

FOCUS ISSUE: CARDIAC IMAGING

Coronary Calcification

Relationship Between Coronary Artery Calcification Detected by Electron-Beam Computed Tomography and Abnormal Stress Echocardiography

Association and Prognostic Implications

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OBJECTIVES	The purpose of this study was to compare the results and prognostic value of electron-beam computed tomography (EBCT) and exercise echocardiography.
BACKGROUND	Although patients with elevated coronary artery calcium scores (CACS) might be referred for exercise echocardiography, the association of EBCT CACS with wall motion score index (WMSI) is not known.
METHODS	Patients without known coronary artery disease who underwent both clinically indicated EBCT and exercise echocardiography within a 3-month period were identified. Exercise WMSI was based on a 16-segment model (normal = 1; abnormal >1). The EBCT CACS was derived with the Agatston scoring system. Follow-up was obtained for the combined end point of death and myocardial infarction.
RESULTS	The study population included 556 patients (age 54 ± 10 years; 65% male). Correlation between EBCT CACS and exercise WMSI was limited ($r = 0.17$, $p < 0.0001$) but statistically significant. The proportion of patients with abnormal exercise WMSI increased with increasing CACS severity (chi-square = 19.1, $p < 0.001$). However, even in those with CACS >400, 66% had normal exercise WMSI. Age, CACS, and chest pain were independently associated with abnormal exercise WMSI. Events occurred in 12 (2%) patients. Wall motion score index (risk ratio [RR] 3.7, $p = 0.023$) and age (RR 1.9, $p = 0.019$) were associated with events.
CONCLUSIONS	Electron-beam computed tomography CACS was predictive of abnormal exercise WMSI, but the majority of patients with elevated CACS had normal WMSI. Wall motion score index and age were the best predictors of events. Prospective studies are indicated to establish the relative roles of these tests in risk stratification. (J Am Coll Cardiol 2006;48:2125-31) © 2006 by the American College of Cardiology Foundation

Early detection of subclinical coronary artery disease (CAD) in at-risk individuals is of paramount importance. Traditional models of risk stratification, such as the Framingham risk score, have limitations in their ability to predict which patients will have clinically manifest CAD (1,2). In up to 50% of patients, acute myocardial infarction (MI) is the first presentation of previously undocumented cardiovascular disease; almost one-half of these patients will die from lethal ventricular arrhythmias (3).

Electron-beam computed tomography (EBCT) is a non-invasive and extremely sensitive technique for detecting coronary artery calcification. In histopathologic studies, this has correlated well with the overall burden of coronary artery atherosclerosis (4,5). However, in a review of 16 studies using coronary angiography as the reference stan-

dard, EBCT had a low weighted average specificity of only 40% with respect to the detection of hemodynamically significant coronary artery lesions ($\geq 50\%$ stenosis) (6).

In contrast, stress echocardiography is better suited to detecting flow-limiting CAD by the finding of new stress-induced regional wall motion abnormalities. However, early atherosclerotic plaque remains largely undetected with this technique.

Thus, EBCT and stress echocardiography offer potential as complementary techniques. This study was undertaken to determine the relationship between coronary artery calcium score (CACS) on EBCT and results of exercise echocardiography. The utility of the 2 techniques for prediction of mortality and cardiac events was also assessed.

METHODS

Patient population. We retrospectively identified patients at our institution who had undergone both clinically indicated EBCT and exercise echocardiography within a

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Abbreviations and Acronyms

CACS	= coronary artery calcium score
CAD	= coronary artery disease
CI	= confidence interval
EBCT	= electron-beam computed tomography
HU	= Hounsfield units
MI	= myocardial infarction
RR	= risk ratio
SPECT	= single-photon emission computed tomography
WMSI	= wall motion score index

