Multislice Computed Tomography in an Asymptomatic High-Risk Population

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Approximately 50% of all acute coronary syndromes occur in previously asymptomatic patients. This study evaluated the value of multislice computed tomography for early detection of significant coronary artery disease (CAD) in high-risk asymptomatic subjects. One hundred sixty-eight asymptomatic subjects with ≥1 major risk factor (hypertension, diabetes, hypercholesterolemia, family history, or smoking) and an inconclusive or unfeasible noninvasive stress test result (stress electrocardiography, echocardiography, or nuclear scintigraphy) were evaluated in an outpatient setting. After clinical examination and laboratory risk analysis, all patients underwent multislice computed tomographic (MSCT) coronary angiography within 1 week. In all subjects, conventional coronary angiography was also carried out. Multislice computed tomography displayed single-vessel CAD in 16% of patients, 2-vessel CAD in 7%, and 3-vessel CAD in 4%. Selective coronary angiography confirmed the results of multislice computed tomography in 99% of all patients. Sensitivity and specificity of MSCT coronary angiography were 100% and 98%, respectively, with a positive predictive value of 95% and a negative predictive value of 100%. In conclusion, MSCT coronary angiography is an excellent noninvasive technique for early identification of significant CAD in high-risk asymptomatic patients with inconclusive or unfeasible noninvasive stress test results. **(Am J Cardiol 2007; 99:325–328)**

Multislice computed tomographic (MSCT) coronary angiography is a relatively new noninvasive technique to define coronary artery disease (CAD). It is considered 1 of the most significant advances in cardiac imaging technology. Previous studies in symptomatic patients have reported an excellent sensitivity and specificity and negative predictive value of multislice computed tomography,[1–5] much better than those of other noninvasive tests, such as exercise electrocardiography and thallium scintigraphy.[6–9] However, there are no data available on the extent and severity of CAD in a high-risk asymptomatic population, particularly by noninvasive means. We postulated that multislice computed tomography, if accurate, could be used as a potent noninvasive diagnostic tool to manage patients at high risk for coronary atherosclerosis.[10,11] This study evaluated the value of multislice computed tomography for early detection of significant CAD in asymptomatic subjects with conventional CAD risk factors and inconclusive or unfeasible noninvasive stress test results.

Methods

Patient population: We enrolled 168 consecutive asymptomatic subjects from June 2004 to April 2005 (89 men, 27 women; mean age 60 ± 7 years, range 36 to 70) who were evaluated in a primary prevention program in an outpatient setting. All subjects were evaluated with clinical examination and laboratory risk analysis. Criteria for inclusion in this study were an age <70 years, absence of a previous diagnosis or symptoms of CAD (such as chest pain), presence of ≥1 CAD risk factor, and an inconclusive or unfeasible stress test result (stress electrocardiography, echocardiography, or nuclear scintigraphy). Diagnosis of diabetes was based on criteria of the American Diabetes Association, i.e., symptoms of diabetes plus random plasma glucose concentration ≥200 mg/dl (11.1 mmol/L) or fasting plasma glucose level ≥126 mg/dl (7.0 mmol/L). Hypertension was defined according to the classification of the American Heart Association. Hypercholesterolemia was defined as a serum total cholesterol level >200 mg/dl and a low-density lipoprotein cholesterol level >100 mg/dl. Smoking was defined as current use of ≥5 cigarettes a day. Family history was defined as having first- or second-degree relatives with premature CAD. Exclusion criteria were presence of arrhythmias, renal insufficiency (serum creatinine >120 mmol/L), known contraindication to iodinated contrast agent, severe claustrophobia, and pregnancy.

In all patients, MSCT coronary angiography was performed within 1 week of outpatient evaluation. Conventional coronary angiography was performed within 1 month of multislice computed tomography. Plasma lipid and C-reactive protein (as a marker of inflammation) levels were measured by the hospital clinical laboratory. Informed con-

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sent was obtained from all patients. The study protocol was approved by the local ethics committee.

MSCT coronary angiographic protocol: Multislice computed tomography was performed with a General Electric LightSpeed-16 scanner (GE Healthcare, Chalfont St. Giles, United Kingdom) as previously described.[4] Electrocardiography was digitized and recorded continuously in all patients. Patients with a heart rate >60 beats/min received 100 mg of metoprolol 1 hour before the MSCT scan. Mean heart rate during multislice computed tomography was 59 ± 6 beats/min (range 53 to 69). Patients were instructed to hold their breath during the scan. First, a noncontrast localization scan was performed that yielded an anteroposterior view of the chest; this allowed us to position the imaging volume, which extended from the distal tract of the ascending aorta to the inferior border of the heart. The volume dataset was acquired in spiral mode with simultaneous acquisition of 16 parallel slices with collimation of 16 × 0.625 mm. Gantry rotation time was 500 ms, peak tube voltage was 140 kV, tube current was 10 to 440 mA in 5-mA increments, and table feed averaged 2.9 mm/rotation. A nonionic, low-osmolality contrast agent (120 ml; Iopamiro 370, Bracco S.P.A., Milan, Italy) was injected (4 ml/s) as a single injection.

