Ambulatory Blood Pressure and Coronary Artery Calcification in Middle-Aged and Younger Adults


**Background:** The objective of this study was to investigate relationships between blood pressure (BP) determined by ambulatory monitoring and coronary artery calcification (CAC) determined by electron beam computed tomography (EBCT) in middle-aged and younger adults without symptoms of coronary artery disease.

**Methods:** Measures of office and ambulatory BP were analyzed in 298 asymptomatic adults (134 women and 164 men) from the white population of Rochester, MN, who were 20 to 60 years old (mean ± SD, 40 ± 9 years). For the ambulatory BP measurements, the active period of the day was defined as the daytime, out-of-bed hours and the inactive period as the nighttime, in-bed hours. Logistic regression was used to assess whether ambulatory measures of BP influenced the probability of having CAC detected by EBCT.

**Results:** After adjusting for sex, age, and office measures of BP, ambulatory diastolic BP during the active and inactive periods were each statistically significant additional predictors of the probability of having CAC. Similarly, after adjusting for sex, age, and ambulatory systolic BP, ambulatory diastolic BPs during each period were also statistically significant additional predictors of the probability of having CAC. In contrast, measures of ambulatory systolic BP, pulse pressure, and diurnal dipping of BP levels from the active to the inactive period did not make statistically significant additional contributions to the probability of having CAC.

**Conclusion:** These findings emphasize the role that the hemodynamic stress of diastolic BP may play in the early development of atherosclerotic coronary artery disease. Am J Hypertens 2002;15:518–524 © 2002 American Journal of Hypertension, Ltd.

**Key Words:** Blood pressure, hypertension, coronary artery calcification, computed tomography.

Atherosclerotic coronary artery disease is a major cause of mortality in the United States. Noninvasive measures of asymptomatic (subclinical) coronary artery disease are crucial for etiologic studies, prevention programs, and risk management. Measurement of coronary artery calcification (CAC) by electron beam computed tomography (EBCT) provides a noninvasive method to study the relationship of subclinical coronary artery disease with its risk factors. After adjustment for verification bias, detection of CAC by EBCT has a 97% sensitivity and a 72% specificity for the presence of obstructive coronary artery disease (ie, ≥50% luminal stenosis). Moreover, EBCT measures of CAC have been shown to predict future occurrence of coronary artery disease events. Hypertension is a major risk factor for the development of coronary artery disease. The relationship between blood pressure (BP) levels in the population and coronary risk is positive and is continuously graded across the entire range of BP levels. In 1983, Perloff et al provided the first evidence that mean levels of systolic and diastolic BP determined by ambulatory monitoring (ABPM) make additional contributions to the prediction of future cardiovascular events after office BP levels were considered. In cross-sectional studies, measures of BP level and variability determined by ABPM have also been related to the presence of subclinical cardiovascular disease including echocardiographic measures of left ventricular mass, ultrasound measures of carotid intimal-medial thickness, and urinary measures of albumin excretion. Although supported by National Institutes of Health grants R01 HL46292, R01 HL30428, R01 HL46190, and M01 RR00585 and by funds from the Mayo Foundation.

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office measures of BP and diagnostic category (hypertension vs. normotension) have been related to EBCT measures of CAC,\(^{11,12}\) no previous studies have investigated the relationship of ambulatory BP to the presence or extent of CAC.

The present study was undertaken to investigate relationships between ambulatory measures of BP and the presence of CAC determined by EBCT in middle-aged and younger adults without symptoms or previous history of coronary artery disease. Our primary objective was to determine whether ambulatory measures of BP contribute to predicting the presence of CAC after adjustment for office BP levels. To accomplish this, we analyzed office and ambulatory measures of BP and EBCT measures of CAC among asymptomatic adults from the general white population of Rochester, MN.

