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Comparison of Electron Beam Computed Tomography Scanning and Conventional Risk Factor Assessment for the Prediction of Angiographic Coronary Artery Disease

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Objective. **To determine whether electron beam computed tomography (CT) adds to conventional risk factor assessment in the prediction of angiographic coronary artery disease.**

Background. **Electron beam CT scanning can be used to predict the severity of coronary atherosclerosis, but whether it does so independently of conventional risk factors is unclear.**

Methods. **Electron beam CT scans were performed and conventional risk factors were measured in 290 men and women undergoing coronary arteriography for clinical indications. The association of the electron beam CT-derived coronary artery calcium score and conventional risk factors with the presence and severity of angiographically defined coronary atherosclerosis was analyzed by logistic regression and receiver-operator characteristics analysis.**

Results. **Age, the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol and the coronary calcium score were significantly and independently associated with the presence of any coronary disease and obstructive coronary disease. In association with any coronary disease, odds ratios for age, the ratio of total cholesterol to HDL cholesterol and calcium score, highest quartile vs. lowest quartile, were 6.01 (95% confidence interval 2.87 to 12.56), 3.14 (1.56 to 6.31) and 94.08 (21.06 to 420.12), respectively. For obstructive coronary disease, highest quartile vs. lowest quartile, the respective odds ratios for age, the ratio of total cholesterol to HDL and calcium score were 3.86 (1.86 to 8.00), 4.11 (1.98 to 8.52) and 34.12 (12.67 to 91.86). Male gender was also significantly associated with any coronary disease (odds ratio 2.19, $p = 0.04$) and obstructive coronary disease (odds ratio 2.07, $p = 0.04$). Cigarette smoking was significantly associated with any coronary disease (odds ratio = 2.74, $p = 0.004$), and diabetes was significantly associated with obstructive disease (odds ratio 3.16, $p = 0.01$). After adjustment for the coronary calcium score and other risk factors, it was determined that triglycerides, family history and hypertension were not significantly associated with any disease state. A coronary calcium score ≥80 (Agatston method) was associated with an increased likelihood of any coronary disease regardless of the number of risk factors, and a coronary calcium score ≥170 was associated with an increased likelihood of obstructive coronary disease regardless of the number of risk factors ($p < 0.001$).**

Conclusion. **Electron beam CT scanning offers improved discrimination over conventional risk factors in the identification of persons with any angiographic coronary disease or angiographic obstructive coronary disease.**

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The electron beam computed tomography (CT)-derived coronary artery calcium score is related to the severity of coronary atherosclerosis (1–9) and predicts future coronary events in both symptomatic and asymptomatic adults (10–13). To date, however, there has been little information regarding the incremental value of electron beam CT scanning relative to conventional risk factor assessment. This gap in knowledge is serious, for the demonstration of predictive value independent of existing, less expensive methods are a necessary step in the validation of any new test.

The purpose of this study was to determine the strength of association of the coronary artery calcium score and conventional risk factors with the presence and severity of angiographically defined coronary artery disease. Variance around the general relationship between coronary calcification and coronary atherosclerosis notwithstanding, we hypothesized that the coronary artery calcium score would add significantly to the accuracy of conventional risk factor assessment.

Methods

Patients. Between June 1994 and September 1995, free electron beam CT scans of the coronary arteries were offered via telephone to patients aged less than 76 years at the time of

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Abbreviations and Acronyms

CT = computed tomography
HDL = high-density lipoprotein
LDL = low-density lipoprotein
ROC = receiver-operator characteristics
SD = standard deviation

scheduling for elective cardiac catheterization for clinical indications at St. Francis Hospital. To restrict the study to patients in whom the diagnosis of coronary disease was not yet proven, patients with prior coronary artery bypass surgery, percutaneous transluminal coronary angioplasty, myocardial infarction or previous cardiac catheterization were excluded. To increase the number of patients with normal coronary arteries and nonobstructive disease, patients with valvular heart disease received a second invitation (in person, from a research nurse) to undergo free electron beam CT scanning after angiography. Electron beam CT scans were performed within 3 months of angiography with the approval of the Institutional Review Board of the St. Francis Hospital and after obtaining written informed consent from the patients.

