Independent and Incremental Value of Coronary Artery Calcium for Predicting the Extent of Angiographic Coronary Artery Disease
Comparison With Cardiac Risk Factors and Radionuclide Perfusion Imaging

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OBJECTIVES
The study was done to test the ability to predict the extent of angiographically determined coronary artery disease (CAD) by quantification of coronary calcium using electron-beam computed tomography (EBCT) and to compare it with more conventional parameters for delineating the angiographic extent of CAD, that is, cardiovascular risk factors and radionuclide single-photon emission computed tomography (SPECT).

BACKGROUND
The angiographic extent of CAD is a powerful predictor of subsequent events. Use of EBCT may be able to define it by virtue of its ability to determine plaque burden.

METHODS
We examined 308 patients presenting with suspected but not previously known CAD who underwent selective coronary angiography. As measures of the angiographic extent of CAD, coronary artery greater even 20 (CAGE$^{\geq 20}$) and CAGE$^{\geq 50}$ scores represented the total number of coronary segments with $\geq 20\%$ or $\geq 50\%$ stenoses, respectively. The EBCT-derived total calcium scores were obtained in 291 patients, risk factors as defined by the National Cholesterol Education Program in 239 patients, and SPECT scans in 136 patients.

RESULTS
Using multiple linear regression analysis, total calcium scores were better independent predictors of both CAGE$^{\geq 20}$ and CAGE$^{\geq 50}$ scores than either a SPECT-derived radionuclide perfusion score or the risk factors age, male gender and ratio of total/high-density lipoprotein (HDL) cholesterol. The association between EBCT and angiographic scores remained highly significant after excluding the influence of all interrelated risk factors and SPECT variables ($r = 0.65; p < 0.001$ for CAGE$^{\geq 20}$ scores, $r = 0.50; p < 0.001$ for CAGE$^{\geq 50}$ scores).

CONCLUSIONS
Coronary calcium predicts the angiographic extent of CAD in symptomatic patients and provides independent and incremental information to the more conventional clinical parameters derived from SPECT or risk assessment. (J Am Coll Cardiol 1999;34:777–86) © 1999 by the American College of Cardiology

Selective coronary angiography represents the current standard for the definition of coronary artery anatomy and extent of coronary artery disease (CAD). The value of noninvasive techniques used to examine patients with chest pain and no known CAD is usually defined with respect to the angiographically identified culprit lesion (or “maximum stenosis”) as the reference standard. We have recently reported that cutpoints of coronary artery calcium quantities determined by electron-beam computed tomography (EBCT) can be used to predict angiographic culprit stenosis severity (1). In contrast, it has been suggested, given normal ventricular geometry and function, that the anatomic extent of angiographic disease may be a more important determinant of morbidity and mortality than culprit lesion severity (2–4). In fact, the angiographic worst stenosis is frequently not the site of subsequent plaque rupture and thrombosis (5,6).

Coronary artery calcium quantities are more closely related to mural atherosclerotic plaque burden than to coronary luminal narrowing (7–9) and may therefore measure more accurately the extent of coronary angiographic disease.

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METHODS

General outline. We determined the angiographic extent of CAD in 308 patients by methods adopted by the Coronary Artery Surgery Study (CASS) (10,11) and the Bypass Angioplasty Revascularization Investigation (BARI) (12,13) investigators. Twenty-seven coronary segments were defined (including right or left dominance and the presence of a ramus intermedius), providing for a complete description of coronary angiographic anatomy.

We examined EBCT-derived coronary artery calcium for predicting the total number of coronary segments with stenoses $\geq 50\%$ (“obstructive stenoses”) or $\geq 20\%$ (“nonobstructive and obstructive stenoses”) luminal diameter narrowing, respectively. To analyze the comparative value of EBCT in this respect, established clinical measures of risk or extent of CAD, assessed by cardiac risk profiles as defined by the National Cholesterol Education Program (NCEP) (14) and radionuclide SPECT scans available in a subset of patients, were also related to the angiographic extent of disease.

Patients. The research protocol was approved by the Mayo Clinic Institutional Review Board. Patient recruitment was done during selected times depending on availability of the EBCT scanner and a study coordinator. In these time intervals, consecutive patients who underwent diagnostic coronary angiography for clinical indications were invited to participate in the research protocol if they had no previous arteriographic documentation or invasive treatment of CAD. Also, no patient had unstable angina or underwent angioplasty at the time of angiography.

