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Quantification of Coronary Artery Calcium by Electron Beam Computed Tomography for Determination of Severity of Angiographic Coronary Artery Disease in Younger Patients

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Objectives. **This study attempted to 1) evaluate five quantitative measures of coronary artery calcium and determine which best agreed with coronary artery disease severity at angiography; and 2) determine optimal quantity cutpoints to distinguish among no, mild and significant disease.**

Background. **Coronary artery calcium identified noninvasively by electron beam computed tomography is a sensitive marker for atherosclerosis. Quantitative assessments of calcium could distinguish among patients with no, mild and significant disease in clinical, screening and research settings.**

Methods. **One hundred sixty patients, 23 to 59 years old, underwent coronary angiography and electron beam computed tomography. *Coronary artery calcium* was defined as dense (>130 Hounsfield units) foci ≥2 mm^2 on the tomogram. Regression and receiver operating characteristic analyses were used to evaluate five quantitative measures of calcium as predictors of the largest stenosis in the coronary arteries and to identify optimal cutpoints for distinguishing among disease categories. *No disease* was defined as no stenosis, *mild disease* as 10% to 49% diameter stenosis in one or more major branches and *significant disease* as ≥50% diameter stenosis in one or more major branches.**

Results. **All measures evaluated performed well. With calcific area as the quantitative measure, the best cutpoint for discriminating between patients with and without disease was the presence of calcium: sensitivity 81%, specificity 86% and overall accuracy 83%. The best cutpoint for discriminating between patients with and without significant disease was 18 mm^2: sensitivity 86%, specificity 81% and accuracy 83%.**

Conclusions. **Because the ranges of calcium quantity overlapped across disease categories, no cutpoints would distinguish among categories with absolute certainty. However, selected cutpoints could rule out disease in most healthy subjects and identify most patients with significant disease.**

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Coronary artery calcium identified noninvasively by electron beam computed tomography is an accurate marker of significant coronary artery disease when significant disease is defined as an angiographic arterial stenosis of at least 50% (1,2) or 70% (3) diameter. However, calcium on an electron beam computed tomogram does not necessarily imply hemodynamically significant disease because this highly sensitive method also detects calcium associated with milder coronary artery disease (2). A quantitative assessment of calcium on electron beam computed tomographic studies may be useful in distinguishing between patients with mild and those with significant coronary artery disease in the clinical setting. It might also prove helpful as a screening tool to detect preclinical coronary artery disease and as a research tool to follow the progression of atherosclerosis in patients over time.

Objective quantification of coronary artery calcium is performed readily with electron beam computed tomography because the rapid scan acquisition time of 100 ms produces high resolution images with little motion artifact. Image processing software is used to count and calculate the X-ray attenuation coefficient (computed tomographic number) of each pixel above a predefined threshold within a calcific plaque. Thus, several different expressions of quantity of calcium within the arterial tree are possible. The total calcium burden in a coronary artery system could be defined as a function of the size, density or number of calcific plaques, or a combination of these variables. Because most studies have focused merely on the presence or absence of coronary artery calcium, the optimal quantitative measure of calcium for differentiation of disease severity has not yet been identified. One approach to defining such a measure would be to identify a quantity that maximizes agreement between quantity of coronary artery calcium on electron beam computed tomography and severity of coronary artery disease at angiography, the

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reference standard for identifying and quantifying coronary artery disease.

Thus, the aims of the present study were to 1) evaluate several quantitative measures of coronary artery calcium and determine which best agreed with angiographic severity of coronary artery disease; and 2) determine the cutpoints in this measure that best distinguished among patients with no, mild (10% to 49% diameter stenosis) and significant (≥50% diameter stenosis) coronary artery disease.