Risk factor assessment. Lipid profiles, consisting of measurements of serum concentrations of total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides, were obtained in the fasting state within 10 days of coronary arteriography. Total cholesterol, HDL cholesterol and triglycerides were measured using a Boehringer Mannheim/Hitachi 717 analyzer and Boehringer Mannheim reagents (catalog numbers 450026, 543004 and 1039031, respectively). Pretreatment lipid values were obtained from the private physicians of patients who were taking lipid-lowering medications at the time of coronary arteriography.

Nonlipid risk factors were recorded by an experienced cardiac nurse at the time of electron beam CT scanning. Hypertension was defined by current use of antihypertensive medications for blood pressure control. Smoking was defined as any current cigarette smoking, and diabetes was defined as the current use of diet or medications to reduce blood sugar. Family history of coronary disease was defined as symptomatic coronary artery disease occurring in first degree male relatives aged <56 years or first degree female relatives aged <66 years.

Electron beam CT scanning. Electron beam CT scanning was performed using an Imatron C-150XP scanner. Forty contiguous 3-mm slices were obtained during a single breath-hold beginning at the carina. Scan time was 100 ms/slice and the scan field was 350 mm, yielding a pixel area of 0.47 mm^2. The coronary artery score was calculated with the Agatston method (14) by a technologist blinded to all clinical and angiographic data. Two contiguous pixels with attenuation coefficient >130 Hounsfield units were required to qualify as a calcium deposit.

Coronary arteriography. Coronary arteriograms were analyzed visually. The worst stenosis in each major coronary arterial segment was estimated by consensus of two observers (A.D.G., L.A.S.) who were blinded to both the calcium score and the clinical status of the patients. Obstructive coronary disease was defined as ≥50% reduction in the diameter of any major coronary arterial segment. Nonobstructive disease was defined as 0 < worst stenosis <50%. Patients with unquantifiable minimal irregularities were classified as having nonobstructive disease. In a previous study, when visual estimates of severity of disease were compared to computer-assisted quantitative coronary angiography performed at a remote site, the same two observers classified 59 of 60 angiograms correctly (15).

Statistical analysis. The primary outcome measures were the independent, relative associations (odds ratios) of the coronary calcium score and conventional risk factors with the presence of any coronary disease, nonobstructive coronary disease or obstructive coronary disease, as determined by coronary arteriography. Multiple logistic regression was used to calculate odds ratios and p values ($p < 0.05$ defined significant associations).

Age, the ratio of total cholesterol to HDL cholesterol, triglycerides and calcium score were treated as continuous variables; gender, family history, hypertension, diabetes and cigarette smoking were treated as dichotomous variables. Total cholesterol was excluded from analysis because it covaried with the ratio of total cholesterol to HDL cholesterol and because of evidence that it is prognostically inferior to the ratio of total cholesterol to HDL cholesterol (16,17). For age, odds ratios were analyzed per additional decade of life, for example, age 60 to 69 vs. 50 to 59. For triglycerides, odds ratios are presented in increments of 1 mg/dl. For the ratio of total cholesterol to HDL cholesterol, odds ratios are presented per additional unit, for example, 5.0 to 5.9 vs. 4.0 to 4.9. For the coronary calcium score, odds ratios are presented on the basis of increments of 200 units, for example, 200 to 399 vs. 0 to 199.

We subsequently analyzed the effect of the total number of risk factors, as defined by the National Cholesterol Education Program (18), on the prediction of any disease and obstructive disease by the coronary calcium score. This analysis differs from the multiple logistic regression described above in that the relationships of the coronary calcium score and conventional risk factors to the different disease states of interest were not adjusted for each other. Instead, the analysis addressed a simple question: Is the predictive value of the coronary calcium score related to the number of risk factors? This analysis helps to illustrate the incremental effect of both coronary calcium and the total number of risk factors in the prediction of disease.

Analyses of risk factors associated with any coronary disease or obstructive coronary disease involved the use of data from all patients (i.e., any coronary disease refers to nonobstructive disease plus obstructive disease vs. normal coronary arteries and obstructive disease is compared to data from subjects with normal coronary arteries and nonobstructive disease).