Materials and Methods

Study Sample

The sample consisted of 298 subjects (134 women and 164 men) who are members of the Rochester Family Heart Study (RFHS) cohort, which includes 3974 members of three-generation pedigrees ascertained through children enrolled in the schools of Rochester, MN.\(^{13,14}\) Between April 1991 and February 1998, a total of 1240 RFHS participants (604 men and 636 women) underwent EBCT for determination of CAC as part of the Epidemiology of Coronary Artery Calcification (ECAC) study.\(^{15}\) Eligibility of RFHS participants for the ECAC study included being >20 years of age at the time of EBCT, not being pregnant or lactating, and never having undergone coronary or non-coronary heart surgery. As a consequence of other study protocols involving RFHS participants,\(^{16,17}\) ABPM recordings were available for 301 ECAC study participants for whom the time between ABPM and EBCT was <1 year. Three of these individuals were excluded from the present analysis because of missing manual or ambulatory BP readings. Five subjects were receiving antihypertensive drug therapy, which was discontinued >4 weeks before ABPM.

Ambulatory Blood Pressure Monitoring

In 243 of the 298 subjects (82%), ABPM was performed using the Del Mar Avionics Pressurometer-IV (Irvine, CA); in the remaining 55 (18%), ABPM was performed using the SpaceLabs model 90202 device (SpaceLabs, Redmond, WA). Both devices have been previously evaluated and were found to have accuracy similar to clinicians’ measurement of BP.\(^{18–20}\) In each subject, the device was attached and removed between 7 and 9 AM on consecutive days and readings were obtained every 10 minutes during the intervening period. During the recording, subjects were instructed not to ingest any medications known to affect BP. They slept overnight in the General Clinical Research Center and were required to recline in bed no later than 10 PM and to remain with the lights and television off until they arose the next morning. At the beginning and end of the recording, BP was measured simultaneously by the ambulatory device and by a study technician using the auscultatory method. Two parallel sets of six readings (two sitting, two standing, and two supine) were obtained in this manner. The mean (±SD) differences between averages of the 12 machine and 12 manual readings did not differ significantly from zero (for systolic BP: −0.07 ± 2.34 mm Hg, \(P = .59\); for diastolic BP: −0.02 ± 1.86 mm Hg, \(P = .82\)). The minimum and maximum differences between machine and manual averages were for systolic BP −5.9 and 12.9 mm Hg, respectively, and for diastolic BP −7.3 and 6.8 mm Hg, respectively. Office BP was defined as the average of the four seated manual readings (two at the beginning and two at the end of the recording). Using the time each subject got into bed as a point of reference, we considered the preceding interval as the active period, and the subsequent interval until the subject arose the next morning as the inactive period. The mean (±SD) number of BPs recorded during the active period was 82 ± 9.7 (range 49 to 120) and during the inactive period was 46 ± 7.5 (range 2 to 64). The diurnal dip in BP was calculated by subtracting the average BP level during the active period from that during the inactive period.

Electron Beam Computed Tomography

Measurement of CAC was performed on Imatron C-100 or C-150 scanners (Imatron Inc., South San Francisco, CA). Subjects were positioned supine, head first, into the scanner opening. Three electrocardiographic leads were attached so that data acquisition could be triggered to late diastole when cardiac motion is minimal. For each scan, subjects were required to hold their breath at the end of complete expiration while 40 contiguous, 3-mm-thick two-dimensional transverse images were obtained from the level of the right branch of the pulmonary artery to the apex of the heart. Scanning was performed during one or two breath holds, and scan time per tomographic level was 100 msec.

The EBCT data were reviewed for technical quality by a radiologist, and then scored by a radiology technologist using customized computer software.\(^{21}\) The technologist was blinded to the identities of study participants. Using a three-dimensional graphics editor, the technologist traces the midlines of the left main, left anterior descending, right, and circumflex coronary arteries. For analyses, CAC was defined as at least one focus located within 5 mm of the midline of a coronary artery, ≥4 pixels in size, and having CT numbers above 130 Hounsfield units for each pixel. Foci ≥4 pixels are more repeatable on examinations taken minutes apart than foci <4 pixels, which are more likely to include noise.\(^{22}\)
Table 1. Characteristics of 298 asymptomatic white subjects, stratified by presence/absence of coronary artery calcification (CAC)