Methods

Study patients. The study sample included 160 subjects who underwent routine angiography for clinical indications at the Mayo Clinic in Rochester, Minnesota between January 1, 1989 and December 31, 1992. Subjects were invited to undergo electron beam computed tomographic examination of the heart after angiography if they were <60 years old and had no previous diagnosis of coronary artery disease and no history of coronary angioplasty, coronary bypass or cardiac transplant surgery. The sample was restricted to subjects <60 years old because the prevalence of coronary artery calcium is close to 100% in older patients (1,4). The protocol was approved by the Mayo Clinic Institutional Review Board. Approximately 58% of invited subjects participated after giving informed, written consent, for a sample of 133 white men and 27 white women (mean [±SD] age 48.5 ± 7.6 years, range 23 to 59). The median time between angiography and electron beam computed tomography was 1 day. The most common indication for angiography was chest pain (105 subjects), followed by abnormal result on stress thallium scan, treadmill test or stress radionuclide angiography (20 subjects), myocardial infarction (12 subjects), evaluation before cardiac transplantation or valve replacement (9 subjects), cardiomyopathy or dyspnea on exertion (4 subjects each), clinical congestive heart failure (3 subjects) and constrictive pericarditis, syncope and family history of premature coronary artery disease (1 subject each).

Coronary arteriographic protocol. Catheterization was performed by the Judkins technique with a minimum of five views of the left coronary system alone and two views of the right coronary system. All stenoses were visually assessed as percent diameter narrowing by the patient's cardiologist and then overread by another cardiologist (R.S.S.). Disease category was determined on the basis of the largest stenosis identified among the major epicardial arteries: *no disease* was defined as no diameter narrowing ≥10% in any major branch, *mild disease* as presence of 10% to 49% diameter narrowing in one or more major branches and *significant disease* as ≥50% diameter narrowing in one or more major branches. When the two readers disagreed as to disease category, a third cardiologist (J.A.R.) examined the arteriographic films and determined the most likely category. The maximal stenosis among all major epicardial arteries (average of the two or three readings) was also recorded.

Electron beam computed tomographic protocol. An electron beam computed tomographic scanner (Imatron C-100) was used to obtain 40 contiguous 3-mm thick transverse images commencing at the root of the aorta cephalad to the coronary sinuses and proceeding caudad through the entire coronary artery tree. Electrocardiographic triggering was used so that all images were obtained at the same phase of the cardiac cycle (80% of the RR interval). Scan acquisition time was 100 ms. Scans were taken using a 26-cm^2 field of view and a 512 × 512 reconstruction matrix so that the area of 1 pixel was equal to 0.258 mm^2. No contrast-enhancing agent was used. Total radiation dose to the skin at the back was estimated to be 10 mGy (1 rad).

Each image was examined by a radiologic technologist who placed a region of interest around each focus of coronary artery calcium, with coronary artery calcium defined as ≥8 contiguous pixels (~2 mm^2) with CT number >130 Hounsfield units (HU) within the borders of a coronary artery. The threshold of 130 HU was originally selected because it is >2 SD above the average CT number of blood and because it has been used in every published study of coronary artery calcium detected by electron beam computed tomography. This definition of calcium has been shown to be highly reproducible and is 83% accurate overall when coronary artery calcium is considered a marker of any coronary artery disease (5). Image processing software provided measurements of the area and average and peak CT number for the pixels >130 HU within each region of interest. Five different measures that assessed the quantity of calcium present in the heart were calculated: 1) *Number of plaques* was calculated as the number of discrete regions of interest in the heart. 2) *Calcific area* was calculated as the total area (mm^2) of pixels >130 HU within all regions of interest; 3) *Average density* was calculated as the average CT number among all pixels >130 HU within all regions of interest, or 130 HU if there was no calcium; 4) *Calcium score* was calculated by multiplying the calcific area (mm^2) of each region of interest by a weighting coefficient based on the peak CT number in the plaque. The weighting coefficient ranged from 1 to 4, where 1 = peak 131 to 199; 2 = peak 200 to 299; 3 = peak 300 to 399; and 4 = peak ≥400 HU. The results were then summed across regions of interest. 5) *Calcium product* was calculated by multiplying the calcific area (mm^2) of each region of interest by the average CT number in the plaque. The results were then summed across regions of interest.

