Diagnostic Accuracy of 64-Slice Computed Tomography Coronary Angiography

A Prospective, Multicenter, Multivendor Study

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Objectives

This study sought to determine the diagnostic accuracy of 64-slice computed tomographic coronary angiography (CTCA) to detect or rule out significant coronary artery disease (CAD).

Background

CTCA is emerging as a noninvasive technique to detect coronary atherosclerosis.

Methods

We conducted a prospective, multicenter, multivendor study involving 360 symptomatic patients with acute and stable anginal syndromes who were between 50 and 70 years of age and were referred for diagnostic conventional coronary angiography (CCA) from September 2004 through June 2006. All patients underwent a nonenhanced calcium scan and a CTCA, which was compared with CCA. No patients or segments were excluded because of impaired image quality attributable to either coronary motion or calcifications. Patient-, vessel-, and segment-based sensitivities and specificities were calculated to detect or rule out significant CAD, defined as ≥50% lumen diameter reduction.

Results

The prevalence among patients of having at least 1 significant stenosis was 68%. In a patient-based analysis, the sensitivity for detecting patients with significant CAD was 99% (95% confidence interval [CI]: 98% to 100%), specificity was 64% (95% CI: 55% to 73%), positive predictive value was 86% (95% CI: 82% to 90%), and negative predictive value was 97% (95% CI: 94% to 100%). In a segment-based analysis, the sensitivity was 88% (95% CI: 85% to 91%), specificity was 90% (95% CI: 89% to 92%), positive predictive value was 47% (95% CI: 44% to 51%), and negative predictive value was 99% (95% CI: 98% to 99%).

Conclusions

Among patients in whom a decision had already been made to obtain CCA, 64-slice CTCA was reliable for ruling out significant CAD in patients with stable and unstable anginal syndromes. A positive 64-slice CTCA scan often overestimates the severity of atherosclerotic obstructions and requires further testing to guide patient management. (J Am Coll Cardiol 2008;52:2135–44) © 2008 by the American College of Cardiology Foundation

Noninvasive coronary angiography using computed tomography (CT) is a recent development, and multiple small single-center studies have been published with different generation scanners, but only 1 multicenter study using a 16-slice scanner has been published (1). Computed tomographic coronary angiography (CTCA) using 4- and 16-slice scanners lacked sufficient robustness to be useful in clinical practice (2,3). The

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Methods

Study design. The study was designed to prospectively include symptomatic patients who presented with stable anginal syndromes and unstable anginal syndromes who were referred for clinically indicated CCA. Patients were requested to undergo an additional CTCA for research purposes in addition to their CCA. The study protocol was approved by the institutional review board of the Erasmus University Medical Center.

Study group. From October 2004 until June 2006, 433 symptomatic patients with stable or unstable anginal syndromes who were between the ages of 50 and 70 years were enrolled in 3 university hospitals. To avoid radiation exposure in young patients, who have a higher lifetime attributable risk than older individuals receiving the same dose, patients enrolled in the study were 50 years or older (17). A maximum age limit was set to minimize the presence of severe coronary calcifications, which especially occur in the elderly and are known to hamper precise coronary stenosis evaluation. Sixty-two patients denied (written) informed consent, and 11 patients were excluded because of CT-related criteria (5 scanner malfunction, 3 poor intravenous access, 2 contrast extravasation, and 1 second-degree atrioventricular block because of beta-blockers). Thus, the remaining study population comprised 360 patients (Fig. 1).

Patients with stable chest pain were categorized as having typical or atypical angina pectoris. Typical angina was defined when the following 3 characteristics were present: 1) substernal discomfort; 2) precipitated by physical exertion or emotion; and 3) relieved with rest or nitroglycerine within 10 min. Atypical angina pectoris was defined when only 1 or 2 of these 3 symptom characteristics were met. Patients presenting with an acute coronary syndrome were categorized as having unstable angina pectoris (in the absence of a troponin increase as measured at 2 separate time intervals) or as non–ST-segment elevation myocardial infarction whenever troponin levels were elevated. Only patients with an acute coronary syndrome that did not require an urgent invasive strategy were included.

Patients with a previous history of percutaneous coronary stent placement, coronary artery bypass surgery, impaired renal function (serum creatinine >120 μmol/l), persistent arrhythmias, inability to perform a breath hold of 15 s, or known allergy to iodinated contrast material, were excluded.

Scan protocol. Each center used a 64-slice CT scanner from a different vendor (Sensation 64, Siemens, Forchheim, Germany; Brilliance 64, Philips Medical Systems, Best, the Netherlands; Toshiba Multi-Slice Aquilion 64 system, Toshiba Medical Systems, Tokyo, Japan). Patients with a heart rate exceeding 65 beats/min received either additional oral or intravenous beta-blockers.

A nonenhanced scan to calculate the total calcium score was performed before the CTCA. The scan parameters of the scanners are shown in Table 1. A bolus-tracking technique was used to synchronize the start of image acquisition with the arrival of contrast agent in the coronary arteries.

The effective dose of the nonenhanced scan and the CTCA was estimated from the product of the dose-length product and a conversion coefficient (k = 0.017 mSv/[mGy × cm]) for the chest as the investigated anatomical region (18).