<table>
<thead>
<tr>
<th>Trait</th>
<th>With CAC (N = 73)</th>
<th>Without CAC (N = 225)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
<td></td>
</tr>
<tr>
<td>Men, %</td>
<td>80.8 7.6</td>
<td>46.7 9.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age, years</td>
<td>44.6 7.6</td>
<td>38.8 9.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>123.2 12.2</td>
<td>115.3 10.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>128.3 10.9</td>
<td>122.4 9.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Inactive</td>
<td>113.3 11.4</td>
<td>106.8 10.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Dip (inactive–active)</td>
<td>−15.0 7.6</td>
<td>−15.6 7.6</td>
<td>.562</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>82.5 7.8</td>
<td>77.7 8.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>83.2 7.5</td>
<td>77.9 7.6</td>
<td>&lt;.0001</td>
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<tr>
<td>Inactive</td>
<td>72.3 7.4</td>
<td>66.8 7.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Dip (inactive–active)</td>
<td>−10.9 5.5</td>
<td>−11.1 5.4</td>
<td>.787</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>40.7 8.1</td>
<td>37.5 8.3</td>
<td>.005</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>45.1 7.2</td>
<td>44.5 7.9</td>
<td>.568</td>
</tr>
<tr>
<td>Inactive</td>
<td>41.0 7.8</td>
<td>40.0 9.3</td>
<td>.413</td>
</tr>
</tbody>
</table>

BP = blood pressure.
Office BP are means of four readings for each subject, two taken at beginning and two at end of ambulatory recording. Active and inactive refer to ambulatory recording periods before and after subjects got into bed. P value is for contrast of means or percentage of men between subjects with and without CAC.

Statistical Analyses

Statistical analyses were performed using SAS version 6.12 (SAS Institute, Cary, NC). A significance level of $P = .05$ was used in all analyses. Means, SD, and ranges were calculated for continuously distributed traits, and percentages were calculated for categoric traits. Subjects with and without CAC detected by EBCT were compared by using $t$ tests to contrast mean values for continuously distributed traits and $\chi^2$ tests to contrast percentages for categoric traits. Pairwise associations between measures of BP were assessed by Pearson’s correlation coefficient.

Logistic regression methods were used to model dependencies of the probability of having CAC on sex, age, and measures of BP. In preliminary analyses (not shown), we found that together male sex and older age were each statistically significant predictors of the probability of having CAC ($P < .001$ for sex; $P < .001$ for age). Consequently, in all analyses of the relationships between measures of BP and CAC (see Results), the variables sex and age were forced into the logistic regression models before entering measures of BP. Wald statistics were calculated for each measure of BP included in the logistic regression models, as was the proportion of interindividual variation ($R^2$) in the presence of CAC explained by variation in predictor traits included in the model.

Results

The 298 subjects had mean ($\pm$SD) age of 40 $\pm$ 9 years (range 20 to 60 years), body mass index of 26.3 $\pm$ 4.8 kg/m$^2$ (range 15.9 to 47.6), waist-to-hip ratio of 0.8 $\pm$ 0.09 (range 0.6 to 1.0), as well as a fasting plasma total cholesterol of 176 $\pm$ 36 mg/dL (range 57 to 331) and glucose of 84.0 $\pm$ 6.7 mg/dL (range 70.1 to 111.6). Of the subjects, 10% had office systolic or diastolic BP levels in the hypertensive range (>140/90 mm Hg), whereas 25% of subjects had ambulatory systolic or diastolic BP averages in the hypertensive range (>135/85 mm Hg during the active period or >120/75 mm Hg during the inactive period$^{26}$). As expected, each measure of BP was significantly and positively correlated with every other measure; correlation coefficients ranged from a minimum of 0.45 for office diastolic and ambulatory systolic BP during the inactive period to a maximum of 0.80 between office and ambulatory diastolic BP during the active period ($P < .0001$ for all coefficients).

Coronary artery calcification was detected by EBCT in 25% of subjects, in whom the mean area of CAC ($\pm$ SD) was 5.94 $\pm$ 27.5 mm$^2$ and the maximum area was 292.3 mm$^2$. Subjects with CAC were significantly more often male, were significantly older, and had significantly higher mean systolic and diastolic BP levels than those without CAC (Table 1). In addition, the mean pulse pressure of office readings (but not ambulatory readings) was also significantly greater in subjects with CAC. In contrast, neither the systolic nor the diastolic measure of dipping of BP from the active to the inactive period differed significantly between those with and without CAC.