After signed informed consent, EBCT scanning was performed on an average of one day following arteriography. The original sample consisted of 339 patients. Results from subsets of this patient population have been published previously (1,15–17). These studies focused on the detection of any angiographically obstructive stenoses or nonobstructive disease (15,16), on epidemiologic aspects of the distribution of coronary calcium in different populations (17) and on the use of different calcium quantity cutoffs for defining the likely severity of angiographic stenoses (1). Thirty-one patients were excluded from the present analysis because they had a clinical diagnosis of prior myocardial infarction or signs of ischemia in the resting electrocardiogram (ECG). In the remaining 308 patients, the most common indication for coronary angiography was chest pain (typical or atypical angina) in 216 patients (70%). Forty-three patients (14%) had abnormal conventional stress tests, 23 (8%) had unexplained exertional dyspnea, 19 (6%) were examined preoperatively (usually for valvular heart disease), 6 (2%) had congestive heart failure and 1 was examined for a disability claim. The EBCT scans analyzed as described below were available for 291 participants. The other participants, having agreed to participate in the study, did not undergo the EBCT examination owing to scheduling conflicts or unavailability of the scanner.

Coronary angiography. Coronary angiography was performed by the Judkins technique with a minimum of five views of the left system and two views of the right system. The angiograms were analyzed on the basis of the coronary segmental classification proposed by the CASS investigators (10,11). The maximum percent diameter stenosis in any of the 27 coronary segments was visually assessed by two experienced angiographers unaware of the results of EBCT scanning. Segments were defined as containing no or trivial stenoses (0% to <20%), stenoses ranging from 20% through 49% (nonobstructive disease) or ranging from 50% to 100% (obstructive disease). In the case of a disagreement in the interpretation of a given angiogram, there was arbitration with the help of a third angiographer, as described previously (1).

The angiographic extent of CAD has been determined in various ways. The most widely published method reflects the extent of potentially flow-limiting luminal narrowing (\( \geq 50\% \) luminal diameter narrowing) and has been called the “coronary artery greater even than 50 (CAGE \( \geq 50 \)) score” by the CASS investigators (10,11). We replicated this CAGE \( \geq 50 \) score by generating the total number of segments with a 50% or greater maximum stenosis per patient. In view of recent reports on clinical events caused by angiographically nonobstructive coronary lesions (5,6), we reasoned that it was necessary to also include lesser narrow-
ings in a score that would better reflect the overall extent of angiographically detectable CAD. By analogy, we created a “CAGE ≥20 score” to represent the extent of reliably identifiable nonobstructive and obstructive disease. The total number of segments with a 20% or greater maximum stenosis was the CAGE ≥20 score.

Electron-beam computed tomography. High-resolution, noncontrast enhanced EBCT examinations (Imatron C-100 scanner, Imatron, South San Francisco, California) were performed in a manner described previously (1,16). In all participants, 40 contiguous, 3-mm thick, transaxial images were done commencing at the root of the aorta and proceeding caudad through the apex of the heart. For each study, a calcium score was determined using the methods of Agatston and colleagues (18). This algorithm has been widely used in research and clinical studies. The calcium score is the product of the area of coronary artery calcium (at least 2 contiguous pixels with a computed tomography [CT] density ≥130 Hounsfield units) and a factor rated 1 through 4 dictated by the maximum CT density within that lesion. A calcium score was calculated for each of the major coronary arteries (left main, left anterior descending, left circumflex and right coronary arteries) and the entire epicardial coronary system (“total calcium score”). All EBCT scans were read without knowledge of the results of the patient’s risk factors (except, obviously, age and gender), radionuclide scan results and angiographic findings.