3-month period from January 1990 to October 2003 ($n = 638$) without intervening MI or coronary revascularization. All patients provided consent to research participation. Patients were excluded for the following reasons (patients might have met ≥ 1 criterion): 1) documented CAD (on the basis of prior MI or previous percutaneous or surgical coronary revascularization) ($n = 74$); 2) Agatston calcium score not reported ($n = 36$); 3) inadequate stress echocardiography images (no evidence of ischemia and ≥ 2 segments not visualized) ($n = 7$); 4) significant valvular heart disease ($n = 2$); and 5) treadmill Bruce protocol not performed ($n = 5$). The remaining 556 patients comprised the final study population. At the time of exercise echocardiography, patient's age, gender, symptom status (none, noncardiac, atypical, or typical chest pain), and presence of other CAD risk factors (hypertension, diabetes mellitus, family history of premature CAD, and history of cigarette smoking) were recorded in a database. Pretest probability of CAD was based on previously published criteria (7).

Exercise echocardiography. Patients underwent symptom-limited exercise treadmill testing according to the Bruce protocol (8). Standard blood pressure and 12-lead electrocardiographic monitoring were performed. The rest and stress exercise echocardiography images were obtained from the parasternal and apical windows at rest and immediately after exercise. Semiquantitative wall motion score index (WMSI) was calculated at rest and after exercise according to a 16-segment model (9). An experienced echocardiographer blinded to the patient's clinical information visually scored wall motion on a 1 to 5 scale for each wall segment (1 = normal, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic, and 5 = aneurysm). The WMSI was calculated at rest and after exercise as the sum of the myocardial wall motion segment scores divided by the number of segments visualized (i.e., normal WMSI = 1). The difference between exercise WMSI and rest WMSI was defined as Δ WMSI. To relate vessel location of coronary artery calcium with exercise echocardiographic distribution of abnormalities, the anteroseptal, anterior, and apical segments were attributed to the left anterior descending coronary artery, the anterolateral and inferolateral segments to the circumflex, and the inferior and inferoseptal segments to the right coronary artery.

EBCT. Electron-beam computed tomography was performed in accordance with previously described methodology (10). Each patient underwent 2 consecutive scans approximately 1 min apart on the same EBCT machine (Imatron C-150, San Francisco, California) with electrocardiographic-triggering at 60% of the R-R interval. Correlation between CACS on serial scans was excellent ($r^2 = 0.96$, $p < 0.001$). Approximately 40 axial slices (3-mm thick) were obtained with 100-ms acquisition times over 1 to 3 breath holds. No intravenous contrast was used.

For each of the major epicardial coronary arteries, foci of calcific plaque(s) with 3 contiguous pixels $\geq 1 \text{ mm}^2$ in area and peak density ≥ 130 Hounsfield units [HU] were identified by a radiology technologist. Each scan was interpreted and verified by an experienced radiologist blinded to the patient's clinical care. Semiautomated computer software derived the vessel-specific CACS by computing the product of the calcific plaque area and the respective density factor on a scale of 1 to 4 (1 = 130 to 199 HU; 2 = 200 to 299 HU; 3 = 300 to 399 HU, and 4 if ≥ 400 HU) (11,12). The total CACS, which was used in the data analyses, was the sum of the calcium scores for all epicardial vessels. If there was a difference in the CACS between serial scans, the higher CACS was used in the analyses. The CACS was stratified as follows: 0 (none); 1 to 10 (minimal); 11 to 100 (mild); 101 to 400 (moderate); and >400 (severe) (12).

Follow-up. Follow-up and verification of events, including all-cause mortality and a combined end point of death and MI, were obtained by review of the patient's medical records. Death was confirmed by review of medical records and documentation by the online Social Security Death Index. Time to first event was used for this analysis. Coronary artery revascularization, either percutaneous or surgical, was also recorded.