Statistics. The Pearson chi-square test and analysis of variance were used to compare prevalence and quantity of coronary artery calcium for each quantitative measure across the three disease categories. Regression and receiver operating characteristic analyses were used to determine which measure of calcium quantity performed best in relation to maximal stenosis found at angiography.

Regression analyses were performed to ascertain which of the five measures of calcium quantity accounted for the most linear variation in maximal stenosis. To reduce skewness in the distributions, natural log transformations of the values plus 1 were taken for all measures except average density. Average density was transformed linearly by subtracting 130 from each value, so that the minimal possible value was set at zero.

Table 1. Ranges (median values) of Five Measures of Calcium Quantity by Disease Category

	No Disease	Mild Disease	Significant Disease
No. of Plaques	0–4 (0)	0–25 (2)	0–45 (12)
Calcific area	0–17 (0)	0–330 (9)	0–757 (108)
Average density	130–357 (130)	130–332 (175)	130–334 (241)
Calcium score	0–63 (0)	0–982 (19)	0–2,759 (327)
Calcium product	0–6,181 (0)	0–71,700 (1,650)	0–219,400 (23,696)

First-order regression equations predicting maximal stenosis were then constructed through the origin for each of the five measures of calcium quantity. The coefficients of determination (R^2) derived from these equations are not equivalent to R^2 statistics from linear regression equations with intercept terms (6), but may be compared with one another to indicate relative goodness of fit.

In contrast to the regression approach, which implicitly assumes that there are no cutpoints of interest in either the predictor (quantity of calcium) or outcome (severity of disease) measure, receiver operating characteristic analysis allows evaluation of the overall performance of diagnostic procedures at a range of possible decision thresholds (7). A decision threshold is the cutpoint in the range such that any value at or above that cutpoint would be considered a positive result and any value below it a negative result. In receiver operating characteristic analysis, multiple decision thresholds are set, with sensitivity and specificity of the diagnostic test calculated at each decision threshold. Points corresponding to sensitivity, or true positive fraction (y axis), and 1 − specificity, or false positive fraction (x axis), are then plotted, and a receiver operating characteristic curve is created linking the points. The area under a receiver operating characteristic curve (the "receiver operating characteristic area") represents the ability of the diagnostic test to discriminate between patients with and without the disease in question (7).

Receiver operating characteristic curves were created for each of the five measures of calcium quantity for any angiographically detectable disease (mild or significant) and for significant disease only. Areas under each curve were calculated using the Systat Signal module (8). The CLABROC algorithm was used to test for differences between areas while accounting for the correlated nature of the data (9).

In the regression and receiver operating characteristic analyses, all measures of quantity of calcium except average density performed similarly well. Thus, the choice of the optimal measure became subjective. Calcific area was selected as the working measure for reasons outlined later in the Discussion section. A two-step receiver operating characteristic analysis was then used to determine the decision thresholds that would best discriminate among patients with no, mild and significant coronary artery disease. First, receiver operating characteristic analysis was used to determine the best decision threshold for discriminating between patients with and without *any* disease. Second, receiver operating characteristic analysis was used to determine the best decision threshold for discriminating between patients with and without *significant* disease. Possible decision thresholds were evaluated at 1-mm^2 increments. Decision thresholds were chosen such that sensitivity, specificity and overall accuracy would all be high.

Results

Relation of calcium to disease category. Of the 160 subjects in the sample, 49 (31%) had no angiographically detected coronary artery disease, 47 (29%) had mild disease only, and 64 (40%) had significant disease. Maximal stenosis ranged from 10% to 47% (median 25%) in the mild disease category and from 50% to 100% (median 90%) in the significant disease category. Overall, the prevalence of coronary artery calcium was 61%. Prevalence of calcium was strongly related to disease category, varying from 14% for no disease to 64% for mild disease and 94% for significant disease ($p < 0.001$).