To determine which measures of office and ambulatory BP were predictive of the probability of having CAC after
adjustment for sex and age, each was entered, one at a time, into a separate logistic regression model that included sex and age (Table 2). Office systolic BP, ambulatory systolic BP during the inactive period, and ambulatory diastolic BP during both the active and inactive periods were each statistically significant additional predictors of the probability of having CAC. Compared with the reduced model that included only sex and age, the model that included ambulatory diastolic BP during the inactive period explained the largest proportion of variation in the presence of CAC, with an increase in the $R^2$ value from 0.178 to 0.207 (Fig. 1 and Table 2). On

<table>
<thead>
<tr>
<th>BP</th>
<th>Odds Ratio*</th>
<th>95% Confidence Interval</th>
<th>P Value†</th>
<th>$R^2$‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>1.20</td>
<td>(1.04, 1.38)</td>
<td>.013</td>
<td>0.197</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>1.14</td>
<td>(0.98, 1.33)</td>
<td>.100</td>
<td>0.184</td>
</tr>
<tr>
<td>Inactive</td>
<td>1.16</td>
<td>(1.01, 1.34)</td>
<td>.039</td>
<td>0.195</td>
</tr>
<tr>
<td>Dip (inactive–active)</td>
<td>1.08</td>
<td>(0.89, 1.31)</td>
<td>.420</td>
<td>0.184</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>1.18</td>
<td>(0.98, 1.42)</td>
<td>.088</td>
<td>0.182</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>1.36</td>
<td>(1.11, 1.67)</td>
<td>.004</td>
<td>0.195</td>
</tr>
<tr>
<td>Inactive</td>
<td>1.40</td>
<td>(1.14, 1.72)</td>
<td>.001</td>
<td>0.207</td>
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<tr>
<td>Dip (inactive–active)</td>
<td>1.08</td>
<td>(0.81, 1.43)</td>
<td>.594</td>
<td>0.181</td>
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<tr>
<td>Pulse pressure</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office</td>
<td>1.16</td>
<td>(0.97, 1.40)</td>
<td>.112</td>
<td>0.191</td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>0.92</td>
<td>(0.74, 1.14)</td>
<td>.430</td>
<td>0.178</td>
</tr>
<tr>
<td>Inactive</td>
<td>0.98</td>
<td>(0.82, 1.16)</td>
<td>.801</td>
<td>0.178</td>
</tr>
</tbody>
</table>

Abbreviation as in Table 1.
Each measure of BP was entered into a separate logistic regression model that also included sex and age.

* Odds ratios are shown for 5-mm Hg increase in each measure of BP.
† P value for Wald statistic.
‡ $R^2$ is proportion of variation in presence of coronary artery calcification attributable to variation in sex, age, and measure of BP included in logistic regression model. $R^2$ for model that included only sex and age was 0.178.
average, the estimated odds ratio for the presence of CAC increased 1.36 times for each 5–mm Hg increase in ambulatory diastolic BP during the active period and 1.40 times for each 5–mm Hg increase during the inactive period (Table 2). In contrast, none of the measures of pulse pressure or of dipping was significantly predictive of the probability of having CAC (Table 2). Consequently, these latter measures of BP were not considered in subsequent analyses.

To determine whether ambulatory BP levels made additional contributions to the prediction of CAC after office measures were considered, we entered each ambulatory measure into separate logistic regression models that included sex, age, and the corresponding office measure of BP (Table 3). Neither the active nor the inactive measure of ambulatory systolic BP was a statistically significant additional predictor of the probability of having CAC, whereas both the active and inactive measures of ambulatory diastolic BP were. Ambulatory diastolic BP levels were also additional predictors of the probability of having CAC when added to separate logistic regression models that included sex, age, and office systolic BP, whereas ambulatory systolic BP levels made no additional contribution to the probability of having CAC after controlling for the effects of sex, age, and office diastolic BP (data not shown).

