Predictive Value of 16-Slice Multidetector Spiral Computed Tomography to Detect Significant Obstructive Coronary Artery Disease in Patients at High Risk for Coronary Artery Disease

Patient- Versus Segment-Based Analysis

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Background—In this study, we investigated the diagnostic value and limitations of multidetector computed tomography (MDCT)–based noninvasive detection of significant obstructive coronary artery disease (CAD) in a consecutive high-risk patient population with inclusion of all coronary segments.

Methods and Results—In a prospective, blinded, standard cross-sectional technology assessment, a cohort of 33 consecutive patients with a positive stress test result underwent 16-slice MDCT and selective coronary angiography for the detection of significant obstructive CAD. We assessed the diagnostic accuracy of MDCT in a segment-based and a patient-based model and determined the impact of stenosis location and the presence of calcification on diagnostic accuracy in both models. Analysis of all 530 coronary segments demonstrated moderate sensitivity (63%) and excellent specificity (96%) with a moderate positive predictive value of 64% and an excellent negative predictive value (NPV) of 96% for the detection of significant coronary stenoses. Assessment restricted to either proximal coronary segments or segments with excellent image quality (83% of all segments) led to an increase in sensitivity (70% and 82%, respectively), and high specificities were maintained (94% and 93%, respectively). In a patient-based model, the NPV of MDCT for significant CAD was limited to 75%. Coronary calcification was the major cause of false-positive findings (94%).

Conclusions—For all coronary segments included, 16-slice MDCT has moderate diagnostic value for the detection of significant obstructive coronary artery stenosis in a population with a high prevalence of CAD. The moderate NPV of patient-based detection of CAD suggests a limited impact on clinical decision-making in high-risk populations. (Circulation. 2004;110:2638-2643.)

Key Words: tomography ■ atherosclerosis ■ coronary disease

Studies with electron beam computed tomography (EBCT) and early versions of multidetector computed tomography (MDCT) scanners equipped with 4 detectors and a temporal resolution of 250 to 330 ms demonstrated the ability of cardiac CT to detect significant coronary stenosis in selected patients with high–image-quality data sets. However, the clinical applicability of these methods was limited because of the fact that roughly one third of all coronary artery segments could not be evaluated owing to stairstep and motion artifacts and the presence of calcification. When all coronary segments were included, diagnostic accuracy significantly decreased for both EBCT and MDCT (sensitivity, 68±4.3% and 63±2.9%, respectively; specificity, 68±0.2% and 71±0.2%, respectively).1

The newest generation of MDCT scanners permits simultaneous acquisition of image data in 16 parallel cross sections with an in-plane resolution of 0.6 mm and a gantry rotation time of 420 ms that results in a temporal resolution of ~210 ms.2 Initial reports have suggested improved diagnostic accuracy for the detection of significant stenosis in assessable segments (92% sensitivity, 93% specificity) compared with selective x-ray coronary angiography.3,4 Although the initial results are promising, a systematic and thorough analysis comparing a segment-based with a clinically more useful patient-based model, which includes all coronary artery segments as well as an assessment of technical limitations and the impact of image quality on diagnostic accuracy, has not been performed.
The aim of this prospective, blinded, standard cross-sectional technology assessment therefore was to test the ability of 16-slice MDCT to detect significant coronary artery stenoses based on the American Heart Association (AHA) classification of coronary artery segments. We evaluated the diagnostic accuracy on a per-segment and per-patient basis and determined the impact and underlying cause of misinterpretation.

Methods

Patients
A cohort of 33 consecutive patients (27 male, 6 female; mean ± SD age, 57 ± 9 years) scheduled for invasive coronary angiography on an inpatient basis because of suspected coronary artery disease (CAD; lead complaint of chest pain on the Canadian Cardiology Society scale of 1 to 3, with proven or suspected stress-induced myocardial ischemia) underwent cardiac MDCT within 1 day of coronary angiography. Patients in unstable clinical condition, without sinus rhythm, with impaired renal function, and possibly pregnant patients were excluded. All patients provided written, informed consent. The institutional review board of the Massachusetts General Hospital approved the study protocol.