Ranges and median values for the five measures of calcium quantity are shown by disease category in Table 1. After transformations described earlier, one-way analysis of variance indicated that each quantitative measure was strongly related to disease category at $p < 0.0001$.

Comparison of quantitative measures. On the basis of linear regression, the amount of variability in maximal stenosis explained by quantity of calcium was high for each measure, ranging from 0.712 to 0.792 (Table 2). The lowest R^2 value was associated with average density, and the highest R^2 value was associated with number of plaques.

The receiver operating characteristic areas for the five quantitative measures of coronary artery calcium were also high, ranging from 0.893 to 0.911 when calcium was evaluated as an indicator of any coronary stenosis (mild or significant) and from 0.841 to 0.914 when calcium was evaluated as an indicator of significant coronary stenosis (Table 3). There were no statistically significant pairwise

Table 2. Regression Values for Five Measures of Calcium Quantity

	R^2 for Maximal Stenosis*
No. of plaques†	0.792
Calcific area†	0.790
Average density‡	0.712
Calcium score†	0.790
Calcium product†	0.777

*$p < 0.0001$. †Log-transformed values. ‡Linearly transformed values.

Table 3. Receiver Operating Characteristic Curves for Five Measures of Calcium Quantity

	Any Disease Versus No Disease	Significant Versus No and Mild Disease
No. of plaques	0.893	0.914
Calcific area	0.896	0.905
Average density	0.896	0.841
Calcium score	0.898	0.898
Calcium product	0.911	0.902

differences between the receiver operating characteristic areas when calcium was evaluated as an indicator of any stenosis, but as an indicator of significant stenosis, average density performed significantly less well than all other measures in pairwise comparisons ($p < 0.05$). The receiver operating characteristic curves for the five measures of calcium quantity were virtually identical. Figure 1 shows the receiver operating characteristic curves for calcific area.

Comparison of cutpoints. Calcific area was selected as the working measure of coronary artery calcium quantity for reasons outlined later in the Discussion section. Calcific area ranged from 0 (no calcium) to 757 mm^2. There was a broad range in calcific area within each disease category, and the ranges overlapped across disease categories, as shown in Figure 2. Still, among subjects with no disease, all had calcific area <40 mm^2, and among subjects with mild disease, only one had calcific area >120 mm^2.

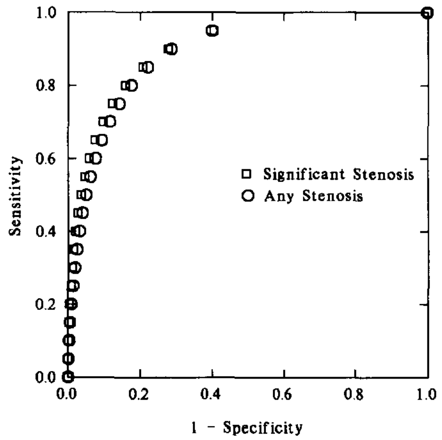
Figure 3 displays the sensitivity, specificity and overall accuracy of calcific area for any angiographically detectable disease (vs. no disease) at varying cutpoints for a "positive" calcium result between 0 and 760 mm^2. Sensitivity, specificity and accuracy were all high at the 2-mm^2 cutpoint (81%, 86% and 83%, respectively), but sensitivity decreased and specificity increased with higher cutpoints for positive calcium test results. Specificity reached 100% at 18 mm^2, at which point sensitivity was 66% and accuracy 76%.

Figure 4 displays the sensitivity, specificity and overall accuracy of calcific area for significant coronary artery disease (vs. mild or no disease) at varying cutpoints. The values for sensitivity, specificity and accuracy were all high at the 18-mm^2 cutpoint (86%, 81% and 83%, respectively). Specificity reached 99% at 108 mm^2, at which point sensitivity was 50% and overall accuracy 79%.