Average follow-up was 4.0 ± 2.1 years for the primary end point of death. Death was confirmed by medical record review and Social Security Death Index or exclusively by medical records for the 77 (13.8%) patients with residence addresses outside the U.S. or Canada. For the combined end point analysis, 81 patients (14.6%) without subsequent clinical evaluation beyond the index EBCT scan were considered lost to follow-up. Mean follow-up in the remaining 475 (85.4%) patients was 2.6 ± 2.3 years.

Statistical analysis. Continuous variables were summarized with mean values \pm SD and nominal or ordinal variables with count and percentage data. Correlation between EBCT CACS and WMSI by exercise echocardiography was reported with the Spearman correlation coefficient. Baseline characteristics between patients with and without severe CACS were compared with a 2-sample t test. Univariate logistic regression analysis was performed to assess the associations of clinical risk variables (age, gender, hypertension, diabetes mellitus, family history of premature CAD, smoking status), symptom status, and CACS with abnormal exercise echocardiography (i.e., WMSI >1).

Table 1. Demographic and Clinical Characteristics Grouped by CACS

Parameter	Overall (n = 556)	CACS ≤400 (n = 494)	CACS >400 (n = 62)	p Value
Age, yrs	53.9 ± 10.1	52.8 ± 9.6	62.6 ± 9.9	<0.001
Male	363 (65.3%)	313 (63.4%)	50 (80.7%)	0.005
Diabetes mellitus	45 (8.1%)	40 (8.1%)	5 (8.1%)	0.99
Smoking	233 (41.9%)	201 (40.7%)	32 (51.6%)	0.10
Systemic hypertension	196 (35.2%)	168 (34.0%)	28 (45.1%)	0.09
Family history of premature CAD	259 (46.6%)	230 (46.6%)	29 (46.8%)	0.97
Hypercholesterolemia	412 (74.2%)	368 (74.7%)	44 (71.0%)	0.53
Beta-blocker	74 (13.3%)	69 (14.0%)	5 (8.1%)	0.19
Calcium channel blocker	33 (5.9%)	27 (5.5%)	6 (9.7%)	0.19
Digoxin	2 (0.4%)	0 (0%)	2 (3.2%)	0.01
Symptom status				
Asymptomatic	343 (61.7%)	298 (60.3%)	45 (72.6%)	0.06
Typical angina	37 (6.7%)	34 (6.9%)	3 (4.8%)	0.79
Atypical/noncardiac chest pain	176 (31.7%)	162 (32.8%)	14 (22.6%)	0.09
Exercise time (min)	10.4 (3.0)	10.5 (2.9)	10.0 (3.6)	0.06

CACS = coronary artery calcium score; CAD = coronary artery disease.

Kaplan-Meier methods were used to estimate survival free of end points. Significant differences in event-free survival curves were assessed with the log-rank test. Univariate and multivariate associations of CACS, WMSI, and clinical risk variables with the occurrence of mortality and the combined end point of death/MI were derived with Cox proportional hazards models.

We used JMP 5.1 statistical software (2003 SAS Institute, Inc., Cary, North Carolina) for all analyses. Significance level for retention of variables in univariate and multivariate analysis was set at a p value of <0.05.

RESULTS

Baseline characteristics. Demographic and clinical baseline characteristics of the study population are shown in Table 1. The mean age of the study population was 54 ± 10 years; 363 (65%) patients were male. Clinical risk variables, except for age and gender, were comparable in patients with and without severe CACS. The majority of patients were asymptomatic (61.7%) and underwent evaluation primarily because of risk factors for CAD. The remaining patients were referred for evaluation of chest pain. Pretest probability of CAD was low in 354 (63.7%) patients, intermediate in 165 (29.7%), and high in 37 (6.6%).

Patients had EBCT performed before (n = 278 [50%]), the same day (n = 126 [22.7%]), and after (n = 152 [27.3%]) exercise echocardiography. Patients who underwent EBCT before compared with after exercise echocardiography had significantly higher CACS (183 ± 21 vs. 101 ± 29, p = 0.03), were more likely to be asymptomatic (64% vs. 53%, p = 0.02), and had lower WMSI (1.04 ± 0.01 vs. 1.16 ± 0.02, p < 0.001).