Study Design
This study was designed as a prospective, blinded, standard cross-sectional technology assessment between 16-slice MDCT and invasive selective coronary angiography ("gold standard").

Data Acquisition
MDCT data were acquired with a Sensation 16 MDCT scanner (Siemens Medical Solutions). According to a previously published protocol, images were acquired with 16 × 0.75-mm-slice collimation, a gantry rotation time of 420 ms, table feed of 2.8 to 3.8 mm per rotation, tube energy of 120 kV, and an effective tube current of 500 mAs. Contrast agent (80 mL of Iodixanol, 320 g/cm²; Visipaque, Nycomed Amersham) was injected intravenously at a rate of 4 mL/sec. Overlapping transaxial images were reconstructed with a medium-sharp convolution kernel (B35f) with an image matrix of 512 × 512 pixels, slice thickness of 1 mm, and an increment of 0.5 mm with an average heart rate of 65 ± 7 bpm. A maximum of 2 segments per patient, with at least 2 independent planes, were included for assessment.

MDCT data were transferred to an offline image analysis workstation (Leonardo; Siemens Medical Solutions). Original axial images, thin-slice (5-mm) maximum-intensity projections (which display a stack of 5 consecutive original slices in 1 image), and multiplanar reformatted reconstructions rendered orthogonal and perpendicular to the vessel course of each respective segment were used for assessment.

The MDCT data sets were evaluated for the presence of significant coronary artery stenosis within all 17 coronary segments (modified 16-segment model of the AHA, with segment 17 being the intermediate branch of the left coronary artery). The presence of stenosis was assessed by visual estimation. Any narrowing of the normal contrast-enhanced lumen to ≤ 50% that could be identified in at least 2 independent planes was defined as significant coronary artery stenosis.

Image Quality
Image quality was assessed for each coronary segment as excellent, limited, or not assessable. Reviewers defined the cause of impaired image quality as the presence of (1) calcified plaque, (2) motion artifacts (ill-defined vessel contours), (3) stairstep artifacts (misalignment of slices obtained from different heartbeats), or (4) image noise/suboptimal contrast enhancement.

In addition, observers provided information on diagnostic certainty with regard to the absence or presence of significant CAD per patient (1 = very uncertain, 2 = uncertain, 3 = unequivocal, 4 = certain, 5 = absolutely certain) and subsequent recommendations for patient management (coronary angiography indicated [yes/no]).

Selective Coronary Angiography
Selective coronary angiography (BICOR Coroskop Hi-P, Siemens Medical Systems) was performed with standard techniques through a transfemoral approach. Seven projections were obtained (left coronary artery, 4 views and right coronary artery, 3 views). However, owing to variability of the position of the heart, the angles of image acquisition were slightly different from patient to patient.

The angiograms were quantitatively assessed with qualitative coronary angiography software (QAPlus, Sanders Data Systems) by an independent and experienced interventional cardiologist unaware of the results of the CT examination. Significant coronary lesions were classified into significant stenosis 50% to 69% or ≥70% of luminal narrowing, thresholds that have been used in other MDCT studies.6–8

Statistical Evaluation
Measures of diagnostic accuracy of MDCT for the detection of significant coronary artery stenosis (sensitivity, specificity, positive predictive value, negative predictive value, and likelihood and diagnostic odds ratios with 95% confidence intervals) were calculated on a per-segment and per-patient basis. To determine the impact of image quality, analysis was carried out with and without the exclusion of segments with limited assessability as well as for proximal segments only. We also determined diagnostic accuracy for 2 routinely used positivity criteria for coronary artery stenosis (≥70% or >50% luminal narrowing), as determined by selective coronary angiography.

Diagnostic certainty scores were compared with a paired 2-tailed t test. A probability value <0.05 was considered to indicate statistical significance. The intraobserver and interobserver variability for the detection of significant coronary artery stenosis was tested with a κ test.