Cardiac risk factors. Cardiac risk factors have been shown previously to predict the extent of angiographic disease, that is, CAGE ≥50 scores (10). To compare the associations of risk factors against coronary calcium scores with CAGE ≥20 or CAGE ≥50 scores, we used the current NCEP definitions (14), taking into account age/gender (men ≥45 years, women ≥55 years), family history of CAD, current cigarette smoking, hypertension (systolic or diastolic blood pressure ≥140 mm Hg and ≥90 mm Hg, respectively, or antihypertensive treatment or both), low high-density lipoprotein (HDL) cholesterol (<35 mg/dl), diabetes mellitus and, as a negative risk factor, high HDL cholesterol (>60 mg/dl). These risk factors were defined precisely as outlined by the NCEP except for “family history.” For this variable, “positive” information such as definite myocardial infarction or sudden death in parents or first-degree relatives up to age 75 for both genders was used. No patients were taking lipid-lowering medications at the time of study entry. In 250 patients, a lipoprotein analysis of fasting total cholesterol, HDL cholesterol and triglycerides was performed. Eleven patients had triglycerides ≥400 mg/dl. Hence, calculations of low-density lipoprotein (LDL) cholesterol levels as proposed by the NCEP were possible in 239 patients, who were accordingly classified into four risk groups, with increasing probabilities of future cardiac events from group 1 to 4 (14,19).

Treadmill exercise testing. Stress testing within three months before coronary angiography was performed in 164 patients (53%). Of these patients, 90 (55%) had a test judged to be unremarkable (n = 49) or nondiagnostic (n = 41), whereas 74 (45%) had a test positive for ischemia. After exclusion of nondiagnostic tests, there was a significant difference in CAGE ≥50 scores between tests positive for ischemia and unremarkable tests (1.53 ± 1.91 vs. 2.99 ± 2.71; p = 0.001). However, this association was weaker than that between radionuclide perfusion studies (see below) and CAGE ≥50 scores. Indeed, in multivariate analysis, treadmill exercise testing did not remain in a model assessing its predictive value compared with radionuclide perfusion testing with regard to CAGE ≥50 scores. To use the “best” conventional test in comparison with EBCT, and because treadmill exercise testing is not an established method for analyzing the extent of angiographic disease, we decided to analyze radionuclide perfusion rather than treadmill exercise testing.

Radionuclide studies. An association between radionuclide SPECT perfusion studies and the extent of angiographic CAD is well established (20). In a subset of patients in which studies were available, we used SPECT as an established noninvasive imaging modality for CAD extent against which EBCT-derived coronary calcium scores could be compared. The SPECT studies were performed before coronary angiography in 136 patients. In 111 patients, the Naughton or Bruce protocols were used for treadmill exercise testing as previously described (21,22). Exercise was continued until standard end points were achieved (21).

In 25 patients, pharmacologic agents were used; adenosine was used (0.14 mg/kg/min) in 15 patients and dipyridamole (up to 0.84 mg/kg) in 10 patients. Patients were injected with 3 mCi of thallium-201 (n = 103) or 20 to 30 mCi of technetium-99 sestamibi (n = 33) intravenously during the last minute of exercise or pharmacologic provocation. Tomographic imaging was accomplished using a rotating gamma camera using the “step-and-shoot” method, acquiring 30 images for 40 s each at 6° intervals over a 180° arc. Short-axis images at the basal, midventricular and apical level were divided into 14 segments as previously described (12). Poststress radionuclide uptake was graded for each segment on a scale of 0 to 4 by consensus of two experienced observers. To obtain a score reflecting increasing severity of regional reductions in post-stress radionuclide uptake, normal or increased uptake was graded “0,” mildly reduced uptake “1,” moderately reduced uptake “2,” markedly reduced uptake “3,” and absent uptake “4.” Delayed images (obtained 4 h after stress for thallium and 24 h for sestamibi) were used to ascertain that segments with mild hypoperfusion also in the delayed images were not scored as reversible perfusion defects. The grading for all 14 segments was summed to generate an overall “radionuclide perfusion score” reflecting the extent (number of segments) and severity (grading) of post-stress reversible hypoperfusion (20).
Statistics. Statistical analyses were performed using the SPSS software package (version 8.0, SPSS, Chicago, Illinois). Values are reported as mean ± SD. To account for the nonnormal distribution of calcium scores, a loge [+] transformation was made. Triglyceride and total cholesterol values were also transformed to the (natural) logarithmic scale. Proportions between categories were analyzed using a chi-square test. To enable comparisons between calcium scores, radionuclide perfusion scores and cardiac risk factors against categories of the angiographic extent of disease in these chi-square analyses, quartiles of the calcium and radionuclide perfusion scores and the NCEP-defined risk groups (14) were used. The contingency coefficient was determined as a measure of the degree of association of the classifications in the contingency table (23). The maximum value of this coefficient is 1.