Table 1. Distribution of Continuous Variable Risk Factors

	Percentile				
	10th	25th	50th	75th	90th
Age (yr)	45	51	60	67	70
Total cholesterol (mmol/liter)	4.27	4.91	5.61	6.49	7.47
Ratio	3.6	4.5	5.6	6.7	8.0
Triglycerides (mg/dl)	74	99	135	192	244
Coronary calcium score	0	5	100	489	1189

To convert total cholesterol from mmol/liter to mg/dl, multiply by 38.7. Ratio refers to the ratio of total cholesterol to HDL cholesterol.

Results

Coronary risk factors, coronary arteriograms and electron beam CT scans were analyzed for 290 patients. The mean (± SD) age was 59 ± 10 years and 206 of the patients (71%) were men. The mean (± SD) time from electron beam CT scanning to coronary arteriography (absolute value) was 17 ± 27 days. There were no coronary events between arteriography and electron beam CT scanning. Obstructive disease was found in 116 patients (40%), nonobstructive disease in 76 patients (26%) and normal coronary arteries in 98 patients (34%). The distribution of continuous variable risk factors (age, total cholesterol, the ratio of total cholesterol to HDL cholesterol, triglycerides and the coronary calcium score) is presented in Table 1.

Coronary calcification and severity of angiographic coronary disease. Coronary artery calcium score increased as a function of the category of angiographic disease (Fig. 1, Table 2, $p < 0.0001$). The calcium scores of patients with angiographically normal coronary arteries and angiographic obstructive disease were widely separated, with a calcium score of 33 representing the 75th percentile for subjects with normal coronary arteries and a calcium score of 147 representing the 25th percentile for subjects with obstructive coronary disease.

Figure 1. Box and whisker plot of the distribution of coronary calcium scores for patients with angiographically normal coronary arteries (n = 98), angiographic nonobstructive coronary disease (n = 76) or angiographic obstructive disease (n = 116). The horizontal line inside the rectangular segment of each box denotes the median value for each category of disease. The lower and upper edges of the rectangular segment represent the 25th and 75th percentiles of the distribution of calcium scores and the flared ends of each box represent the 10th and 90th percentiles. The whiskers encompass the entire range of each population.

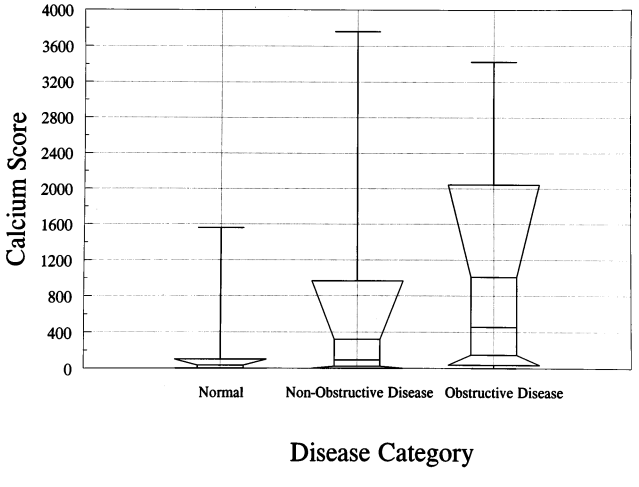

Table 2. Distribution of Coronary Calcium Scores for Each Category of Disease

	Percentile			
	n	25th	50th	75th
Normal	98	0	3	33
Nonobstructive	76	21	95	317
Obstructive	116	147	465	1007

Coronary calcium score and conventional risk factors: relation to angiographic coronary disease. By multiple logistic regression, age, male gender, the ratio of total cholesterol to HDL cholesterol and the coronary calcium score were all significantly and independently associated with the presence of any coronary disease and obstructive coronary disease (Tables 3 and 4). Cigarette smoking was associated with the presence of any coronary disease and diabetes mellitus was associated with the presence of obstructive disease.

For the prediction of any coronary disease, the area under the receiver-operator characteristics (ROC) curve for the calcium score, 0.86, was higher than that for the ratio of total cholesterol to HDL cholesterol, 0.64 ($p < 0.0001$). The area under the ROC curve for the prediction of obstructive coronary disease was also higher for the calcium score than for the ratio of total cholesterol to HDL cholesterol (0.84 vs. 0.63, $p < 0.0001$).