Total amount of calcium in the coronary tree was quantified using SmartScorePro (GE Healthcare) according to a scoring system originally developed by Agatston et al[12] for electron beam computed tomography (Agatston score equivalent).

Image reconstruction: Electrocardiographically gated image reconstruction was done with a desktop environment (ImageWork, General Electric). We used 2 reconstruction algorithms depending on heart rate. If heart rate was <60 beats/min, a single sector for image reconstruction was used with a temporal resolution of 250 ms; if heart rate was 60 to 70 beats/min, 2 sectors for image reconstruction were used with a temporal resolution of 125 ms. Transaxial images were reconstructed with a slice thickness of 0.625 mm at 0.4-mm increments, thus optimizing the position of the reconstruction window by an increment or a decrement of 10% in a range of 40% to 80%. The image dataset was transferred to a dedicated work station (Advantage Window 4.1, General Electric) for postprocessing.

Depending on vessel morphology and quality of data, several postprocessing techniques were applied to assess arterial and venous conduits. These included thin-slab, maximum intensity projection, reconstruction of multiple curved cross sections, vessel tracking, and 3-dimensional volume rendering.

MSCT data analysis: Two radiologists and 2 cardiologists experienced in MSCT coronary angiography independently evaluated the images. In a patient-based analysis, stenosis assessment was performed using a modified American Heart Association/American College of Cardiology segmentation model.[4] Only side branches ≥1.5 mm diameter were evaluated. Each segment was first evaluated as interpretable or not. Subsequently, the presence of significant narrowing (≥50% decrease in lumen diameter) was determined in assessable segments. We evaluated patients as having no significant stenosis or 1-, 2-, or 3-vessel CAD. Further, the patient population was divided into subgroups on the basis of the number of associated CAD risk factors.

Table 1
Comparison between multislice computed tomography and coronary angiography

No. of Narrowed Coronary Arteries (by MSCT)	No. of Coronary Arteries With ≥50% Narrowing (by coronary angiography)				
	0	1	2	3	Total
Normal	123	0	0	0	123
1	2	23	1	0	26
2	0	0	11	1	12
3	0	1	0	6	7
Total	125	24	12	7	168

MSCT = multislice computed tomography.

Selective coronary angiography: In all subjects, conventional coronary angiography was carried out using Philips Integris 5000 equipment (Medical Philips System, Best, The Netherlands). Vascular access was obtained using the femoral approach. Coronary angiograms were evaluated by an experienced angiographer and coronary vessel segments were classified as for MSCT coronary angiography. Quantitative coronary analysis was performed offline by a resident MPS (Medical Philips System) program using the catheter tip for calibration. Stenoses were quantified only in vessels >1.5 mm in diameter. A decrease in diameter >50% was defined as a significant stenosis.

Statistical analysis: A patient-based analysis was performed. MSCT data were considered correct in the individual patient analysis if ≥1 significant stenosis was detected on MSCT images or if multislice computed tomography ruled out the presence of any significant stenoses. Normally distributed data were reported as mean ± SD and categorical variables were expressed as number and percentage of the cohort. Bivariate correlation was performed with Spearman's ρ. All analyses were performed using SPSS 13 (SPSS, Inc., Chicago, Illinois). All analyses were 2-tailed, and statistical significance was set at a p value <0.05.

Results

Multislice computed tomography showed no significant CAD in 73% of patients but identified significant 1-vessel disease in 16% of patients, 2-vessel disease in 7%, and 3-vessel disease in 4%. Four patients had significant left main CAD, and these patients were classified as having 2-vessel disease. Disease in the proximal left anterior descending coronary artery was identified in 5 patients (3%).

Selective coronary angiography confirmed the results of multislice computed tomography in 99% of all patients and confirmed the extent of disease correctly in 97% of patients (Table 1). Two patients with 1-vessel CAD detected by multislice computed tomography were shown not to have significant CAD by selective coronary angiography. Another patient with 1-vessel CAD on multislice computed tomography was found to have 2-vessel CAD on selective coronary angiography. One patient with 2-vessel CAD de-

Table 2
Comparison of type 2 diabetics and nondiabetics

No. of Narrowed Coronary Arteries	Multislice Computed Tomography		Coronary Angiography	
	NG (n = 68)	T2DM (n = 100)	NG (n = 68)	T2DM (n = 100)
0	86.8%	64.0%	86.8%	66.0%
1	10.3%	19.0%	11.5%	16.0%
2	1.5%	11.0%	0%	12.0%
3	1.5%	60%	1.5%	6.0%

NG = normoglycemia; T2DM = type 2 diabetes.