CACS and WMSI: correlation and distribution. Exercise echocardiograms showed abnormal wall motion in 98 (17.6%) patients; new exercise-induced regional wall motion abnormalities occurred in 80 (14.4%) of these. The percentage of wall segments abnormal at peak exercise averaged 5.8 ± 16.3% for the entire study population, 32.8 ± 25.1%

for the 98 patients with abnormal studies, and 35.3 ± 26.3% for the 80 patients with ischemia. In the patients with abnormal studies, exercise WMSI was 1.4 ± 0.4. In those with ischemia, exercise WMSI was 1.5 ± 0.4 and the change in WMSI from rest to stress was 0.27 ± 0.24. The overall correlation between EBCT CACS and exercise WMSI was poor (r = 0.17, p < 0.0001) but statistically significant. Patients with normal exercise WMSI (n = 458, 82.4%) had CACS ranging from 0 to 2,500 (median 10.1); patients with CACS = 0 (n = 172, 30.9%) had exercise WMSI ranging from 1 to 2.2 (median 1.0). The correlation between CACS and ΔWMSI was also weak (r = 0.13, p = 0.003).

Coronary artery vessel-specific analyses revealed that patients with any wall motion abnormality in the left anterior descending coronary artery distribution had a higher left anterior descending calcium score than patients with normal wall motion in this territory (198 vs. 109, p < 0.03). Similarly, patients with abnormal wall motion in the right coronary artery territory also had a significantly higher right coronary artery calcium score (87 vs. 50, p = 0.03). Similar analysis by circumflex territory revealed a nonsignificant trend (47 vs. 33, p = 0.06).

When patients were grouped according to CACS, the proportion of patients with abnormal exercise WMSI in-

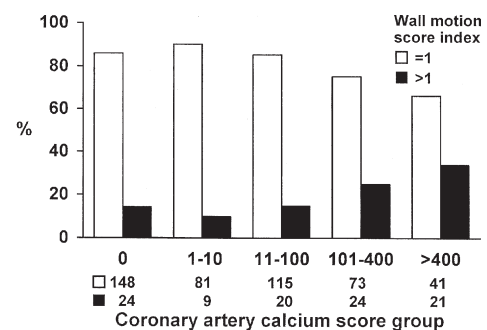


Figure 1. Distribution of exercise wall motion score index by calcium score.

Table 2. Predictors of Exercise WMSI >1

Variable	Univariate		Multivariate		
	Chi-Square	p Value	Chi-Square	p Value	Odds Ratio
Clinical variables					
Age (per 10-yr increase)	31.4	<0.001	19.6	<0.001	43.1
CACS (per 100-U increase)	20.0	<0.001	5.9	0.02	18.4
History of chest pain	3.0	0.08	4.8	0.03	1.7
Systemic hypertension	2.2	0.14			
Gender	2.0	0.15			
Smoking	1.2	0.27			
Diabetes mellitus	0.7	0.40			
Family history of premature CAD	0.2	0.70			
Exercise variables					
Exercise time (min)	26.6	<0.001			
Peak heart rate (beats/min)	14.6	<0.001			
Peak rate pressure product	6.2	0.013			
Functional aerobic capacity (%)	3.1	0.08			

CACS = coronary artery calcium score; CAD = coronary artery disease; WMSI = wall motion score index.

creased with increasing CACS severity (chi-square = 19.1, $p < 0.001$) (Fig. 1). The percentage of wall segments abnormal at peak exercise increased with increasing CACS group (chi-square = 6.1, $p < 0.001$), from $3.9 \pm 1.2\%$ for CACS = 0 to $13.7 \pm 2.0\%$ in patients with CACS >400. Exercise WMSI >1.25 (n = 48, 8.6%) was noted in 5.2% of patients with CACS = 0 versus 24.2% of patients with CACS >400 (chi-square = 15.5, $p < 0.001$). However, the majority of patients in each CACS group had normal exercise WMSI. Even in patients with severe CACS, 66% of patients had normal exercise WMSI.