Multiple linear regression analysis was performed to examine the independent relation of cardiac risk factors, radionuclide perfusion scores and total calcium scores with CAGE ≥20 and CAGE ≥50 scores, respectively. In this case, mostly continuous variables were analyzed, and the following cardiac risk factors were entered independently into the model: age (years), gender (male/female), smoking (never/former/active), hypertension (present/absent), diabetes mellitus (present/absent), family history (present/absent), calculated LDL cholesterol (mg/dl) and triglycerides (mg/dl, loge-transformed). Total cholesterol (mg/dl, loge-transformed) and HDL cholesterol (mg/dl) were also entered or, alternatively, the ratio of total cholesterol/HDL cholesterol, depending on the best predictive values achieved. Only independently predictive risk factor variables were forced into the regression models together with radionuclide perfusion and calcium scores.

Finally, we analyzed the partial correlation between total calcium scores and CAGE ≥20 and CAGE ≥50 scores, respectively, after exclusion of all interrelated co-factors that might influence these relationships. This was done by correlating the residuals of two regression models. These residuals were the difference between individual predicted values and the actually observed values. One model tested the associations of individual risk factors and radionuclide perfusion scores with CAGE ≥20 or CAGE ≥50 scores, respectively, and the other model tested the associations of individual risk factors and radionuclide perfusion scores with total calcium scores. The residuals of these models represented the part of information inherent in the angiographic or calcium scores, respectively, independent from the risk factor and radionuclide perfusion variables. Residual values were negative for predicted values lower than observed values and positive for predicted values greater than observed values. Plotting these residuals against each other then showed the association between calcium scores and angiographic scores truly independent from any interrelationships with risk factors or radionuclide perfusion variables. For all statistical evaluations, a value of two-tailed p < 0.05 was considered significant.

RESULTS

Patient demographics. BASIC DEMOGRAPHICS. Basic patient demographics are given in Table 1. Left ventricular ejection fraction was normal in most patients. There were no statistical differences in any of the variables listed in Table 1 in subgroups of patients who had complete risk factor analysis and/or SPECT studies, indicating very comparable demographics across these subgroups. Table 2 gives angiographic characteristics. The median number of segments with ≥20% maximum stenosis per patient (i.e., the median CAGE ≥20 score) was 4 (the 25th and 75th percentiles were 2 and 7, respectively). The median CAGE ≥50 score was 1 (the 25th and 75th percentiles were 0 and 4, respectively). The numbers of patients in each category of CAGE ≥20 and CAGE ≥50 scores are shown in Figure 1A and B, respectively.

ELECTRON-BEAM COMPUTED TOMOGRAPHY. Of the 291 patients with EBCT scans, 262 (90%) had a positive score (i.e., a total calcium score >0). Positive total calcium scores
ranged from 0.5 through 7,633. The mean and median scores were 447 ± 807 and 144, respectively. The 25th and 75th percentiles were 7.5 and 545, respectively.

**CARDIAC RISK FACTORS.** Individual risk factors are listed in Table 1. Patient classification according to the risk groups specified by the NCEP (14,19) resulted in a fairly homogeneous distribution of the 239 patients with available lipoprotein values across the four risk groups. Eighty-seven (36%) patients were in group 1, 27 (11%) in group 2, 62 (21%) in group 3 and 69 (22%) in group 4.

**RADIONUCLIDE IMAGING.** Of the 136 patients with radionuclide stress imaging before coronary angiography, 112 (82%) had reversible reduced tracer uptake in at least one segment. The radionuclide perfusion score in these patients ranged from 1 through 34. The mean and median scores were 8.6 ± 8.0 and 6.0, respectively. The 25th and 75th percentiles were 2.0 and 14.8.

Table 3 provides an overview of the results of total calcium score quartiles, NCEP risk groups and radionuclide perfusion score quartiles grouped as a function of CAGE ≥20 or CAGE ≥50 scores. Chi-square analysis showed significant correlations of total calcium scores and, to a lesser degree, radionuclide perfusion scores with both CAGE ≥20 and CAGE ≥50 scores. The NCEP risk groups were significantly related to CAGE ≥20, but not CAGE ≥50 scores.

