentage (frequency).
‡Includes antihypertensive medications used at baseline and any time during follow-up.

**Figure.** Adjusted odds of a CAC score >0 by selected blood pressure measures.
the presence of any CAC and MAP, being on a hypertension medication, a diagnosis of prehypertension, or a diagnosis of hypertension.

The analyses in Table 3 combined those who reported taking and not taking a blood pressure medication. To explore potential differences attributable to blood pressure medication, we conducted stratified analyses by medication status (data not shown). After the same multivariable adjustment as applied to the analyses described above, the magnitudes of the associations were modestly different by medication status, but the trend and overall findings were not materially different. That is, for both those taking and those not taking a blood pressure medication, SBP was significantly associated with the presence of any CAC, and the magnitude of the effect increased with higher levels of SBP. For DBP, the association with CAC was inverse such that higher levels of DBP were significantly associated with a reduced odds for CAC.

We then examined the association among the different blood pressure measures and the extent of CAC (Table 4). Because the results for baseline and last available blood pressure were similar, we present those using the baseline values only. Compared with a CAC score equal to 0 and after adjustment for age, race/ethnicity, diabetes, dyslipidemia, smoking, BMI, family history of CHD, education, income, and CEE treatment assignment as well as additional covariates specific to particular risk factors (see below).

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in this study of a subgroup of postmenopausal women from the WHI CEE clinical trial who were 50 to 59 years of age at baseline and studied for CAC, increasing SBP was associated with the presence and extent of CAC. Conversely, higher levels of DBP were associated with lower odds for CAC, suggesting that PP may be significantly associated with CAC. Indeed, with adjustment for multiple CVD risk factors, there was a significant trend between increasing odds for CAC with increasing levels of PP. More specifically, a PP ≥55 mm Hg was associated with 2-fold higher odds for the presence of any CAC. Conversely, there was no significant association between MAP and CAC. Together, these results suggest a complex relationship between different blood pressure measures and CAC such that both SBP and higher levels of PP may be clinically relevant for the prevention of coronary artery disease in postmenopausal women.

### Discussion

In this study of a subgroup of postmenopausal women from the WHI CEE clinical trial who were 50 to 59 years of age at baseline and studied for CAC, increasing SBP was associated with the presence and extent of CAC. Conversely, higher levels of DBP were associated with lower odds for CAC, suggesting that PP may be significantly associated with CAC. Indeed, with adjustment for multiple CVD risk factors, there was a significant trend between increasing odds for CAC with increasing levels of PP. More specifically, a PP ≥55 mm Hg was associated with 2-fold higher odds for the presence of any CAC. Conversely, there was no significant association between MAP and CAC. Together, these results suggest a complex relationship between different blood pressure measures and CAC such that both SBP and higher levels of PP may be clinically relevant for the prevention of coronary artery disease in postmenopausal women.

### Table 4. Multivariable Associations Between Blood Pressure Measures and the Extent of CAC

<table>
<thead>
<tr>
<th>Blood Pressures (mm Hg)</th>
<th>CAC Score 1 to 99</th>
<th>CAC Score ≥100</th>
<th>( P^* )</th>
<th>P-het†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>Odds Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>SBP‡ (ref: &lt;110)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>110 to 119</td>
<td>1.60</td>
<td>0.90, 2.86</td>
<td>1.50</td>
<td>0.74, 3.06</td>
</tr>
<tr>
<td>120 to 129</td>
<td>1.93</td>
<td>1.07, 3.48</td>
<td>1.47</td>
<td>0.70, 3.07</td>
</tr>
<tr>
<td>130 to 139</td>
<td>2.07</td>
<td>1.04, 4.12</td>
<td>2.20</td>
<td>0.98, 4.91</td>
</tr>
<tr>
<td>≥140</td>
<td>3.78</td>
<td>1.78, 8.01</td>
<td>2.11</td>
<td>0.86, 5.20</td>
</tr>
<tr>
<td>DBP§ (ref: &lt;70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70 to 74</td>
<td>0.90</td>
<td>0.51, 1.56</td>
<td>1.32</td>
<td>0.65, 2.66</td>
</tr>
<tr>
<td>75 to 79</td>
<td>1.01</td>
<td>0.57, 1.79</td>
<td>1.52</td>
<td>0.74, 3.10</td>
</tr>
<tr>
<td>80 to 84</td>
<td>0.54</td>
<td>0.29, 0.98</td>
<td>1.52</td>
<td>0.75, 3.09</td>
</tr>
<tr>
<td>≥85</td>
<td>0.37</td>
<td>0.19, 0.73</td>
<td>0.66</td>
<td>0.29, 1.54</td>
</tr>
<tr>
<td>PP¶ (ref: &lt;40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 to 44</td>
<td>1.34</td>
<td>0.80, 2.26</td>
<td>1.30</td>
<td>0.68, 2.48</td>
</tr>
<tr>
<td>45 to 49</td>
<td>1.27</td>
<td>0.75, 2.15</td>
<td>1.95</td>
<td>1.07, 3.55</td>
</tr>
<tr>
<td>50 to 54</td>
<td>1.56</td>
<td>0.87, 2.81</td>
<td>1.45</td>
<td>0.70, 2.99</td>
</tr>
<tr>
<td>≥55</td>
<td>2.15</td>
<td>1.30, 3.57</td>
<td>1.63</td>
<td>0.88, 3.04</td>
</tr>
<tr>
<td>MAP∥ (ref: &lt;85)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85 to 89</td>
<td>1.07</td>
<td>0.62, 1.84</td>
<td>0.90</td>
<td>0.45, 1.81</td>
</tr>
<tr>
<td>90 to 94</td>
<td>1.65</td>
<td>0.97, 2.81</td>
<td>1.59</td>
<td>0.83, 3.04</td>
</tr>
<tr>
<td>95 to 99</td>
<td>1.15</td>
<td>0.63, 2.08</td>
<td>1.86</td>
<td>0.96, 3.61</td>
</tr>
<tr>
<td>≥100</td>
<td>1.01</td>
<td>0.59, 1.73</td>
<td>1.06</td>
<td>0.56, 2.00</td>
</tr>
<tr>
<td>Antihypertensive medication use¶ (ref=no)</td>
<td>0.96</td>
<td>0.63, 1.48</td>
<td>1.68</td>
<td>1.04, 2.7</td>
</tr>
<tr>
<td>Hypertension status (ref: SBP/DBP &lt;120/80 and no medications)</td>
<td>0.94</td>
<td>0.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehypertensive: SBP=120 to 139; DBP=80 to 89 and no medications</td>
<td>0.95</td>
<td>0.61, 1.48</td>
<td>1.44</td>
<td>0.83, 2.47</td>
</tr>
<tr>
<td>Hypertensive: ≥140/90 or on medication</td>
<td>1.23</td>
<td>0.79, 1.91</td>
<td>1.90</td>
<td>1.10, 3.28</td>
</tr>
</tbody>
</table>