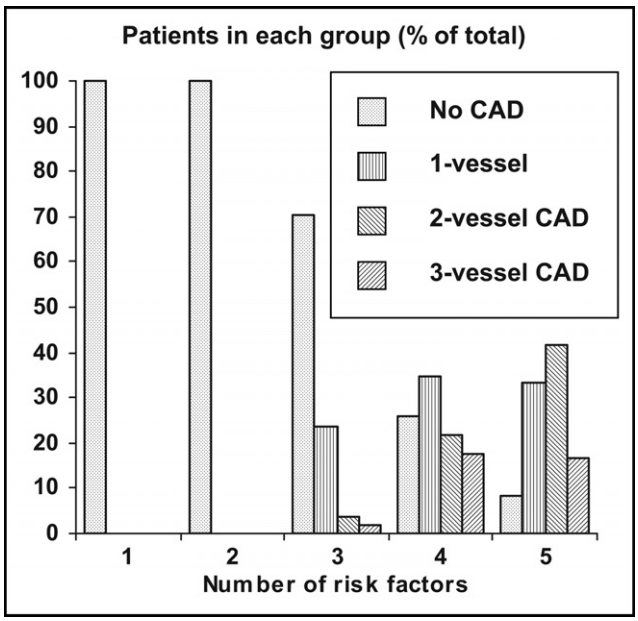

Figure 1. Correlation between numbers of risk factors and extent of CAD (Spearman $\rho = 0.66$, $p < 0.01$).

tected by multislice computed tomography was found to have 3-vessel CAD by coronary angiography, and 1 patient with 3-vessel disease on multislice computed tomography was shown to have 1-vessel CAD by coronary angiography.

In patients with type 2 diabetes mellitus (n = 100), multislice computed tomography identified 19 patients with 1-vessel CAD, 11 with 2-vessel CAD, and 6 with 3-vessel CAD (Table 2). In all but 2 patients with 1-vessel disease, the presence of CAD was confirmed by selective coronary angiography. One patient with 1-vessel CAD by multislice computed tomography was shown to have 2-vessel CAD by coronary angiography. All patients with type 2 diabetes mellitus with 3-vessel CAD on multislice computed tomography were confirmed to have 3-vessel CAD by coronary angiography.

Overall, MSCT angiography had a sensitivity of 100% and specificity of 98% with a positive predictive value of 95% and a negative predictive value of 100% for the diagnosis of CAD.

Thirty-nine patients with significant CAD by coronary angiography underwent myocardial revascularization (coronary artery bypass surgery in 12 patients and percutaneous transluminal coronary angioplasty in 27 patients). Four patients were treated with medical therapy alone.

A strong correlation between conventional CAD risk factors and number of diseased vessels was evident (Figure 1). Procam and Framingham scores correlated with number of diseased vessels. No correlation was found between coronary calcium score or C-reactive protein and extent of CAD (data not shown).

Discussion

It is common experience that conventional stress tests, such as exercise electrocardiography, stress echocardiography, and nuclear scintigraphy, are often not feasible or equivocal. For these reasons, we examined the value of MSCT angiography in this patient population.

This study shows that multislice computed tomography can define significant CAD in high-risk asymptomatic patients with CAD risk factors and an inconclusive or unfeasible stress test result by noninvasive means. Overall accuracy of defining significant coronary lesions, with selective coronary angiography as the reference, was extremely high. Further, multislice computed tomography accurately diagnosed the presence of CAD in 100% of patients.

Multislice computed tomography provides data on the presence or absence of CAD accurately and noninvasively in a symptomatic population.[3–9,13] Ropers et al[5] showed sensitivity and specificity of 91% and 93%, respectively, of MSCT technology. Nieman et al[13] reported a somewhat higher sensitivity and a lower specificity with a negative predictive value of 97%. A previous study from our group[4] showed a negative predictive value of 98%. Schuijf et al[14,15] found a 97% negative predictive value of multislice computed tomography in symptomatic hypertensive and diabetic patients.

We found a significant correlation of traditional risk factors with the presence of CAD. We also established that multiple traditional risk factors have a cumulative or synergistic effect on the development of coronary atherosclerosis. It was heartening to see that the time-tested conventional risk factors correlated with the presence of coronary atherosclerosis even when the patients were asymptomatic.

We also found a significant correlation between Procam and Framingham risk scores and extent of CAD. However, risk-prediction algorithms derived from large epidemiologic studies only yield a statistical probability of the presence of coronary atherosclerosis. Use of multislice computed tomography permits visualization of the coronary artery, quantification of CAD, and a certain diagnosis. The introduction of data from the noninvasive MSCT technology into the CAD risk score has the potential to provide a new algorithm for risk stratification based on actual anatomy beyond just a statistical probability.

A special comment needs to be made about the diabetic population. The American Heart Association/American College of Cardiology guidelines stress the need to treat diabetic patients as equivalent to patients with CAD.[16] We observed that 36 of 100 asymptomatic diabetic patients had significant CAD; importantly, 17 of these had 2- or 3-vessel CAD.

Studies in larger patient cohorts may be needed to con-

firm these data in this high-risk population. Radiation exposure remains a limitation of the widespread use of multislice computed tomography. Patients are exposed to a relatively large amount of radiation during multislice computed tomography because of continuous x-ray exposure and overlapping data acquisition at a slow spiral feed. Newer MSCT scanners using an electrocardiographically gated dose modulation software will decrease radiation emission by almost 50% and decrease the need for strict heart rate control.

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