**Prediction of angiographic measures of disease.**

**CALCICM SCORES VERSUS ANGIOGRAPHIC SCORES.** The relationship between loge-transformed total calcium scores and CAGE ≥20 or CAGE ≥50 scores was best described by a quadratic (second-order polynomial) function ($r = 0.77$, Fig. 2A). The relationship between loge-transformed total calcium scores and CAGE ≥50 scores was characterized by a relatively flat first portion of the curve, which then became exponential with increasing extent of angiographic disease (Fig. 2B). This was again best described by a quadratic function ($r = 0.68$). The association of total calcium scores was better with CAGE ≥20 than with CAGE ≥50 scores ($z$-statistic = 2.30; $p = 0.022$).

**RISK FACTORS VERSUS ANGIOGRAPHIC SCORES.** Independent risk factor predictors of both CAGE ≥20 and CAGE ≥50 scores were age, male gender, the ratio of total

**Table 2. Angiographic Characteristics (n = 308)**

<table>
<thead>
<tr>
<th></th>
<th>No. of Patients (%)</th>
<th>CAGE ≥20 Score Mean ± SD</th>
<th>CAGE ≥50 Score Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/near normal coronary</td>
<td>59 (19)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>arteries (&lt;20% luminal diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stenosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonobstructive coronary artery</td>
<td>69 (22)</td>
<td>2.90 ± 1.63</td>
<td>—</td>
</tr>
<tr>
<td>disease (20%–49% luminal diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stenosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Vessel disease (≥50% maximum</td>
<td>47 (15)</td>
<td>4.62 ± 2.24</td>
<td>1.36 ± 0.74</td>
</tr>
<tr>
<td>diameter stenosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-Vessel disease (≥50% maximum</td>
<td>61 (20)</td>
<td>6.13 ± 2.19</td>
<td>2.66 ± 0.91</td>
</tr>
<tr>
<td>diameter stenosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Vessel disease (≥50% maximum</td>
<td>72 (23)</td>
<td>8.87 ± 2.41</td>
<td>5.94 ± 2.06</td>
</tr>
<tr>
<td>diameter stenosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1.** (A) Absolute number of patients in each category of CAGE ≥20 scores. (B) Absolute number of patients in each category of CAGE ≥50 scores.
cholesterol over HDL cholesterol and calculated LDL cholesterol, respectively (Table 4). Stepwise linear regression analysis eliminated calculated LDL cholesterol from both models.

**RISK FACTORS AND RADIONUCLIDE PERFUSION SCORES VERSUS ANGIOGRAPHIC SCORES.** Radionuclide perfusion scores (reducing the number of available observations to 118) were entered in addition to age, gender and the ratio of total cholesterol/HDL cholesterol. Radionuclide perfusion scores were independently predictive of both CAGE ≥20 and CAGE ≥50 scores, although the previously mentioned risk factors retained their predictive significance (Table 4).

**RISK FACTORS, RADIONUCLIDE PERFUSION SCORES, AND TOTAL CALCIUM SCORES VERSUS ANGIOGRAPHIC SCORES.** When total calcium scores were added to the model, only age remained predictive of CAGE ≥20 scores besides total calcium scores, and only radionuclide perfusion scores remained predictive of CAGE ≥50 scores besides total calcium scores (Table 4). The T-values, indicating the degree of association, were about two times greater for total calcium scores than for either age or radionuclide perfusion scores. Figure 3 shows that after exclusion of all interrelated co-factors in this analysis—that is, after exclusion of cardiac risk factors and radionuclide perfusion scores—there was still a highly significant correlation between total calcium scores and either CAGE ≥20 scores or CAGE ≥50 scores (r = 0.65) or CAGE ≥50 scores (r = 0.50; p = 0.065 vs. CAGE ≥20 scores).

**DISCUSSION**

As opposed to prior studies, the current investigation used very detailed information on the angiographic extent of CAD as the standard against which risk factors, SPECT and EBCT were compared. It demonstrated in a clinical population of symptomatic patients without documented prior CAD that coronary calcium scores have independent and incremental value for predicting the extent of any (CAGE ≥20 score) or obstructive (CAGE ≥50 score) angiographic CAD compared with cardiac risk factors or radionuclide perfusion studies.