Results
MDCT was performed without complications in all 33 patients. The mean heart rate at scan time was 60 ± 7 bpm (range, 51 to 73 bpm). The mean scan duration was 20 ± 3 seconds. In 24 patients, all 3 coronary arteries could be best visualized between 55% and 65% of the RR cycle. In 9 patients, the right coronary artery was best visualized at 35% of the RR cycle.

Seventeen AHA coronary segments were analyzed in all patients, independent of image quality (n = 530). Thirty-one segments could not be delineated on coronary angiography. Analysis was repeated with the exclusion of 92 segments (17%) with impaired image quality by MDCT (n = 438). Among excluded segments, 46 were the left circumflex, 24 the left anterior descending, and 24 the right coronary artery, with segment 10 (n = 6), segment 12 (n = 10), and segment 16 (n = 6) the most commonly affected.
Patient-Based Analysis

The prevalence of significant CAD (at least 1 stenosis $>50\%$ diameter reduction) among 33 patients was 67%. On the basis of invasive coronary angiography, 22 patients had significant coronary artery disease (1-vessel disease in 8 patients, 2-vessel disease in 7, and 3-vessel disease in 7).

All Segments

MDCT correctly identified significant CAD (presence of at least 1 stenosis $>50\%$ diameter reduction) in 19 patients and correctly ruled out CAD in 9 patients. In 2 patients, MDCT failed to detect significant CAD (mid-right coronary artery stenosis in 1 patient, mid-left circumflex and intermediate branch stenosis in another). In 3 patients (total of 5 vessels), MDCT detected CAD despite a normal coronary angiogram (2 proximal left circumflex, 1 proximal right coronary artery, 1 mid-right coronary artery, 1 mid-left anterior descending).

Proximal Segments

Fourteen patients had significant CAD in proximal coronary segments (1–2, 5–7, 11, 13; CAD prevalence, 42%). MDCT correctly detected significant CAD in 12 patients and correctly ruled out significant CAD in 17 patients. In 2 patients, MDCT failed to detect significant CAD, and in 2 patients, MDCT detected CAD despite the absence of significant epicardial coronary stenosis (stenosis $>50\%$ diameter reduction) on the coronary angiogram. Overall, MDCT was more sensitive than specific for the detection of significant CAD in this high-risk patient population. Sensitivity and specificity were insensitive to the positivity criteria as defined by coronary angiography (>50% versus >70% stenosis).

Segment-Based Analysis

Coronary angiography by quantitative methods identified 54 significant lesions ($>50\%$) in 530 segments (prevalence, 9%). Proximal lesions ($n=33$ in segments 1–2 [$n=14$], 5–7 [$n=13$], 11 [$n=4$], and 13 [$n=2$]) were more frequent than distal lesions ($n=19$). Forty-six lesions ($28$ in proximal segments, 18 in distal segments) had $>70\%$ luminal obstruction. Table 1 provides detailed data on false- and true-positive/negative findings of MDCT for the detection of significant obstructive CAD in all segments, proximal segments, and evaluable segments compared with selective invasive coronary angiography. MDCT test characteristics are summarized in Table 2.

All Segments

MDCT correctly detected 34 lesions and failed to detect stenoses in 20 segments with $>50\%$ stenosis (sensitivity, 63%). The sensitivity increased slightly to 67% for lesions of $>70\%$ stenosis. Specificity was not different for the detection of stenosis $>50\%$ and $>70\%$ luminal narrowing (95% and 96%, respectively). The sensitivity of MDCT did improve by 19% and 22% (for $>50\%$ and $>70\%$ stenosis, respectively) when only proximal segments were evaluated, primarily because most lesions that were not detected by MDCT occurred in distal segments ($n=13$ and $n=12$ for $>50\%$ and $>70\%$ stenosis, respectively).