ref indicates reference category.

*From adjusted multivariable nominal polychotomous logistic regression model, test to determine whether risk factor is predictive of either CAC response category adjusted for age, race/ethnicity, diabetes, dyslipidemia, smoking, BMI, family history of CHD, education, income, and CEE treatment assignment as well as additional covariates specific to particular risk factors (see below).

†From adjusted multivariable nominal polychotomous logistic regression model, test to determine whether odds ratios differ between CAC category for any level of risk factor.

‡Also adjusted for DBP and antihypertension medication use.

§Also adjusted for SBP and antihypertension medication use.

∥Also adjusted for antihypertension medication use.

¶Also adjusted for SBP and DBP.
because the value in our study is similar to or greater than those from others.

With increasing age, arterial compliance decreases, resulting in an increase in SBP, a decrease to DBP, and therefore an increase in PP. These physiological changes are the basis for findings of increases in SBP and concomitant decreases in DBP in those older than 50 years of age in both sexes and multiple ethnic groups. Accordingly, central measures of blood pressure, including PP, have found significant associations with prevalent coronary artery disease and incident CVD. Similarly, previous studies have demonstrated a significant association between reduced arterial compliance and coronary artery disease and CAC. This is especially relevant given the age distribution of our participants who were all postmenopausal and 50 years of age or older at the time of the baseline blood pressure measurements.

Other studies of clinical CVD have reported results that are consistent with ours. Using data from the Framingham Heart Study, Franklin et al found PP to be significantly associated with an increased risk for incident CHD and that this association was independent of SBP level. Moreover, “there was no added value of SBP for predicting CHD risk over and above PP.” In a separate study and compared with SBP, DBP, and MAP, PP was the strongest predictor of the progression of calcium attributable to atherosclerosis in the abdominal aorta. Conversely, MAP has been found to be associated with incident CVD in younger but not older men. These results, combined with previous reports on PP, demonstrate increasing evidence that among individuals 50 years of age or older, PP is an independent predictor of atherosclerosis, coronary artery disease, and CHD.

The strengths of our study include an ethnically diverse population, a prospective design, data on a wide range of covariates, and women representing a wide range of CVD risk, especially because many previous studies on CAC are composed of subjects who either self-referred or were referred on the advice of their health care provider. Conversely, the results of this study are limited to women, and some previous studies suggest there may be differences in the associations between central measures of blood pressure and coronary artery disease. Finally, calcium detected by CT is primarily attributable to intimal changes associated with atherosclerosis. However, this technique does not distinguish between intimal calcification attributable to atherosclerosis and Mockeberg’s medial calcinosis. Because the latter occurs principally in those with diabetes or chronic kidney disease and is located in the lower extremities (below the knee), we believe the probability of misclassification is low in our study.

Perspectives

In summary, we found increasing prevalence and severity of CAC with higher levels of SBP and PP but an inverse association between CAC prevalence and DBP. Accordingly, ISH was associated with an increased odds for CAC. These results suggest that PP and ISH are relevant in the risk assessment for CAC in women 50 years of age or older. Accordingly, in the context of prevention of coronary artery disease, clinicians should be cognizant of the age-related differences in risk associated with the different blood pressure measures.

Acknowledgments

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Disclosures

None.

References


24. Waddell TK, Dart AR, Medley TL, Cameron JD, Kingswell BA. Carotid pressure is a better predictor of coronary artery disease severity than brachial pressure. *Hypertension*. 2001;38:927–931.


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