Usefulness of Electron Beam Computed Tomography Scanning for Distinguishing Ischemic From Nonischemic Cardiomyopathy

MATTHEW J. BUDOFF, MD, DAVID M. SHAVELLE, MD, DANIEL H. LAMONT, MD, H. TINA KIM, BS, PAMELA AKINWALE, JOHN M. KENNEDY, MD, BRUCE H. BRUNDAGE, MD, FACC

Torrance, California

Objectives. This study was undertaken to evaluate the ability of electron beam computed tomography (EBCT) to distinguish ischemic from nonischemic causes of cardiomyopathy by evaluating heart failure patients for coronary calcification (CC).

Background. The etiology of heart failure, whether coronary-induced or nonischemic, may be difficult to discern clinically. Differentiation of ischemic from nonischemic etiology is clinically important for both therapeutic and prognostic implications. With its ability to noninvasively discern and quantitate coronary artery calcification, EBCT correlates well with angiographic stenosis and thus may be useful in differentiating ischemic and nonischemic cardiomyopathies.

Methods. One hundred and twenty-five patients with cardiomyopathy (ejection fraction <0.40) and known coronary anatomy underwent EBCT coronary scanning to evaluate for CCs within 3 months of coronary angiography.

Results. Of the 72 patients who were found to have ischemic cardiomyopathy, 71 patients had CC by EBCT (sensitivity 99%, p < 0.001), mean score 798 ± 899. In comparison, among the 53 patients without significant coronary artery disease (CAD) (nonischemic cardiomyopathy), the mean score was significantly lower (17 ± 51; p < 0.0001), and 44 patients had a CC score of 0 (no CC present). The specificity of EBCT to exclude CAD in patients with cardiomyopathy was 83%, using a threshold CC score of 0, and 92% for scores <80 (p < 0.001). Overall accuracy for determining the etiology of cardiomyopathy (differentiating ischemic from nonischemic) was 92% for this technique.

Conclusions. This prospective, blinded study indicates that EBCT detected CC accurately and can noninvasively distinguish between cardiomyopathy because of CAD and nonischemic causes of left ventricular dysfunction.

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The etiology of heart failure, whether coronary-induced or nonischemic, may be difficult to discern clinically. Patients with dilated cardiomyopathy (DC) may have chest pain or electrocardiographic changes suggestive of coronary artery disease (CAD), and patients with CAD-induced congestive heart failure may present without angina or evidence of ischemia or infarction (1–4). Differentiation of ischemic from nonischemic etiology has both therapeutic and prognostic implications (5,6). Because ischemic cardiomyopathy (IC) has the potential for revascularization and thus improvement of the heart failure, the etiology of the heart failure is often sought.

Clinicians have sought a noninvasive method to discern those patients who are more likely to have obstructive CAD. Regional wall motion abnormalities, as seen by radionuclide angiography or two-dimensional echocardiography, were thought to be specific to coronary-induced areas of myocardial infarction (7). However, these regional abnormalities have been recognized as occurring in patients with nonischemic cardiomyopathy as well (8,9). Two-dimensional echocardiography, in combination with Doppler and color flow imaging, although commonly used by clinicians, has failed in some studies to differentiate patients with DC from those with IC (10,11). Studies report that up to two-thirds of patients with nonischemic cardiomyopathy have regional wall motion abnormalities at rest (9,12). Because of limitations of the noninvasive tests, coronary angiography, with increased risk in these patients, is frequently undertaken (13,14).

In 1959, Blankenhorn and Stern (15) reported an association between coronary calcification (CC) and coronary atherosclerosis at autopsy (15). Since that time, multiple histology studies have demonstrated a strong correlation between the presence of coronary calcium and obstructive CAD (16–19). Electron beam computed tomography (EBCT), by acquiring x-ray images of the coronary arteries, detects the presence of coronary calcium, which is invariably an indicator of intimal atherosclerosis (20). With its ability to noninvasively discern and quantitate coronary artery calcification, EBCT correlates well with angiographic stenosis (21), and has been used to diagnose patients with obstructive CAD with high sensitivities (Fig. 1) (22,23).
to evaluate the ability of EBCT to distinguish ischemic from nonischemic causes of cardiomyopathy.

**Methods**

**Patient population.** The study group consisted of 125 patients with cardiomyopathy and known coronary anatomy who underwent EBCT scanning to assess this technique. Inclusion criteria were: 1) a ventricular ejection fraction <0.40; 2) underwent coronary catheterization for evaluation of the etiology of heart failure; and 3) underwent EBCT coronary scanning to evaluate for the presence and amount of CC within 3 months of angiography. All patients were New York Heart Association functional class II to IV at the time of angiography. Patients whose EBCT scans were performed more than 3 months before or after the coronary angiogram were excluded from the study. All subjects signed a written consent form approved by the Institutional Review Board at Harbor-UCLA Medical Center.