**Angiographic measures of the extent of CAD.** CAGE ≥20 and CAGE ≥50 scores provide a comprehensive representation of the coronary tree, describing the overall number of coronary segments with any stenoses or potentially flow-limiting stenoses, respectively. Although there is a positive relation of maximum stenosis severity with CAGE ≥20 and CAGE ≥50 scores, it is important to note...
that these angiographic measures reflect distinctly different aspects of angiographically assessed CAD (i.e., severity vs. extent of angiographic CAD). Measures of the angiographic extent of CAD used in clinical practice, such as the number of major vessels with significant disease, appear to have incremental prognostic value beyond the use of maximum (“culprit”) stenosis severity alone (2,3,24,25). The angiographic extent of disease has been established as an important predictor of prognosis in prospective investigations close to following the patient’s natural history (2,25,26).

In addition, theoretical considerations suggest the importance of accounting for the extent of disease. Vulnerable coronary plaques display variable angiographic characteristics (27), and stenosis severity cannot be used to predict subsequent events reliably (5,6). A greater amount of overall plaque formation may be associated with a greater number of individually vulnerable plaques (28). Finally, acute myocardial infarction has been described as a result of multifocal, “systemic” coronary disease activity (29).

Coronary calcium scores as a measure of the angiographic extent of disease. The association of coronary calcium scores with CAGE \( \geq 20 \) scores was significantly stronger than with CAGE \( \geq 50 \) scores. Histopathologic site-by-site comparisons have shown that the amount of coronary artery calcium is related directly to atherosclerotic plaque burden rather than directly to the degree of luminal narrowing (7,9,30). Analysis of luminal narrowing by coronary angiography tends to underestimate coronary atherosclerotic plaque burden. Because of various mechanisms related to the angiographic technique itself (31) and the pathogenesis of coronary atherosclerosis (31,32), obstructive stenoses are often only visualized in patients with substantial plaque burdens. Thus, CAGE \( \geq 20 \) scores should be antic-
never- and former smokers (n = 231), active smokers (n = 73) had significantly lower CAGE 20 scores (3.95 vs. 4.92, p = 0.04), CAGE 50 scores (1.53 vs. 2.31, p = 0.01) and maximum percent stenosis (47% vs. 58%, p = 0.03). Accordingly, this limits the use of NCEP-defined risk factors for prediction of angiographic CAD. In many ways, radionuclide perfusion studies examine functional aspects of the coronary circulation.

In addition to epicardial coronary luminal stenosis morphology, severity and the number of stenoses, microvascular disease or functional abnormalities of the coronary circulation may affect myocardial radionuclide uptake (36). Coronary calcium scores and risk factor assessment may then provide information on underlying atherosclerotic plaque burdens complementing the physiologic assessment of the coronary circulation provided by SPECT imaging. It should also be kept in mind that patients with unremarkable SPECT studies were probably underrepresented owing to the effect of referral bias in this angiographic population (37).

Study limitations. Complete results of cardiac risk factor analysis, SPECT perfusion imaging and EBCT coronary calcium scores were only available in a subset of 118 patients. Our results in this limited number of patients, however, were very consistent with the results in the overall study population with respect to risk factor and coronary calcium associations with the angiographic extent of CAD.

The general bias found in patient populations referred for coronary angiography does not permit extrapolation of our data to broader populations. The previously stated specific referral bias pertaining to patients undergoing SPECT imaging usually results in a decreased specificity for detec-

Table 4. Multiple Linear Regression Analysis to Determine Independent Predictors of the Number of Angiographic Segments with 20% or Greater Maximum Stenosis (CAGE ≥20 score) or 50% or Greater Maximum Stenosis (CAGE ≥50 score)