To determine whether ambulatory systolic and diastolic BP levels made additive contributions to the prediction of CAC, we entered both measures into the same sex- and age-adjusted logistic regression model (Table 4). For both the active and inactive periods, ambulatory diastolic BP levels were statistically significant additional predictors of the probability of having CAC after adjusting for the corresponding ambulatory systolic BP levels. In a separate model (not shown) that included sex, age, and office systolic and diastolic BP levels, neither of the latter could be distinguished as making an additional statistically significant contribution to the prediction of CAC. Because of the particularly high correlation between the active and inactive measures of ambulatory BP (for systolic BP, \( r = 0.76 \); for diastolic BP \( r = 0.77 \)), we did not determine whether both together made additive contributions to the prediction of CAC.

### Discussion
The results of the present study provide evidence that average BP levels determined by ABPM improve the ability to predict the presence of CAC beyond what is possible with office BP levels. After adjustment for sex and age, ambulatory systolic and diastolic BP levels were predictive of CAC; however, only the ambulatory diastolic BP levels were predictors after additional adjustment for

<table>
<thead>
<tr>
<th><strong>Ambulatory BP</strong></th>
<th><strong>Odds Ratio</strong></th>
<th><strong>95% Confidence Interval</strong></th>
<th><strong>P Value†</strong></th>
<th><strong>R^2 Reduced Model‡</strong></th>
<th><strong>R^2 Full Model§</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic, active period</td>
<td>0.97</td>
<td>(0.77, 1.22)</td>
<td>0.776</td>
<td>0.197</td>
<td>0.198</td>
</tr>
<tr>
<td>Systolic, inactive period</td>
<td>1.05</td>
<td>(0.87, 1.28)</td>
<td>0.607</td>
<td>0.197</td>
<td>0.199</td>
</tr>
<tr>
<td>Diastolic, active period</td>
<td>1.50</td>
<td>(1.09, 2.07)</td>
<td>0.013</td>
<td>0.182</td>
<td>0.196</td>
</tr>
<tr>
<td>Diastolic, inactive period</td>
<td>1.47</td>
<td>(1.13, 1.91)</td>
<td>0.004</td>
<td>0.182</td>
<td>0.209</td>
</tr>
</tbody>
</table>

Abbreviation as in Tables 1 and 2.
* Odds ratios are shown for 5-mm Hg increase in each measure of BP.
† P values for Wald statistic.
‡ R^2 for reduced logistic regression model that included sex, age, and office BP.
§ R^2 for full logistic regression model that included sex, age, office BP and corresponding ambulatory measure of BP.

### Table 4. Sex- and age-adjusted dependence of coronary artery calcification on ambulatory systolic and diastolic BP in 298 asymptomatic white subjects

<table>
<thead>
<tr>
<th><strong>Ambulatory BP</strong></th>
<th><strong>Odds Ratio</strong></th>
<th><strong>95% Confidence Interval</strong></th>
<th><strong>P Value†</strong></th>
<th><strong>R^2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Active period model</td>
<td></td>
<td></td>
<td></td>
<td>0.195</td>
</tr>
<tr>
<td>Systolic</td>
<td>0.94</td>
<td>(0.75, 1.18)</td>
<td>0.596</td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>1.44</td>
<td>(1.07, 1.93)</td>
<td>0.015</td>
<td></td>
</tr>
<tr>
<td>Inactive period model</td>
<td></td>
<td></td>
<td></td>
<td>0.208</td>
</tr>
<tr>
<td>Systolic</td>
<td>1.01</td>
<td>(0.85, 1.21)</td>
<td>0.881</td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>1.39</td>
<td>(1.08, 1.79)</td>
<td>0.011</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation as in Tables 1–3.
* Odds ratios are shown for 5-mm Hg increase in each measure of BP.
† P values for Wald statistic.
office BP. The superior predictive power of ambulatory diastolic BP levels, during both the active and inactive periods, was further supported by their contributions to the probability of having CAC after ambulatory systolic levels were considered. In contrast, ambulatory systolic BP levels made no additional contribution to the prediction of CAC after ambulatory diastolic BP levels were considered. To our knowledge, this is the first study to investigate the relationship between ambulatory BP levels and subclinical coronary artery disease measured by the presence of CAC.