The strength of association of the coronary calcium score with the presence of any coronary disease and obstructive coronary disease is illustrated by comparing the odds ratios for

Table 3. Association of Risk Factors for Coronary Disease and the Coronary Calcium Score With the Presence of Any Angiographic Coronary Artery Disease by Multiple Logistic Regression

	Any Coronary Disease	
	Odds Ratio (95% CI)	p
Age (10)	2.21 (1.50–3.26)	0.0001
Gender	2.19 (1.03–4.64)	0.04
Ratio (1)	1.42 (1.11–1.81)	0.005
Triglycerides (1)	1.00 (0.99–1.01)	0.82
Family history	1.01 (0.52–2.00)	0.96
Hypertension	1.29 (0.66–2.53)	0.45
Diabetes	3.10 (0.81–11.90)	0.10
Smoking	2.74 (1.38–5.46)	0.004
Calcium score (200)	2.67 (1.65–4.3)	0.0001

Ratio refers to the ratio of total cholesterol to HDL cholesterol. Numbers in parentheses next to risk factors refer to the increments used in analyzing the relationship between the risk factor of interest and the disease state of interest. Thus, age was analyzed on the basis of, and the odds ratios refer to, increments of 10 years. Odds ratios for the ratio of total cholesterol to HDL cholesterol and triglycerides refer to the risk associated with increases of 1 unit and 1 mg/dl units, respectively. Calcium score was analyzed on the basis of increments of 200 units.

Table 4. Association of Risk Factors for Coronary Disease and the Coronary Calcium Score With the Presence of Angiographic Obstructive Coronary Artery Disease by Multiple Logistic Regression

	Obstructive Coronary Disease	
	Odds Ratio (95% CI)	p
Age (10)	1.95 (1.36–2.80)	0.0003
Gender	2.07 (1.03–4.20)	0.04
Ratio (1)	1.35 (1.10–1.66)	0.004
Triglycerides (1)	1.00 (.99–1.01)	0.87
Family history	1.52 (0.81–2.83)	0.19
Hypertension	1.52 (0.84–2.77)	0.17
Diabetes	3.16 (1.26–7.93)	0.01
Smoking	1.57 (0.83–2.96)	0.17
Calcium score (200)	1.40 (1.21–1.60)	0.0001

Ratio refers to the ratio of total cholesterol to HDL cholesterol. Numbers in parentheses next to risk factors refer to the increments used in analyzing the relationship between the risk factor of interest and the disease state of interest. Thus, age was analyzed on the basis of, and the odds ratio refer to, increments of 10 years. Odds ratios for the ratio of total cholesterol to HDL cholesterol and calcium score refer to the risk associated with increases of 1 unit and 200 units, respectively. The odds ratio for triglycerides is based on increments of 1 mg/dl.

patients in the highest quartile to patients in the lowest quartile (Table 5). This analysis included all coronary disease risk factors, but results are presented only for those continuous variable risk factors independently associated with all categories of coronary disease, that is, age, the ratio of total cholesterol to HDL cholesterol and the coronary calcium score. After adjustment for all other risk factors, the odds ratios for the coronary calcium score are an order of magnitude higher than the odds ratios for age and the ratio of total cholesterol to HDL cholesterol.

To illustrate the additive value of the coronary calcium score relative to conventional risk factors, the effect of coronary calcium score was analyzed on the basis of the number of conventional risk factors, as defined by the National Cholesterol Education Program (18). Hypercholesterolemia was defined according to the number of nonlipid risk factors, that is, an LDL cholesterol ≥4.14 mmol/liter (160 mg/dl) was counted as a risk factor in the presence of two or more nonlipid risk factors, and a low-density lipoprotein (LDL) cholesterol ≥4.91 mmol/liter (190 mg/dl) was counted as a risk factor regardless of the number of nonlipid risk factors. Calcium scores of 80 and 170 were used as cut points denoting the presence of any disease and obstructive disease, respectively, because in separate analyses they maximized overall accuracy in this population (Fig. 2 and 3). For patients with any number of observed risk factors in this population (zero to six), a coronary calcium score ≥80 was associated with a higher probability of any coronary disease ($p < 0.001$, Fig. 4). Similarly, for patients with one to six risk factors (the range observed in patients with obstructive disease), a coronary calcium score ≥170 was associated with a higher probability of obstructive disease ($p < 0.001$, Fig. 5). In both cases, the positive predictive value of a score above the threshold was independent of the number of risk factors, whereas the negative predictive value was inversely related to the number of risk factors ($p < 0.01$).