<table>
<thead>
<tr>
<th></th>
<th>CAGE ≥20 Scores</th>
<th></th>
<th></th>
<th></th>
<th>R²</th>
<th></th>
<th></th>
<th></th>
<th>R²</th>
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<td></td>
<td>C</td>
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<td>P</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>0.17</td>
<td>0.02</td>
<td>9.61</td>
<td>0.00</td>
<td>0.32</td>
<td>0.01</td>
<td>7.34</td>
<td>0.00</td>
<td>0.23</td>
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<tr>
<td>Male gender</td>
<td>1.94</td>
<td>0.47</td>
<td>4.15</td>
<td>0.00</td>
<td>1.40</td>
<td>0.36</td>
<td>3.92</td>
<td>0.00</td>
<td>0.05</td>
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<tr>
<td>Total/HDL cholesterol</td>
<td>0.25</td>
<td>0.12</td>
<td>2.20</td>
<td>0.03</td>
<td>0.16</td>
<td>0.09</td>
<td>1.81</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl, calculated)</td>
<td>0.01</td>
<td>0.01</td>
<td>2.20</td>
<td>0.03</td>
<td>0.01</td>
<td>0.00</td>
<td>1.99</td>
<td>0.05</td>
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<tr>
<td>Age (yr)</td>
<td>0.16</td>
<td>0.03</td>
<td>6.27</td>
<td>0.00</td>
<td>0.37</td>
<td>0.09</td>
<td>4.67</td>
<td>0.00</td>
<td>0.29</td>
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<tr>
<td>Male gender</td>
<td>1.75</td>
<td>0.66</td>
<td>2.64</td>
<td>0.01</td>
<td>1.25</td>
<td>0.50</td>
<td>2.48</td>
<td>0.02</td>
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<tr>
<td>Total/HDL cholesterol</td>
<td>0.38</td>
<td>0.15</td>
<td>2.54</td>
<td>0.01</td>
<td>0.25</td>
<td>0.11</td>
<td>2.20</td>
<td>0.03</td>
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<td>Radionuclide perfusion score</td>
<td>0.12</td>
<td>0.03</td>
<td>3.42</td>
<td>0.00</td>
<td>0.09</td>
<td>0.03</td>
<td>3.56</td>
<td>0.00</td>
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<td>Age (yr)</td>
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<td>2.60</td>
<td>0.01</td>
<td>0.60</td>
<td>—</td>
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<td>—</td>
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<td>Male gender</td>
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<td>Total/HDL cholesterol</td>
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</tr>
<tr>
<td>Total calcium score (log,-transformed)</td>
<td>0.88</td>
<td>0.11</td>
<td>7.85</td>
<td>0.00</td>
<td>0.50</td>
<td>0.10</td>
<td>5.26</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Before entering the other variables into the regression model, the most important cardiac risk factor predictors were determined. Then, first radionuclide perfusion scores and finally, EBCT calcium scores were added. T-values were derived from testing the null hypothesis that the independent variable (i.e., risk factors, radionuclide perfusion scores or EBCT calcium scores) did not contribute to predicting the dependent variable (i.e., CAGE ≥20 or CAGE ≥50 scores). Large T-values can be interpreted as indicating a true association between the independent and dependent variables. P-values were calculated as the probability of committing a type I error, based on T. Independent variables can be interpreted as predicting the dependent variable when p < 0.05.

C = coefficient; HDL = high-density lipoprotein; LDL = low-density lipoprotein, SE = standard error.

Table 4. Coronary Calcium and Extent of Disease

JACC Vol. 34, No. 3, 1999
September 1999:777–86
scores are shown. The explanations provided for factors and radionuclide perfusion scores against total calcium scores (Y-axis) and the residuals from regressing cardiac risk factors and radionuclide perfusion scores against CAGE total calcium scores (X-axis). The residuals from regressing cardiac values are a result of predictions greater than actual observations. Predictions with lower values than actual observations, and positive unstandardized residuals were used. Negative values are a result of scores. The scales are comparable with those in Figure 2, because unstandardized residuals were used. Negative values are a result of predictions with lower values than actual observations, and positive values are a result of predictions greater than actual observations. (B) Independent relation between CAGE ≥50 scores (Y-axis) and total calcium scores (X-axis). The residuals from regressing cardiac risk factors and radionuclide perfusion scores against CAGE ≥50 scores (Y-axis) and the residuals from regressing cardiac risk factors and radionuclide perfusion scores against total calcium scores are shown. The explanations provided for (A) also apply here.

Clinical implications. Our results indicate that coronary artery calcium quantities determined by EBCT predict the angiographic extent of CAD in symptomatic patients, providing independent and incremental information compared with established cardiac risk factors and SPECT imaging. In view of the unfavorable prognosis conveyed by a greater extent of coronary disease (2,3,24–26), an estimate of its extent may facilitate clinical decision making regarding treatment options of varying aggressiveness.

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