**Electron beam computed tomography.** The EBCT studies were performed with an Imatron (South San Francisco, California) C-150 XL ultrafast computed tomographic scanner in the high-resolution volume mode using a 100-ms exposure time. Electrocardiographic triggering was used so that each image was obtained at the same point in diastole, corresponding to 80% of the RR interval for standardized calcium scoring (21). Coronary artery visualization was obtained without contrast medium injection, and 30 consecutive images were obtained at 3-mm intervals beginning 1 cm below the carina and progressing caudally to include the proximal and midcoronary arteries. Total radiation exposure using this technique was <1 rad per patient.

A CT threshold of 2 pixels and 130 Hounsfield units (Hu) was utilized for identification of a calcific lesion. Each focus exceeding the minimum criteria was scored using the algorithm developed by Agatston et al. (24), calculated by multiplying the lesion area by a density factor derived from the maximal Hounsfield unit within this area. The density factor was assigned in the following manner: 1 for lesions whose maximal density were 130 to 199 Hu, 2 for lesions 200 to 299 Hu, 3 for lesions 300 to 399 Hu and 4 for lesions >400 Hu. A total calcium score was determined by summing individual lesion scores from each of four anatomic sites (left main, left anterior descending, circumflex and right coronary arteries). The EBCT scoring was performed by a cardiologist blinded to the clinical, electrocardiographic and angiographic information.

**Angiographic protocol.** All patients underwent coronary angiography. Patients were referred for coronary angiography based upon the primary physicians’ concern for ischemia. Positive noninvasive stress testing, abnormal echocardiograms and clinical history were all used for referring patients for cardiac catheterization. The coronary angiograms were analyzed by an experienced reader blinded to the results of the EBCT coronary scan. Each epicardial coronary vessel (left main, left anterior descending, circumflex and right coronary artery) was assessed, and the visual estimation of the percent luminal reduction for each lesion was reported. Multiple projections were acquired to discern the maximal coronary artery luminal narrowing. The reader recorded the maximum stenosis in each vessel. Angiographic abnormalities were con-

**Abbreviations and Acronyms**

<table>
<thead>
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<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
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<td>CC</td>
<td>coronary calcification</td>
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<td>DC</td>
<td>dilated cardiomyopathy</td>
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<td>EBCT</td>
<td>electron beam computed tomography</td>
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<td>Hu</td>
<td>Hounsfield unit</td>
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<td>IC</td>
<td>ischemic cardiomyopathy</td>
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<td>LBBB</td>
<td>left bundle branch block</td>
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Figure 1. Electron beam CT coronary scan of a 48-year-old man with IC with three-vessel obstructive CAD on catheterization. Extensive calcifications of the left main, left anterior descending (LAD) and circumflex artery are seen. The total score of this patient was 1,295.
sidered significant if ≥50% luminal diameter stenosis was found in any vessel.

Classification of cardiomyopathy. Classification of the etiology of left ventricular dysfunction was based entirely on arteriographic findings. Patients were considered to have a cardiomyopathy secondary to CAD if a significant stenosis (≥50% luminal artery stenosis) was present in one or more major coronary arteries with a wall motion abnormality in the dependent myocardial territory. Conversely, patients were considered to have DC if coronary angiography failed to reveal significant CAD.

Statistical analysis. All values are reported as mean ± SD. Data were analyzed using chi-square and Fisher exact test for comparing categorical variables. All tests of significance were two-tailed, and significance was defined at the 0.05 level or below.

Results

Patients had a mean age of 55 years (range 23 to 74) and all had history of congestive heart failure class II to IV prior to angiography. By coronary angiographic criteria, 72 patients had IC and 53 had DC. Of the patients with IC, 12 had single-vessel disease, 25 had double-vessel disease and 35 had triple-vessel disease. In 62 patients, CAD involved the left anterior descending artery, the left circumflex artery in 54 patients and the right coronary artery in 51 patients; 3 patients had significant disease of the left main coronary artery.

Fifty-three patients had no obstructive CAD on angiography and were classified as DC. The etiology of the heart failure in the patients without obstructive coronary artery disease was as follows: 30 had idiopathic DC, 7 had alcoholic cardiomyopathy, 6 had significant valvular disease, 6 had hypertensive cardiomyopathy and 4 had congenital heart disease (atrial or ventricular septal defects). The prevalence of hypertension was 68% in those persons with documented obstructive CAD on angiography (ischemic group). There was no congenital heart disease or significant valvular disease in the ischemic group.