Calcium quantity cutpoints were chosen where sensitivity, specificity and overall accuracy were all high. Using this strategy, a reasonable decision threshold for distinguishing between patients with and without disease was 2 mm^2. For distinguishing significant from mild or no disease, a reasonable decision threshold was 18 mm^2. The final result from applying these cutpoints is illustrated in Figure 5. Of the 49 patients with no angiographically detectable disease, 42 (86%) were classified correctly, as 86% was the specificity at the 2-mm^2 cutpoint chosen in the first step in the analysis. Because sensitivity at this cutpoint was 81%, 90 of the 111 patients with disease (81%) were classified correctly. Similarly, of the 64 patients with significant disease, 55 (86%) were correctly classified, as sensitivity was 86% at the 18-mm^2 cutpoint chosen in the second step of the analysis. Misclassification was most likely to occur in the mild disease group: Only 12 patients (26%) were classified correctly.

Viewed another way, the probabilities of accuracy were 67% for a prediction of no coronary artery disease (42/63 = 67%), 50% for a prediction of mild disease (12/24 = 50%) and 75% for a production of significant disease (55/73 = 75%). The true and predicted disease categories were strongly related by the Pearson chi-square test ($p < 0.001$), and the overall accuracy for the entire sample was 68% ([42 + 12 + 55]/160 = 68%).

Figure 1. Receiver operating characteristic curves, calcific area.



Discussion

The present analysis was undertaken to identify threshold amounts of coronary artery calcium that could be used to accurately classify patients with no, mild or significant coronary artery disease. This task required identification of a quantitative calcium measure that would agree well with results from coronary angiography.

Selection of quantitative measure. All measures evaluated except average density performed extremely well in predicting severity of coronary artery disease, both as continuous variables (R^2 values for predicting maximal stenosis close to 80%) and as categoric variables (receiver operating characteristic areas for disease categories close to 90%). Calcific area was chosen as the working measure of calcium quantity because it is simple to calculate and it avoids some of the pitfalls associated with the other quantitative measures evaluated.

Number of plaques is subject to criticism as a quantitative measure of coronary artery calcium for two reasons. First, the number of regions of interest on an electron beam computed tomographic scan does not necessarily equal the number of

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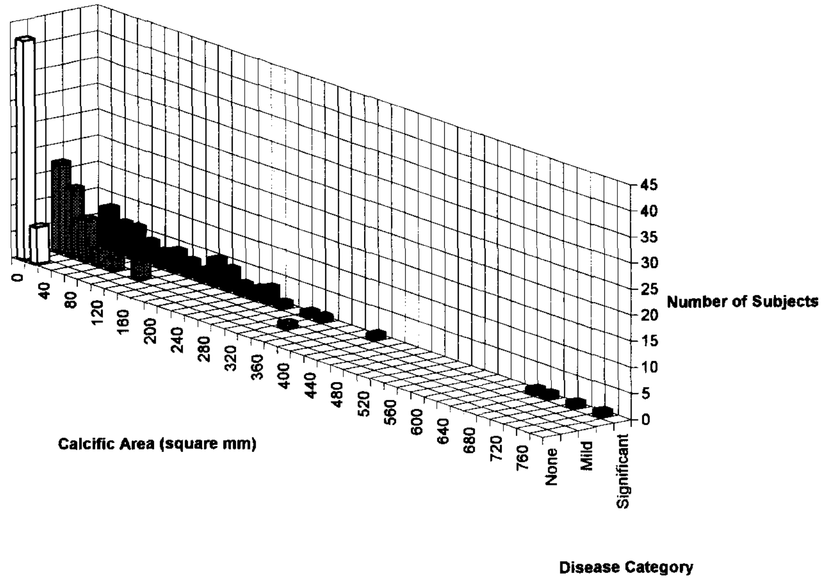