The characteristics of our sample may account for the greater predictive power of ambulatory diastolic versus systolic BP levels. Our sample consisted mostly of normotensive adults <60 years old, none of whom had symptoms or signs of atherosclerotic coronary artery disease. In contrast, studies that have implicated systolic BP as a stronger predictor of target organ disease and clinical cardiovascular events (coronary heart disease, heart failure, stroke, end-stage renal disease, and all-cause mortality) than diastolic BP have involved older cohorts with a greater prevalence of hypertension. Subjects in these cohorts probably also had more advanced subclinical target organ disease.

A recent analysis of data from the Framingham Heart Study has demonstrated age-dependency of the relationships between measures of BP and risk of future coronary heart disease events. Among subjects <50 years of age, when systolic and diastolic BP levels were both entered into a prediction model, diastolic BP was predictive of coronary heart disease but systolic BP was not. Between 50 and 59 years of age, neither systolic nor diastolic BP was more strongly predictive than the other; and at age ≥60 years, higher systolic BP and lower diastolic BP were predictive of coronary heart disease. Age-related differences in the pattern of pulse wave reflection (from the periphery to the heart) may account for these changes in the predictive relationships for office measures of BP.

The age distribution in our sample may also account for the lack of relationships between CAC and office or ambulatory measures of pulse pressure. From 30 to 50 years of age, systolic and diastolic BP rise linearly and in parallel within the population, reflecting a progressive increase in peripheral vascular resistance in this age range. In contrast, after age 50 to 60 years, as systolic BP continues to rise, diastolic BP declines and, consequently, pulse pressure widens. This age-related shift in the proportion of hemodynamic load resulting from steady-state diastolic stress due to resistance in small arteries and arterioles to a greater proportion of the hemodynamic load resulting from pulsatile systolic stress reflects the loss of compliance (increasing stiffness) in larger conduit arteries. Thus, it is reasonable to conclude that the age range of our sample may also be responsible for the lack of relationships between CAC and measures of pulse pressure.

Among hypertensive subjects, nondipping has also been associated with older age, higher BP levels, and the presence of target organ disease. The pathophysiologic basis of these associations remains uncertain; however, they may also reflect age-related increases in large artery stiffness (such as increases in carotid artery wall thickness and plaque), which can impair baroreceptor function. Thus younger age, lower BP, and less advanced atherosclerosis in our subjects may also account for the lack of relationships between CAC and nocturnal dipping of BP.

Our study has several limitations. First, the relatively small sample size did not allow sex-specific analyses or simultaneous consideration of other established predictors of coronary artery disease including measures of body size, plasma lipids or glucose, or cigarette smoking. The small sample size also precluded exploring possible interactions between the effects of BP and other predictors of CAC including age, body size, and plasma lipids. Finally, a different method of ambulatory BP recording (oscillometric versus auscultatory) was used in a minority of subjects (18%), which could have altered the distribution of ambulatory BP levels and reduced the power to detect or accurately estimate relationships with CAC. It is noteworthy in this regard that none of the prediction models explained more than 21% of total variation in the probability of having CAC.

In summary, this is the first published report of a relationship between ambulatory BP levels and subclinical coronary artery disease as measured by the presence of CAC. Although this was not a longitudinal study, our findings underscore the potentially important role that graded increases in the hemodynamic stress of diastolic BP may play in the development of atherosclerotic coronary artery disease in middle-aged and younger asymptomatic individuals. With the aging of the population and the consequent focus on systolic BP and pulse pressure as predictors of clinical cardiovascular disease events in elderly individuals, approaches to reduce cardiovascular disease morbidity and mortality should not fail to note that elevated diastolic BP in early and middle adulthood is the most common, potentially modifiable antecedent of systolic hypertension and widened pulse pressure in elderly individuals.

Acknowledgment
We gratefully acknowledge support of the General Clinical Research Center at the Mayo Clinic.

References