Symptomatic versus asymptomatic patients. Compared with the 213 (38.3%) patients with chest pain, the 343 (61.7%) patients without chest pain had higher CACS (187 vs. 106, $p = 0.03$). In contrast, there was a nonsignificant trend toward a more abnormal exercise WMSI in patients with as opposed to those without chest pain (1.1 vs. 1.06, $p = 0.07$). In patients with chest pain, the correlation between CACS and exercise WMSI was limited ($r = 0.26$, $p < 0.0001$) but better than that for asymptomatic patients ($r = 0.11$, $p = 0.047$). The correlation between CACS and Δ WMSI was significant in patients with chest pain ($r = 0.21$, $p = 0.003$) but not in asymptomatic patients ($r = 0.09$, $p = 0.12$).

Association of clinical variables and CACS with abnormal WMSI. Univariate and multivariate predictors of abnormal exercise WMSI are shown in Table 2. All variables listed in Table 2 were considered potential predictors in a multivariate model. Only age, CACS, and presence of chest pain were independently associated with abnormal exercise WMSI.

In incremental analysis, the global chi-square value for all clinical risk variables forced into a multivariate model was 37.8 ($p < 0.001$) for prediction of abnormal WMSI. When the calcium score was added to this model, the predictive value was further enhanced (chi-square = 44.1, $p < 0.001$).

Follow-up and outcome events. During follow-up, 12 (2%) patients had events, including 7 with death and 5 with

nonfatal MI, 1 of whom died 11 months later. Five of the patients who died and 4 of the patients with nonfatal MI had a history of chest pain before EBCT and exercise echocardiography. Coronary revascularization was performed in 18 patients, including early (<3 months) revascularization in 9 patients (7.3 ± 8.6 days from date of testing) and revascularization after MI in 4 patients.

Mortality. None of the 172 patients with a zero CACS died during follow-up. Estimated 5-year mortality rates were 0.7% for a CACS ≤ 100 and 5.6% for a CACS >100 (chi-square = 2.7, $p = 0.10$).

The difference in event-free survival curves for death between patients with normal and those with abnormal exercise WMSI approached but did not achieve statistical significance (chi-square = 3.6, $p = 0.06$). Estimated 5-year event rate for mortality was 2.0% for normal exercise WMSI compared with 3.1% for abnormal exercise WMSI.

Combined events. The occurrence of death/MI was significantly different in patients with a CACS ≤ 100 versus a CACS >100 (chi-square = 5.5, $p = 0.02$) (Fig. 2) but not in patients with normal exercise WMSI versus abnormal exercise WMSI (chi-square = 1.9, $p = 0.17$). The estimated 5-year event rate for patients with a CACS

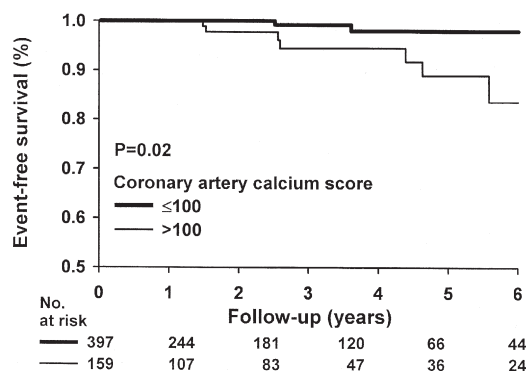


Figure 2. Survival free of death/myocardial infarction stratified by coronary artery calcium score.