Figure 1. A–D, Patient with 94% stenosis of proximal left anterior descending coronary artery (LAD) detected both on MDCT and selective coronary angiography. A, Axial thin-slice maximum-intensity projection (5-mm) MDCT image showing significant narrowing of vessel lumen, with residual contrast filling in presence of eccentric, noncalcified plaque (arrow). B, Curved multiplanar reconstruction along centerline of LAD, demonstrating contrast enhancement of mid and distal LAD segments. C, Volume-rendered 3D image (surface shadowing display) of heart, demonstrating tomographic view of lesion (arrow). D, Invasive selective coronary angiography demonstrates eccentric stenosis of proximal LAD with residual filliform lumen (arrow). Quantitative coronary angiography determined 94% luminal obstruction. All other abbreviations are as defined in text.

Figure 2. A–C, Patient without stenosis of the proximal right coronary artery (RCA) as determined by selective coronary angiography. A, Axial thin-slice maximum-intensity projection (5-mm) MDCT image demonstrates significant calcified plaque in the proximal RCA (arrow). B, Cross-sectional reconstruction perpendicular to centerline of RCA demonstrates massive calcification, apparently without residual contrast-filled coronary lumen. C, Invasive selective coronary angiography demonstrates normal angiogram without luminal obstruction of the proximal RCA. All other abbreviations are as defined in text.
>70% stenosis, respectively). The mean diameter reduction of stenoses (>50%) that were missed by MDCT (76±14%) was not significantly different from the stenoses that were detected (78±17%, P=0.56).

**Evaluable Segments**

After exclusion of 92 segments classified as “unevaluable” by MDCT, coronary angiography identified 43 significant lesions (>50%) in 438 segments (prevalence, 10%). There were 7 obstructive coronary lesions noted in segments that could not be evaluated by MDCT. MDCT correctly detected 30 lesions and failed to detect stenosis in 13 segments (sensitivity, 70%). In 371 segments, stenosis was ruled out correctly by MDCT, and in 22 segments, the degree of narrowing was overestimated (specificity, 94%). The sensitivity of MDCT for the detection of significant luminal narrowing did slightly increase after exclusion of segments with limited assessability, whereas specificity was not affected.

Overall, MDCT was more specific than sensitive for the detection of coronary lesions on a segmental basis. For evaluable segments, sensitivity (70% versus 71%) and specificity (94% versus 94%) were insensitive to positivity threshold (>50% versus >70% stenosis as detected by coronary angiography, respectively).

**Diagnostic Certainty**

Both observers were confident in their final diagnosis with regard to the presence or absence of significant CAD per patient (mean value for observer 1, 4.02±1.09; for observer 2, 4.09±0.87; P=0.66). In patients in whom CAD was either missed or overestimated, diagnostic certainty was lower than in patients diagnosed correctly (3.71±1.16, P<0.2).

**Underlying Cause of False-Negative and False-Positive Findings**

We determined the underlying cause with regard to the presence of calcification, image noise/motion, and location in the 20 segments with false-negative and the 19 segments with false-positive MDCT results. Calcification was identified as the underlying reason for overestimation of coronary lumen obstruction in the overwhelming majority of false-positive findings (94%) (Figure 2). On the contrary, calcification was much less of a factor in false-negative findings (14%). Instead, image noise and suboptimal contrast enhancement in small vessels (<1.5-mm diameter) was the predominant cause of underestimation (66%) (Figure 3), eg, left circumflex with right dominant vessel supply. In some cases (20%), the great cardiac vein overlapped the left circumflex (segment 13) or the intermediate branch (segment 17) and caused false-negative results.

Overall, pitfalls occurred independent of vessel type (right coronary artery, n=14; left anterior descending and intermediate branch, n=12; and left circumflex, n=13). However, the first diagonal branch, the proximal left circumflex segment, and the intermediate branch were the most frequent locations for false-positive findings, whereas the mid-right coronary artery, the mid-left anterior descending, and the first obtuse marginal branch were the most frequent locations for false-negative findings.

**Intraobserver and Interobserver Agreement**

Intraobserver agreement was excellent (κ=0.81), whereas interobserver agreement was good (κ=0.68), based on the comparison of all coronary segments.