Figure 2. Calcific area by disease category. Each tick on the **x axis** represents 20 mm^2, except for the **first tick**, which separates 0 mm^2 from 2 to 19 mm^2.

distinct calcific plaques in the coronary arteries. When a large focus of calcium extends beyond the 3-mm thickness of a tomogram, it appears on more than one image and is counted as more than one region of interest. (A similar inflation effect could occur when calcific area is used as the quantitative measure.) Second, as plaques grow over time, nearby plaques coalesce (10). Thus, a greater amount of calcium can be associated with a smaller number of plaques.

Most electron beam computed tomographic studies of coronary artery calcium have used the calcium score (1-4,10-12). However, this measure has been criticized on the grounds that it uses an arbitrarily scaled weighting coefficient and that the contribution of calcium density is based entirely on the single brightest pixel within each region of interest (4,11,13).

Finally, the calcium product, like the calcium score, combines area and density but does not involve an arbitrary weighting coefficient, nor does it share the potential measurement error associated with splitting plaques over several images because the partial volume effect will decrease average density as total plaque area increases. However, this measure is more difficult to conceptualize and does not perform significantly better than calcific area.

Selection of cutpoints. The results indicated that quantity of coronary artery calcium was strongly related to severity of coronary artery disease in regression analyses. Because there was overlap in quantity of calcium across disease categories, a receiver operating characteristic approach was used, and sensitivity, specificity and overall accuracy were calculated along the full range of possible cutpoints. Using a strategy of choosing cutpoints where sensitivity, specificity and overall accuracy were all high, 2 mm^2 (i.e., any calcium) was the best cutpoint for distinguishing between patients with and without

Figure 3. Any versus no disease: sensitivity, specificity and accuracy.

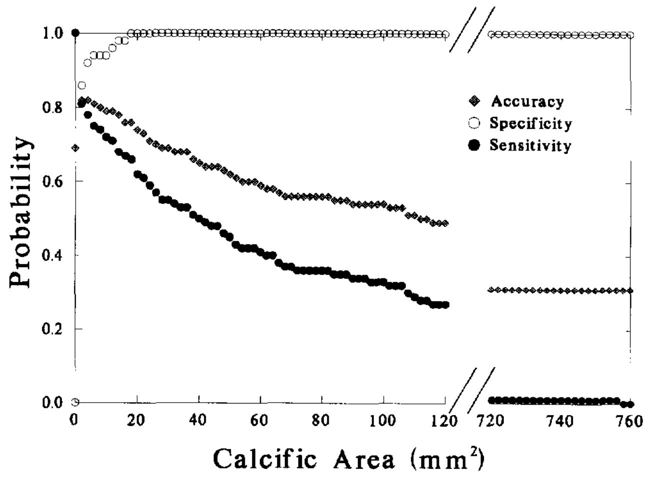
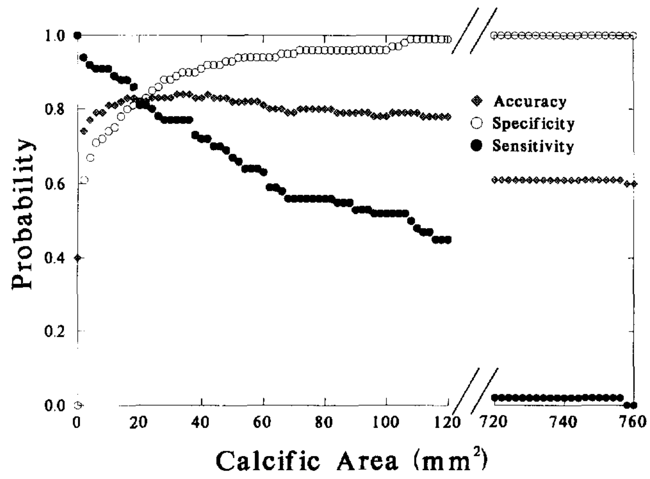


Figure 4. Significant versus no and mild disease: sensitivity, specificity and accuracy.