Table 3. Univariate Predictors of Death and Combined End Point

Variable	Death			Death/MI		
	RR	95% CI	p Value	RR	95% CI	p Value
WMSI (per 1-U increase)	4.2	1.3–12.4	0.022	3.7	1.2–9.4	0.023
Age (per 10-yr increase)	2.1	1.1–4.2	0.028	1.9	1.1–3.6	0.019
Exercise time (per min)	0.8	0.6–1.0	0.056	0.8	0.7–1.0	0.075
Family history of premature CAD	0.3	0.0–1.3	0.115	0.9	0.3–2.8	0.860
History of chest pain	2.7	0.6–18.4	0.206	3.3	1.0–15.1	0.052
Diabetes mellitus	3.1	0.5–13.7	0.208	1.3	0.2–5.0	0.750
Smoking	0.5	0.1–2.2	0.363	0.8	0.2–2.4	0.632
CACS (per 100-U increase)	1.1	0.9–1.2	0.469	1.1	1.0–1.1	0.226
Gender	1.7	0.4–11.5	0.509	1.4	0.4–5.3	0.575
Systemic hypertension	0.9	0.2–3.6	0.861	1.3	0.4–4.3	0.610

CI = confidence interval; MI = myocardial infarction; RR = risk ratio; other abbreviations as in Table 2.

≤100 was 1.9% compared with 11.0% for patients with a CACS >100.

Prognostic value of combining CACS and WMSI. Patients with a CACS >100 and exercise WMSI >1 were more than 4 times more likely to have death/nonfatal MI at 5 years when compared with patients with a CACS ≤100 and normal exercise WMSI. Estimated 5-year event-free survival curves were significantly different (chi-square = 5.4, $p = 0.02$). In patients with normal WMSI, moderate to severe calcium scores conferred a higher probability of events compared with patients with lower scores (chi-square = 10.0, $p = 0.002$). When patients with abnormal exercise WMSI were dichotomized by CACS, the difference in event-free curves was not statistically significant (chi-square = 0.16, $p = 0.69$).

Predictors of events. Clinical variables associated with death and the combined end point of death/MI are shown in Table 3. Whereas exercise WMSI was strongly related to death (risk ratio [RR] 3.7, 95% confidence interval [CI] 1.2 to 9.4, $p = 0.023$) and to combined events (RR 2.8, 95% CI 1.2 to 6.1, $p = 0.025$), CACS was not associated with either end point.

Among the variables considered in Table 3 as potential predictors in a multivariate model, only exercise WMSI (RR 3.9/1-unit increase, 95% CI 1.1 to 8.9, $p = 0.04$) remained independently associated with the combined end point of death/MI, even after adjusting for CACS.

DISCUSSION

This study of 556 primarily asymptomatic patients demonstrates that EBCT CACS has statistically significant but limited correlation with exercise WMSI as determined by exercise echocardiography ($r = 0.17$, $p < 0.0001$). The correlation was better ($r = 0.26$) in the subgroup with chest pain. The proportion of patients with abnormal exercise WMSI tended to increase with increasing CACS, but even in patients with a severe CACS, the majority of patients had a normal WMSI. Symptoms, age, and CACS were independently associated with abnormal exercise WMSI. In addition, in this population in which event rates were low, exercise WMSI but not CACS was independently associated with the end point of death or MI.

The limited correlation of CACS and exercise WMSI is not an unexpected finding. Coronary artery calcium score provides detail on the anatomical presence of coronary calcification that might or might not coexist with hemodynamically significant, flow-limiting stenosis. Two-thirds of patients with a severe CACS had normal exercise WMSI. In patients with normal exercise WMSI, 25% of patients had a CACS >100 and 9% of patients had a severe CACS. Such findings might be viewed as complementary rather than as discrepant results. In such patients, although stress echocardiography indicates that ischemia-provoking lesions are likely not present, the CACS derived by EBCT suggests significant atherosclerosis that might necessitate additional risk factor modification.