Mean age of the patients with DC was 51 ± 12 years versus 58 ± 12 years in patients with CAD (p = 0.005). The mean left ventricular ejection fraction averaged 31 ± 9% in patients with DC and 33 ± 8% in patients with CAD (p = NS). Clinical variables are outlined in Table 1.

EBCT results. Significant CAD (≥50% obstruction in ≥1 coronary artery) was found in 72 patients. Of these 72 patients with IC, 71 patients had CC by EBCT (sensitivity 99%, p < 0.001), mean score 798 ± 899 (see Fig. 1). Of the 53 patients without significant CAD, 44 had a CC score of zero. The mean score for patients without significant CAD (nonischemic cardiomyopathy) was 17 ± 51, significantly less than patients with cardiomyopathy because of CAD (p < 0.0001). The specificity of EBCT to exclude CAD in patients with cardiomyopathy was 83% using a threshold CC score of 0 and 92% for scores ≥80 (p < 0.001). A receiver operating characteristic curve was created to determine the predictive power of the EBCT score for obstructive CAD as a function of the minimum score required to define a positive study. Table 2 displays the

| Table 1. Clinical Characteristics in Patients With Dilated Ischemic Cardiomyopathy |
|-------------------------------|------------------|-------------------|
|                                | Dilated Cardiomyopathy (n = 53) | Ischemic Cardiomyopathy (n = 72) | p Value |
| Age (yrs)                      | 51 ± 12           | 58 ± 10           | 0.005   |
| LVEF (%)                       | 31 ± 9            | 33 ± 8            | NS      |
| Men/women                      | 29/24             | 52/20             | 0.04    |
| Median Score                   |                   |                   |
| Men                            | 476               | 0                 | NS (men vs. women) |
| Women                          | 510               | 0                 |         |
| Percent with CC                |                   |                   |
| Men                            | 83%               | 98%               | NS (men vs. women) |
| Women                          | 83%               | 100%              |         |
| Coronary score (Agatston method) | 17 ± 51           | 797 ± 899         | <0.0001 |

Values are mean ± SD. CC = coronary calcification; LVEF = left ventricular ejection fraction by angiographic ventriculography; NS = not significant.

| Table 2. Cut Points for Electron Beam Computed Tomographic Coronary Calcium Scores for Differentiating Ischemic and Nonischemic Cardiomyopathy |
|-------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| EBCT CC Score Cut Points      | Sensitivity (%)   | Specificity (%)   | Positive Predictive Value (%) | Negative Predictive Value (%) | Accuracy (%) |
| ≥0                             | 99                | 83                | 89                  | 98                  | 92               |
| ≥50                            | 92                | 91                | 93                  | 89                  | 91               |
| ≥80                            | 90                | 92                | 94                  | 88                  | 91               |
| >220                           | 72                | 100               | 100                 | 73                  | 84               |

CC = coronary calcification; EBCT = electron beam computed tomography.
sensitivity, specificity and accuracy for a variety of cutpoints for EBCT score.

Overall accuracy for determining the etiology of cardiomyopathy (differentiating ischemic from nonischemic) was 92% for this technique. There were no significant differences among median values, prevalence of calcification, sensitivities or specificities in men and women in this study. Positive predictive value was 89% and negative predictive value (for a negative test having no obstructive CAD) was 98% in this population. The mean calcium scores ($\pm$SD) for each level of angiographic stenosis are outlined in Figure 2.

In addition to higher EBCT scores, the number of calcified vessels also predicted with higher specificities those patients with heart failure of ischemic etiology. Patients with calcium present in two or more coronary arteries (counting left main, anterior descending, circumflex and right coronary as separate arteries) had an overall specificity of 87%, with a sensitivity of 92%. No patients with DC had calcification in all four coronary vessels (100% specific for IC in this study).