**Discussion**

In our analysis of 33 patients with a high prevalence of CAD (67%), we found a moderate positive predictive value (64%) and sensitivity (63%) and a high negative predictive value (96%) and specificity (96%) for 16-slice MDCT in the detection of significant coronary stenosis in an evaluation of all 17 segments of the coronary artery tree. Increased temporal and spatial resolution led to a decrease in the number of segments with impaired image quality (17%) compared with
TABLE 2. Diagnostic Accuracy and Predictive Value of MDCT for Detection of Significant Stenosis (>50% Luminal Narrowing) on Selective Angiography

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>+LR</th>
<th>-LR</th>
<th>DOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All segments</td>
<td>0.63 (0.50–0.76)</td>
<td>0.96 (0.94–0.98)</td>
<td>0.64</td>
<td>0.96</td>
<td>15.77</td>
<td>0.39</td>
<td>40.89</td>
</tr>
<tr>
<td>Evaluable only</td>
<td>0.70 (0.57–0.82)</td>
<td>0.94 (0.92–0.97)</td>
<td>0.58</td>
<td>0.97</td>
<td>12.46</td>
<td>0.32</td>
<td>38.92</td>
</tr>
<tr>
<td>Proximal segments</td>
<td>0.82 (0.70–0.94)</td>
<td>0.93 (0.90–0.97)</td>
<td>0.68</td>
<td>0.97</td>
<td>12.46</td>
<td>0.19</td>
<td>64.04</td>
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<tr>
<td>Patient-based analysis</td>
<td></td>
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</tr>
<tr>
<td>All segments</td>
<td>0.86 (0.72–1.01)</td>
<td>0.82 (0.60–1.04)</td>
<td>0.90</td>
<td>0.75</td>
<td>4.75</td>
<td>0.17</td>
<td>28.5</td>
</tr>
<tr>
<td>Proximal segments</td>
<td>0.86 (0.67–1.04)</td>
<td>0.89 (0.76–1.03)</td>
<td>0.86</td>
<td>0.89</td>
<td>8.14</td>
<td>0.16</td>
<td>51.00</td>
</tr>
</tbody>
</table>

For segment-based analysis for all segments, analysis of 530 segments according to modified AHA classification of coronary segments; evaluable only, 438 segments (92 segments were excluded because of impaired image quality); proximal segments, 1, 2, 5, 6, 7, 11, 13. For patient-based analysis, there were 33 consecutive patients. PPV indicates positive predictive value; NPV, negative predictive value; +LR, positive likelihood ratio; −LR, negative likelihood ratio; and DOR, diagnostic odds ratio. All other abbreviations are as defined in text. Values in parenthesis represent upper and lower bound for 95% confidence interval.

A patient-based analysis of the absence/presence of significant CAD demonstrated good diagnostic accuracy; however, the negative predictive value was only moderate (75%). Given the high pretest probability of disease in our population, the test appears to be of limited diagnostic value in patients at high risk for significant CAD. Confidence of the observers with regard to the final diagnosis for the presence or absence of significant CAD per patient was similar between correct and incorrect assessments. We identified calcification as the major underlying cause for overestimation of luminal narrowing and motion/noise and contrast-related image deterioration as the major reason for false-negative MDCT findings. We also demonstrated that current CT technology is insensitive to the degree of significant narrowing (50% versus 70% in selective angiography).

Previous studies were limited to the evaluation of high image quality data sets in selected patients and was performed on a per-vessel basis in evaluable proximal segments. Our analysis systematically lays out the differences between a segment-based and a patient-based approach based on all 17 coronary segments, as well as the impact of coronary calcification and poor image quality on diagnostic accuracy in a consecutive patient cohort.

Our results demonstrate that negative and positive predictive values of MDCT for the detection of significant CAD are different from previously established segment-based analyses and a patient-based analysis. Segment-based analysis demonstrated a low positive but a high negative predictive value. In contrast, detection or exclusion of significant CAD per patient demonstrated a moderate negative predictive value (75%) and a high positive predictive value. Per-patient analysis had better sensitivity than per-segment analysis. It should be noted that an increase in sensitivity is merely dependent on the prevalence of 1-, 2-, or 3-vessel disease, with maximal differences in 3-vessel disease.