Clinical variables and CACS were independently associated with abnormal WMSI. Coronary artery calcium score remained independently predictive of WMSI >1 even when added to a global model of all clinical risk variables.

Event-free survival curves for patients with moderate to severe CACS versus patients with CACS ≤100 demonstrated a significant divergence in the first 5 years of follow-up. At 5 years of follow-up, patients with a CACS >100 were more than 5 times more likely to experience a combined event compared with patients with a CACS ≤100 (11.0% vs. 1.9%). However, in a multivariate analysis in which clinical variables were included, WMSI but not CACS was related to death and combined events.

Previous studies. To our knowledge, no previous studies have investigated the relationship between calcium scores on EBCT and exercise WMSI on stress echocardiography. Three studies have examined the association between EBCT calcium scores and findings on stress nuclear single-photon emission computed tomography (SPECT) (13–15). Analogous to our study with exercise echocardiography, in general, these studies have all demonstrated that higher calcium scores are associated with increased severity of stress-induced ischemia on stress SPECT, but the majority of patients with a positive CACS had normal SPECT.

Previous studies have evaluated the prognostic power of EBCT or exercise echocardiography, but no previous study has evaluated both techniques. A few large prospective

studies have assessed EBCT in relation to cardiac risk factors with respect to death and cardiovascular outcomes in asymptomatic subjects (1,16-19). Detrano et al. (16) studied 1,196 asymptomatic, high-risk patients and found that EBCT CACS did not provide incremental prognostic information beyond risk-factor assessment with respect to cardiac death/MI. However, Shaw et al. (17) demonstrated that CACS did provide incremental prognostic information with respect to all-cause mortality (receiver-operating characteristic curve for risk factors 0.72 vs. 0.78 with addition of CACS, $p < 0.001$). Kondos et al. (18) found that CACS was incrementally predictive for death/MI/revascularization. In a study of over 1,300 patients, Greenland et al. (1) demonstrated that CACS provided incremental prognostic information when added to the Framingham risk score, except in patients at low risk for cardiac events.

Exercise echocardiography has been validated in multiple prognostic studies with respect to cardiovascular outcomes (7,20-23). McCully et al. (7) reported a 2.6% event rate at 3 years for cardiac death/MI/coronary revascularization in patients with normal exercise echocardiography. In a study of 2,632 patients ≥ 65 years of age, Arruda et al. (22) showed that exercise WMSI was independently associated with cardiac events (RR 2.78, $p = 0.001$) in a multivariate model that included clinical and exercise electrocardiographic variables. In a study of 1,618 low-risk patients, Elhendy et al. (20) found that exercise WMSI was independently associated with cardiac events (RR 2.1/0.5 units, $p = 0.003$) but noted that <one-half of patients with events were identified by abnormal stress echocardiography.

Study limitations. The study is limited by its retrospective design and selection bias. Patients underwent both techniques for clinical reasons, but the order of testing and reasons for referral varied by patient. Patients who had EBCT before stress echocardiography, as opposed to after, were more likely to be asymptomatic, had higher CACS, and lower WMSI. Quantitation of calcium on EBCT is subject to error (24), but consecutive EBCT scans for each patient had excellent reproducibility in our study ($r^2 = 0.96$, $p < 0.001$). Follow-up data were derived through review of our institution's medical record system, autopsy reports, and use of the Social Security Death Index. Events might be underestimated if patients had undocumented events or medical care with external providers. Lastly, in this predominantly asymptomatic patient group without known CAD, there were few events during follow-up. This precluded robust multivariate analysis with respect to the end point of death.

Conclusions. Although EBCT CACS and exercise echocardiography WMSI demonstrate limited correlation, these 2 techniques offer complementary information. Wall motion score index but not CACS was independently associated with the combined end point of death/MI. However, in this largely asymptomatic population, most patients with coronary artery calcification had a normal exercise echocardiogram and a low event rate during follow-up.

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