Table 5. Odds Ratio for Any Coronary Disease and Obstructive Coronary Disease, Highest Quartile Vs. Lowest Quartile, by Multiple Logistic Regression

	Odds Ratios (95% CI)	
	Any CAD	Obstructive CAD
Age	6.01 (2.87–12.56)	3.86 (1.86–8.00)
Ratio	3.14 (1.56–6.31)	4.11 (1.98–8.52)
Calcium score	94.08 (21.06–420.12)	34.12 (12.67–91.86)

All coronary artery disease (CAD) risk factors included in this analysis, results reported only for continuous variable risk factors consistently and independently associated with all categories of CAD. Ratio refers to the ratio of total cholesterol to HDL cholesterol.

Discussion

This study demonstrates significant and independent associations between the electron beam CT coronary calcium score and presence of any angiographic coronary disease and angiographic obstructive coronary disease in a symptomatic population. The strength of these associations may be appreciated by consideration of the odds ratios listed in Table 5. In turn, these odds ratios represent the interaction of the range of values of the risk factors in Table 1 and the odds ratios listed in Tables 3 and 4. For example, although the odds ratios for the increments of age and coronary calcium score are similar with respect to the presence of any angiographically evident coronary disease, the broader range of coronary calcium scores amplifies the differences in the odds of any coronary disease. Thus, compared to patients with coronary calcium scores of zero (the lowest decile), the odds of finding any coronary disease increased to 7.1 (i.e., 2.67^2) for patients with calcium scores of 400 to 599 and to 362 (2.67^6) for patients with calcium scores of 1,200 to 1,399 (9% of patients had calcium scores above 1,200). In contrast, the odds of any angiographic coronary disease were only about 23.9 (i.e., 2.21^4) for patients in their 70s compared to patients in their 40s, and about 5.8 (1.42^5) for patients with ratios of total cholesterol to HDL cholesterol above 8.0 compared to patients with ratios below 3.6 (i.e., the highest decile vs. the lowest decile). Despite the substantial variance in coronary calcium scores associated with any particular coronary disease state (Fig. 1, Table 2) for which the use of electron beam CT scanning has been criticized (19), the coronary calcium score is independently and powerfully predictive of coronary disease and atherosclerotic plaque burden.

A second way of evaluating the incremental value of electron beam CT is to examine the predictive value of the coronary calcium score as a function of the number of risk factors. This approach is advantageous in that the raw data are visually appreciable, whereas logistic regression is not. Tables 4 and 5 indicate that in a population with high pretest likelihood of disease, the likelihood of any angiographic coronary disease or angiographic obstructive coronary disease is