Most studies so far have been conducted in patients referred for invasive coronary angiography, a population at high risk for significant CAD. Subsequently, the prevalence of CAD in most studies was even higher than in this study (mean prevalence, 72% versus 67%). Given the high pretest probability of CAD, reliable exclusion of significant CAD (high negative predictive value) per patient would represent the most valuable diagnostic information in this patient cohort. Obviously, this question cannot be addressed by a segment-based analysis. Because of a moderate negative predictive value (75%), coronary CT angiography may be of limited diagnostic value in patients at high risk for significant CAD.

Instead, CT-based coronary angiography may be more useful in the diagnostic workup of patients at intermediate risk for CAD (eg, younger symptomatic subjects with multiple risk factors). In those patients, not only is the prevalence of coronary calcification, a major contributor to false-positive findings, lower but also a high positive rather than a high negative predictive value of MDCT would result in significant changes in patient management, ie, referral for coronary angiography. Although it might be difficult to perform large-scale prospective trials in view of the dynamic technical development of CT technology, such trials are necessary to establish cardiac MDCT as a clinical application and more important, to identify the group of patients in whom cardiac CT has the most diagnostic value. In addition, it is likely that 16-slice scanners will continue to be used by many institutions for cardiac imaging.

We confirm the findings of initial reports on 16-slice MDCT by demonstrating that improved image quality achieved by better spatial and temporal resolution led to a significant decrease in the number of segments that could not be evaluated compared with 4-slice MDCT or EBCT. Our finding of 17% is slightly higher than previously reported (7% to 12%) but can also be attributed to the fact that previous studies were restricted to coronary vessels >1.5 mm in diameter.

Similar to previous reports, we have demonstrated that 16-slice MDCT permits the detection of significant CAD in proximal segments with higher sensitivity (82%) and specificity (93%) compared with studies with 4-slice MDCT technology. However, despite the relatively low number of unevaluable segments, the sensitivity for segment-based detection of significant CAD including all 17 coronary segments remains limited (63%).

Whereas previous studies simply mentioned calcification and motion artifacts as major confounders of image quality,
we thoroughly analyzed sources of misinterpretation and could demonstrate that coronary calcification is the major reason for overestimation of luminal narrowing but that it has relatively little impact on the failure to detect coronary stenosis. Although it was beyond the goal of this study, evaluation of different display settings may play a key role in potentially overcoming this limitation. On the contrary, reduced image quality due to noise, coronary motion, and suboptimal contrast enhancement can lead to failure to detect significant stenosis.

Our data demonstrate that qualitative assessment of the presence of significant stenosis may be insensitive to the severity of luminal obstruction, ie, between >50% and >70% of luminal narrowing with current CT technology. In fact, even in a proximal coronary vessel with a 3- to 4-mm lumen diameter, the difference between a 50% and a 70% stenosis is very small in terms of diameter (0.6 mm and 0.8 mm, respectively). However, whether spatial resolution of current 16-slice MDCT technology is sufficient for quantitative evaluation of the degree of stenosis was not explored in this study.

Limitations
The number of patients and thus, the number of analyzed coronary segments was relatively small. Because of the lack of standardized evaluation algorithms, MDCT analysis was based on visual assessment of individual image display settings. The accuracy for calcium detection may have been artificially low, because no unenhanced scan was performed: smaller calcified plaques with a density equal to the contrast-enhanced lumen may thus have been missed by MDCT. However, small calcifications may not result in overestimation of the degree of stenosis. In addition, the frequent use of β-blockers to lower heart rate is a limitation of the technique.

Conclusions
In conclusion, 16-slice MDCT has moderate diagnostic value for the detection of coronary stenoses when all coronary segments are included in the analysis. In a patient population with a high prevalence of hemodynamically significant CAD, the moderate negative predictive value for patient-based detection of CAD suggests a limited impact on clinical decision-making in high-risk populations.

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References
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