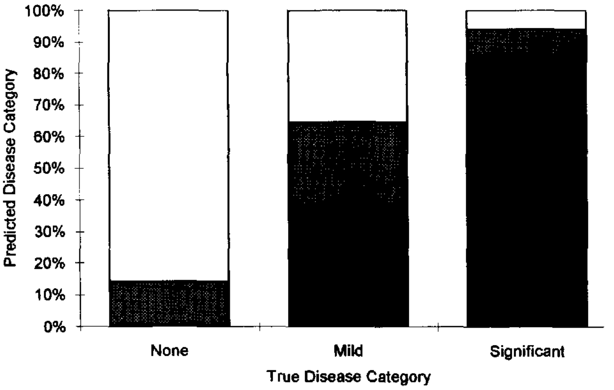


Figure 5. True and predicted disease categories: no (**open bars**), mild (**crosshatched bars**) and significant (**solid bars**) coronary artery disease.

any disease, and 18 mm^2 was the best cutpoint for distinguishing between patients with and without significant disease.

The finding that the best cutpoint for distinguishing between patients with and without any disease is the presence of any calcium is consistent with observations from necropsy studies that coronary artery calcium is invariably associated with atherosclerosis (14). Although there were eight patients with calcium who had no disease detected on angiography in the present sample, it is probable that these patients had atherosclerosis that was not detected either because of compensatory enlargement of the arteries according to the process described by de Feyter et al. (15) or because diffuse atherosclerosis caused narrowing of the entire lumen so that no local stenosis was visible.

Significance of early detection. Although evaluations of screening tests for coronary artery disease often focus on their ability to detect significant disease, identification of patients in the earliest stages of disease may prove important as a public health measure. Risk reduction interventions, such as life-style changes and lipid-lowering treatments, have been shown to be effective in asymptomatic as well as symptomatic patients (16–20). Appropriate targeting of these interventions to patients most at risk could be a valuable strategy in reducing later morbidity and mortality from coronary artery disease.

Generalizability of results. It has been reported (4) that both prevalence and quantity of coronary artery calcium are higher in male and older patients than in female and younger patients (4). Within the present sample, neither age nor gender was related to accuracy of the decision cutpoints chosen. However, caution should be used in extending conclusions drawn from the present sample of subjects <60 years old to older patients until further studies have shown whether the same cutpoints are applicable. Future studies of female subjects will be needed to support the use of the same decision points for female and male subjects.

A related issue is that electron beam computed tomographic results are affected by various factors, such as scanner used, time since scanner calibration, patient girth, partial volume and random noise (21). Thus, inherent error in calcium measurements made using this technique reduces the researcher's ability to choose cutpoints between disease categories that are 100% accurate, even within age-restricted samples. These factors also diminish the ability to choose an ideal definition of coronary artery calcium, as evidenced by an optimal definition, which is just 83% accurate relative to coronary angiography (5). However, a new examination technique that utilizes a calcium calibration phantom is expected to increase accuracy of electron beam computed tomographic studies (21) and may allow refinement of the definition of coronary artery calcium and cutpoints in the future.

Conclusions. There were no threshold amounts of coronary artery calcium that could be used to distinguish between subjects in different disease categories with absolute certainty. However, a zero amount of coronary artery calcium was highly predictive of no coronary artery disease. Although a moderate amount of calcium (2 to 17 mm^2) was not strongly predictive of mild disease, ≥18 mm^2 calcium was suggestive of significant coronary artery disease. These findings indicate that the amount of calcium can be used to rule out coronary artery disease in most subjects without disease and to identify most subjects with significant coronary artery disease in a clinical sample <60 years old.

We acknowledge the contribution of Dr. Jerome Breen to this work.