**Discussion**

The incidence and prevalence of cardiomyopathy appear to be increasing (25). The CASS study (26) and PRAISE trial (27) have demonstrated that the treatment benefit may vary with the etiology of the heart failure. Various noninvasive imaging modalities have been investigated in an effort to find an accurate and cost-effective method for distinguishing IC from nonischemic DC. This is of paramount importance in persons presenting with heart failure, as revascularization is one of the few interventions demonstrated to significantly reduce mortality. Left ventricular dysfunction secondary to CAD needs to be identified with high sensitivity so revascularization can be considered in these patients. One traditional approach to screening patients at risk for coronary events is the use of exercise testing. However, cardiomyopathy patients often have reduced exercise capacity (28) and abnormal electrocardiograms (29), requiring a more expensive imaging modality. Up to 60% of patients with severe cardiomyopathy have left bundle branch block (LBBB) (11), which can mask the evidence of previous infarction and make the interpretation of electrocardiographic changes with exercise testing (without imaging) impossible (10). Noninvasive imaging exercise techniques such as thallium-201 myocardial scintigraphy and exercise echocardiography have been used to try to distinguish IC from DC with variable success; however, reduced exercise capacity (28), reduced coronary flow reserve (30,31) and LBBB (29) have all led to increased false positive results and reduced specificity for both nuclear and echocardiographic stress tests. These tests have further reduced specificity and predictive values with increasing left ventricular dysfunction (32,33). Dobutamine (34) stress tests have been used; however, there is an increased incidence of ventricular arrhythmias (12) and these tests are less diagnostic in cases with LBBB (29). Dipyridamole-thallium-201 (28,35) and positron emission tomography (36) both have less side effects and accuracy up to 90% in differentiating cardiomyopathies; however, both require intravenous injections and are both time consuming and quite costly, especially compared to EBCT ($375 to $400 per study, total patient time less than 5 min).

Electron beam computed tomography, with its ability to distinguish and quantify calcium in the coronary arteries, has been used to diagnose those patients with obstructive CAD with high sensitivities. Electron beam CT is an imaging technique that allows rapid, accurate, noninvasive identification and quantification of coronary artery calcium, a marker of atherosclerosis. Electron beam CT-detected CC has been compared to angiography and demonstrated sensitivities for obstructive CAD ranging from 88 to 100% (18–21). With high sensitivities for disease, a negative test has a low probability of being associated with obstructive CAD, with negative predictive values approaching 100% in many studies. This rapid image acquisition avoids the artifacts resulting from the motion of the heart and allows very small calcium deposits on the epicardial coronary arteries to be seen. The presence of calcium in the coronary arteries, especially in multiple arteries.
or in large quantity, implies an ischemic etiology to the cardiomyopathy with high accuracy in this study. Although a significant portion of the population will have some coronary calcium, the quantification can help further distinguish the two similar clinical entities. Utilization of a lower EBCT score (i.e., zero) would impart a higher sensitivity and negative predictive value for CAD, thus allowing the vast majority of patients with significant disease to undergo revascularization. The power of a negative test would be maximized, and receiver operating characteristic curve analysis demonstrates the highest area under the curve for scores > 0. Higher specificities can be obtained with higher EBCT score cut points (Table 2).

The other intrinsic advantages of EBCT coronary scanning is that there is no need for exercise or intravenous catheters, it is not dependent upon concurrent medications or electrocardiographic findings and has no reported adverse side effects.

**Study limitations.** This is a single-center experience involving patients referred for angiography for evaluation of heart failure. Differentiation of ischemic from nonischemic DC solely on the basis of angiographic criteria is not entirely precise. Cardiomyopathy of unknown cause may coexist with CAD, so that the CAD may not be the cause of ventricular dysfunction (37). Conversely, myocardial infarctions can occur at a site with nonobstructive CAD (at locations with <50% stenosis by angiography) (38), or secondary to spasm, cocaine, emboli, etc. Many of the ischemic patients had hypertension, a potential cause of nonischemic cardiomyopathy. The three patients in this study that had nonobstructive CAD on angiography were classified as DC (because of angiographic criteria for etiology); however, autopsy study of patients can confirm the exact etiology of cardiomyopathy. In this study, all three patients with nonobstructive CAD had coronary calcium by EBCT. Although the “true” etiology of heart failure might never be known, EBCT allows for precise identification of those patients with obstruction on angiography who potentially might benefit from revascularization.

**Conclusions.** Electron beam CT has achieved a substantial degree of standardization and ease of implementation sufficient to make it applicable to wide populations in the evaluation of cardiomyopathies. Electron beam CT, an inexpensive and fast technique, can potentially help obviate the need for invasive coronary angiography in patients in whom the clinical etiology of the cardiomyopathy is not apparent. This prospective, blinded study indicates that EBCT detected CC accurately, and noninvasively distinguished between cardiomyopathy because of CAD and nonischemic causes of left ventricular dysfunction in this study. Cost-effectiveness modeling with this modality needs to be performed before widespread use of this clinical tool can be warranted.

**References**