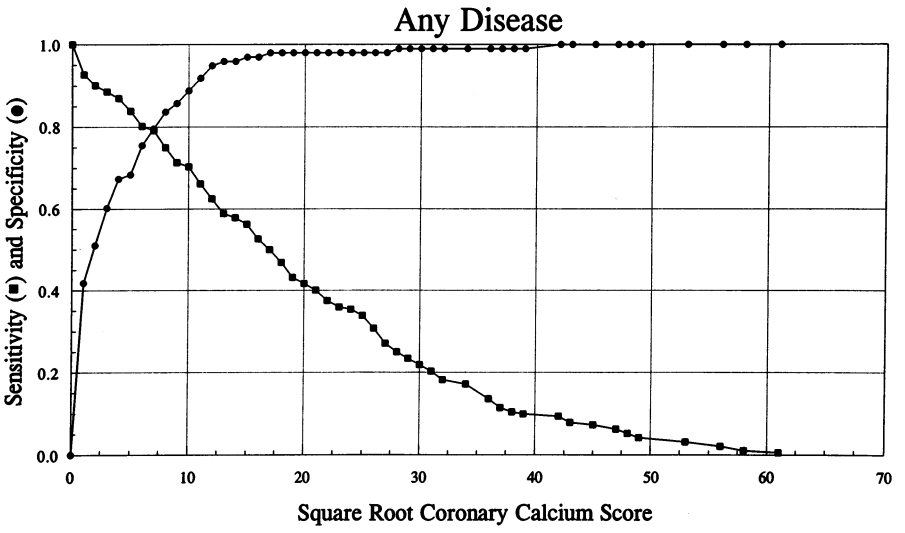

Figure 2. Sensitivity and specificity of electron beam CT scanning for the detection of any angiographic coronary disease. Values for sensitivity and specificity are presented as a function of the square root of the coronary calcium score. The sum of sensitivity and specificity were maximized at a calcium score of 80.

constant across a broad range of risk factors for subjects with coronary calcium scores in excess of 80 and 170, respectively. Conversely, the negative predictive value of the coronary calcium score is inversely proportional to the number of risk factors. These findings are consistent with the relationship of coronary calcification to coronary atherosclerosis. For practical purposes, coronary calcification means coronary atherosclerosis (20,21). At the same time, variance around the general relationship between coronary calcification and coronary atherosclerosis means that Bayes' theorem applies, and the pretest likelihood of disease will influence both the positive and the negative predictive value of any threshold calcium score. (Lack of effect of the number of risk factors on positive predictive value may have been the result of very high pretest probability in the case of any angiographic coronary disease and inadequate sample size in the case of angiographic obstructive disease.) These findings are of clinical importance because they imply that electron beam CT scanning will be most valuable when applied to persons at intermediate risk, that is, those with a few but not many risk factors for coronary artery disease.

In that the coronary calcium score emerged from comparisons with conventional risk factors as the most powerful predictor of angiographic obstructive coronary disease, these results are similar to those recently reported by Kennedy et al. (22) in 368 patients. However, that study lacked measurements of HDL cholesterol and did not analyze relationships between conventional risk factors and any angiographic coronary disease.

The high odds ratio associated with age may be a reflection of patient selection and local practice. This was a study of outpatients without previously documented coronary disease undergoing elective cardiac catheterization. Most of the patients were scheduled for catheterization for the evaluation of chest pain, and virtually all of those with chest pain had already undergone either exercise thallium scintigraphy or stress echo-

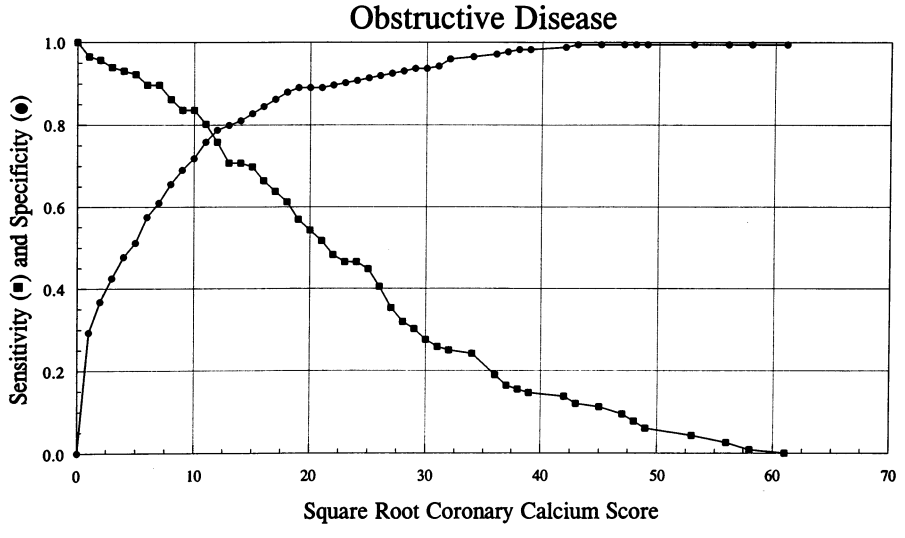

Figure 3. Sensitivity and specificity of electron beam CT scanning for the detection of any angiographic obstructive coronary disease. Values for sensitivity and specificity are presented as a function of the square root of the coronary calcium score. The sum of sensitivity and specificity were maximized at a calcium score of 170.