References

1. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
2. Breen JF, Sheedy PF, Schwartz RS, et al. Coronary artery calcification detected with ultrafast CT as an indication of coronary artery disease: work in progress. Radiology 1992;185:435–9.
3. Tanenbaum SR, Kondos GT, Veselik KE, Prendergast MR, Brundage BH, Chomka EV. Detection of calcific deposits in coronary arteries by ultrafast computed tomography and correlation with angiography. Am J Cardiol 1989;63:870–2.
4. Janowitz WR, Agatston AS, Kaplan G, Viamonte M. Differences in prevalence and extent of coronary artery calcium detected by ultrafast computed tomography in asymptomatic men and women. Am J Cardiol 1993;72:247–54.
5. Bielak LF, Kaufmann RB, Moll PP, McCollough CH, Schwartz RS, Sheedy PF. Small lesions in the heart identified at electron beam CT: calcification or noise? Radiology 1994;192:631–6.
6. Kvalseth TO. Cautionary note about R^2. Am Statistician 1985;39:279–85.
7. Erdreich LS, Lee ET. Use of relative operating characteristic analysis in epidemiology: a method for dealing with subjective judgement. Am J Epidemiol 1981;114:649–62.
8. Stenson H. SIGNAL: A Supplementary Module for SYSTAT and SYGRAPH. Evanston (IL): SYSTAT, Inc., 1988.
9. Metz CE, Wang P-L, Kronman HB. A new approach for testing the significance of differences between ROC curves measured from correlated data. In: Deconinck F, editor. Information Processing in Medical Imaging: Proceedings of the 8th Conference, Brussels, 1983. Boston: Nijhoff, 1984: 432–45.
10. Janowitz WR, Agatston AS, Viamonte M. Comparison of serial quantitative evaluation of calcified coronary artery plaque by ultrafast computed tomography in persons with and without obstructive coronary artery disease. Am J Cardiol 1991;68:1–6.
11. Megnien JL, Sene V, Jeannin S, et al. Coronary calcification and its relation

to extracoronary atherosclerosis in asymptomatic hypercholesterolemic men. Circulation 1992;85:1799–807.

12. Goel J, Wong ND, Eisenberg H, Hagar J, Kelly K, Tobis JM. Risk factor correlates of coronary calcium as evaluated by ultrafast computed tomography. Am J Cardiol 1992;70:977–80.
13. Kaufmann RB, Sheedy PF, Breen JF, et al. Electron beam computed tomography of the heart to detect calcification: interobserver and intraobserver reliability for scoring quantification. Radiology 1994;190:347–52.
14. Blankenhorn D. Coronary arterial calcification, a review. Am J Med Sci 1961;242:41–9.
15. de Feyter PJ, Serruys PW, Davies MJ, Richardson P, Lubsen J, Oliver MF. Quantitative coronary angiography to measure progression and regression of coronary atherosclerosis: value, limitations, and implications for clinical trials. Circulation 1991;84:412–23.
16. Ornish D, Brown SE, Scherwitz LW, et al. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet 1990;336:129–33.
17. The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. JAMA 1984;251:351–64.
18. Cashin-Hemphill L, Mack WJ, Pogoda JM, Sanmarco ME, Azen SP, Blankenhorn DH. Beneficial effects of colestipol-niacin on coronary atherosclerosis: A 4-year follow-up. JAMA 1990;264:3013–7.
19. Hjermann I, Velve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease: report from the Oslo Study Group of a randomised trial in healthy men. Lancet 1981;2: 1303–10.
20. Brown G, Albers JJ, Fisher LD, et al. Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. N Engl J Med 1990;323:1289–98.
21. McCollough CH, Kaufmann RB, Cameron BM, Katz DJ, Sheedy PF, Peyser PA. Electron beam CT: use of a calibration phantom to reduce variability in calcium concentration. Radiology. In press.