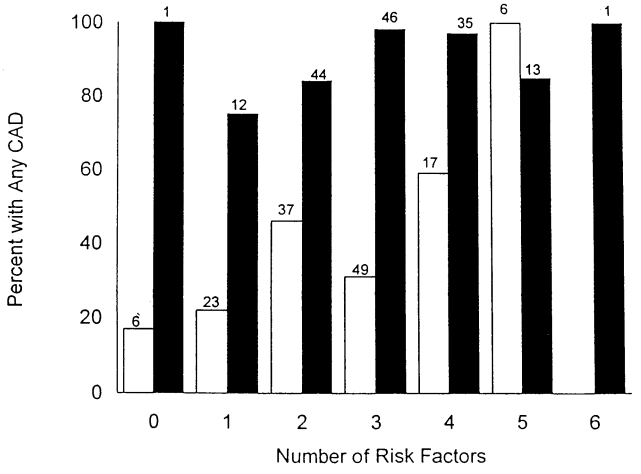

Figure 4. Percentage of patients with any coronary disease as a function of the number of risk factors and the coronary calcium score. **Solid bars** refer to patients with calcium scores ≥80; **open bars** refer to patients with calcium scores <80. Numbers at the top of each bar refer to the number of patients in each group. The likelihood of any coronary disease was independent of the number of risk factors for patients with calcium scores ≥80, whereas the likelihood of any coronary disease was related to the number of risk factors for those with calcium scores <80. The value of p refers to the difference between the likelihood of disease among those with calcium scores above and below 80, after adjustment for the number of risk factors. $p < 0.001$.

cardiography. Among patients aged less than 50 years, 66% had angiographically normal coronary arteries and only 16% had angiographic obstructive disease. These figures are consistent with the local practice of referring younger patients with chest pain and equivocal stress test results for coronary angiography.

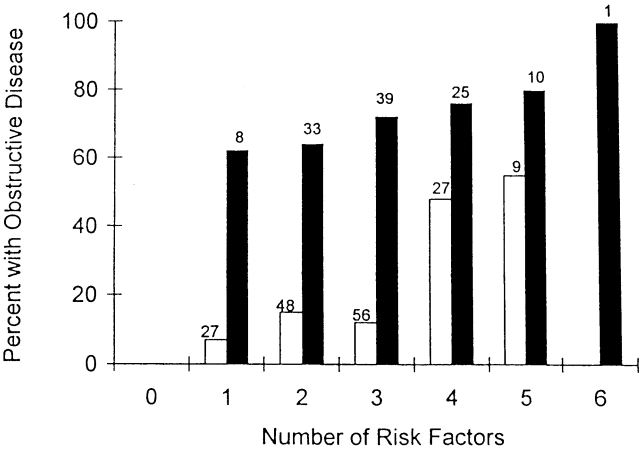

Figure 5. Percentage of patients with obstructive coronary disease as a function of the number of risk factors and the coronary calcium score. **Solid bars** refer to patients with calcium scores ≥170; **open bars** refer to patients with calcium scores <170. Numbers at the top of each bar refer to the number of patients in each group. No patient with obstructive disease had no risk factors. Interpretation as in Figure 2. $p < 0.001$.

Ultimately, the incremental value of electron beam CT scanning must be determined on the basis of correlations with clinical events occurring in asymptomatic populations. In that this study was conducted in a symptomatic population with an angiographic end point, its application is limited. Nevertheless, this study fulfills a corollary of the hypothesis that electron beam CT scanning of the coronary arteries adds significantly to the prognostic power of conventional risk factor assessment, for if electron beam CT scanning does truly add to the prognostic power of conventional risk factor assessment, then the relationship between angiographically defined coronary disease and coronary events (23,24) mandates that the coronary calcium score should also be an independent risk factor for the presence and severity of coronary disease. Thus, this study contributes evidence in support of the hypothesis that electron beam CT scanning adds unique and important information to what can be determined on the basis of conventional risk factor assessment. These data are consistent with reports of unprecedented prognostic accuracy associated with electron beam CT scanning of asymptomatic populations over 1 to 6 years (11,12). Risk factors for coronary disease cannot be equated with actual disease, whereas coronary calcification is a marker for coronary atherosclerosis, regardless of the number of risk factors.

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References

1. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Edwards WD, Schwartz RS. Coronary artery calcium area by electron beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. Circulation 1995;92:2157–62.
2. Guerci AD, Spadaro LA, Popma JJ, et al. Relation of coronary calcium score by electron beam computed tomography to arteriographic findings in asymptomatic and symptomatic adults. Am J Cardiol 1997;79:128–33.
3. Breen JF, Sheedy PF, Schwartz RF, et al. Coronary artery calcification detected with ultrafast CT as an indication of coronary artery disease. Radiology 1992;185:435–9.
4. Agatston AS, Janowitz WR, Kaplan G, Gasso J, Hildner F, Viamonte M. Ultrafast computed tomography-detected coronary calcium reflects the angiographic extent of coronary arterial atherosclerosis. Am J Cardiol 1994;74:1272–4.
5. Devries S, Wolfkiel C, Fusman B, et al. Influence of age and gender on the presence of coronary calcium detected by ultrafast computed tomography. J Am Coll Cardiol 1995;25:76–82.
6. Rumberger JA, Sheedy PF, Breen JF, Schwartz RS. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effect of patient's sex on diagnosis. Circulation 1995;91: 1363–7.
7. Kajinami K, Seki H, Takekoshi N, Mabuchi H. Noninvasive prediction of coronary atherosclerosis by quantification of coronary artery calcification using electron beam computed tomography. J Am Coll Cardiol 1995;26: 1209–21.
8. Budoff MJ, Georgiou D, Brody A, et al. Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease. A multicenter study. Circulation 1996;93:898–904.
9. Chou TM, Redberg RF, Ko E, et al. Screening for coronary atherosclerosis by detection of calcium on electron beam computed tomography: correlation with intravascular ultrasound in asymptomatic patients with primary hyperlipidemia (abstr). Circulation 1996;94 Suppl I:I–360.

10. Detrano R, Hsiai T, Wang S, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27:285–90.
11. Arad Y, Spadaro LA, Goodman K, et al. The predictive value of electron beam CT of the coronary arteries: 19 month follow-up of 1173 asymptomatic subjects. Circulation 1996;93:1951–3.
12. Agatston AS, Janowitz WR, Kaplan GS, et al. Electron beam CT predicts future coronary events (abstr). Circulation 1996;94 Suppl I:I–360.
13. Detrano RC, Wong N, Tang W, Doherty TM. Determining coronary event risk in asymptomatic high risk subjects: a risk factor versus an anatomic approach [abstract]. Circulation 1997;96:I–404.
14. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
15. Guerci AD, Spadaro LA, Popma JJ, et al. Accuracy of electron beam computed tomographic scanning of the coronary arteries in the diagnosis of obstructive and nonobstructive coronary disease in symptomatic adults. (Submitted)
16. Grover SA, Coupal L, Hu XP. Identifying adults at increased risk of coronary disease. How well do the current cholesterol guidelines work? JAMA 1995;274:801–6.
17. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease. Predicting risks by levels and ratios. Ann Int Med 1994;121:641–7.
18. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Summary of the second report of the National Cholesterol Education Program (NCEP) Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). JAMA 1993;269:3015–23.
19. Wexler L, Brundage B, Crouse J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Circulation 1996;94:1175–92.
20. Blankenhorn DH. Coronary arterial calcification: a review. Am J Med Sci 1961;242:1–10.
21. Rifkin RD, Parisi AF, Folland E. Coronary calcification in the diagnosis of coronary artery disease. Am J Cardiol 1979;44:141–7.
22. Kennedy J, Shavelle R, Wang S, Budoff M, Detrano RC. Coronary calcium and standard risk factors in symptomatic patients referred for coronary angiography. Am Heart J 1998;135:696–702.
23. Proudfit WL, Bruschke AVG, Sones FM. Clinical course of patients with normal and moderately abnormal coronary arteriograms: 10-year follow-up of 521 patients. Circulation 1980;62:712–8.
24. Emond M, Mock MB, Davis KB, et al. and participants in the Coronary Artery Surgery Study (CASS). Long term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. Circulation 1994;90;2645–57.