Image reconstruction. To acquire optimal motion-free images, datasets were reconstructed with retrospective electrocardiographic gating using an absolute reverse or percentage technique. Datasets were reconstructed immediately after the scan following a stepwise approach. Initially, a single dataset was reconstructed during the mid-to-end diastolic phase (350 ms before the next R-wave or at 65% to 70% of the R-R interval). In case of insufficient image quality of 1 or more coronary segments, additional datasets were reconstructed in the diastolic phase (between 250 ms and 450 ms before the next R-wave or between 60% and 80% of the R-R interval). In case of persistent artifacts related to coronary motion, an alternative approach using an absolute forward or percentage technique (between 250 and 400 ms after the previous R-wave or between 20% and 40% of the R-R interval) was used to obtain datasets during the end-systolic phase. If necessary, multiple datasets of a single patient were used separately to obtain optimal image quality for all coronary segments. These best selected datasets were stored on CD or DVD and used for CTCA analysis.

Quantitative coronary angiography (QCA). All were carried out within 2 weeks before or after CCA. Three experienced cardiologists (C.A.M., K.N., J.M.W.) unaware of the results of CTCA received the CCAs on a CD and identified and analyzed all coronary segments using a modified 17-segment American Heart Association classification (19) on a separate workstation. Segments were visually classified as normal (smooth parallel or tapering
borders, visually <20% narrowing) or as having nonsignificant or significant coronary obstruction (visually >20% narrowing). The stenoses in segments visually scored as having >20% narrowing were quantified by a validated QCA algorithm (CAAS, Pie Medical, Maastricht, the Netherlands) (20).

Stenoses were evaluated in the worst angiographic view and classified as significant if the lumen diameter reduction exceeded ≥50%.

**CT image evaluation.** The total calcium scores of all patients were calculated using dedicated software. The CTCA scans of a certain study center were always graded by a team from another study center. Two observers graded each CTCA scan, and in case of disagreement consensus was obtained by a third reader. Experienced observers (W.B.M., M.F.M., J.D.S., N.R.M., A.M.V., J.W.J.) unaware of the results of the CCA evaluated the CTCA datasets on an offline workstation (Leonardo, Siemens, Forchheim, Germany).

Image quality was evaluated on a per-segment basis and classified as good (defined as absence of any image-degrading artifacts related to motion, calcification, or noise), moderate (presence of image-degrading artifacts, but evaluations possible with moderate confidence), or poor (presence of image-degrading artifacts and evaluation possible with low confidence). The influence of calcium on a per-segment basis was evaluated and graded as none (not calcified), moderate (calcium present and covering <50% of lumen), and high (calcium covering >50% of lumen in all planes including in cross section).

The axial source images, as well as multiplanar or curved reformatted reconstructions and maximum intensity projections, were used to evaluate the CT dataset for the presence of significant segmental stenosis. Segments were scored as having significant CAD if there was ≥50% diameter reduction of the lumen by visual assessment. Segments distal to a chronic total occlusion were excluded. An intention-to-diagnose design was used; thus, all scanned patients including all vessels and segments were analyzed even if the image quality was poor because of extensive calcification, coronary motion, or breathing artifacts.
**Power calculation.** We assumed a 70% prevalence of significant CAD in this study population. Sample size calculations showed that 320 patients were necessary to estimate the sensitivity and specificity of CTCA versus CCA as reference standard with a 95% confidence interval of 6% (i.e., a standard error of approximately 3%) above and below the expected CTCA sensitivity and specificity of 90%. To allow for possible incomplete data, we included 40 extra patients.

**Statistical analysis.** Descriptive statistics were performed for patients, coronary vessels, and segments. All 360 patients and all coronary segments were included in the analysis. Categorical patients’ demographics and characteristics, expressed as numbers and percentages, were compared using chi-square tests. Continuous variables were expressed as mean (standard deviation) and compared with an unpaired 2-sided Student *t* test. For the evaluation of patient demographics and characteristics, values of *p* < 0.01 were considered statistically significant. Diagnostic performance of CTCA for the diagnosis of significant CAD compared with the standard of reference QCA on CCA was determined with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), and their corresponding 95% confidence intervals (CIs).

**Table 2 Definitions of Descriptive Parameters Used in the Different Diagnostic Analyses**

<table>
<thead>
<tr>
<th>True-Positive</th>
<th>True-Negative</th>
<th>False-Positive</th>
<th>False-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient analysis</strong></td>
<td>At least 1 significant stenosis in a patient detected by CTCA and CCA regardless of location of stenosis</td>
<td>No significant stenosis in a patient detected either by CTCA or CCA</td>
<td>Significant stenosis detected by CTCA and no significant stenosis detected by CCA</td>
</tr>
<tr>
<td><strong>Vessel analysis</strong></td>
<td>At least 1 significant stenosis in a vessel detected by CTCA and CCA regardless of location of stenosis</td>
<td>No significant stenosis in a vessel detected either by CTCA or CCA</td>
<td>Significant stenosis detected by CTCA and no significant stenosis detected by CCA</td>
</tr>
<tr>
<td><strong>Segment analysis</strong></td>
<td>Significant stenosis in a segment detected by CTCA and CCA</td>
<td>No significant stenosis in a segment detected either by CTCA or CCA</td>
<td>Significant stenosis detected by CTCA and no significant stenosis detected by CCA</td>
</tr>
</tbody>
</table>

In CTCA, significant stenosis is defined as a 50% lumen diameter reduction of the lumen by visual assessment. In CCA, significant stenosis is defined as a 50% lumen diameter reduction as quantified with quantitative coronary angiography.
Diagnostic Performance of 64-Slice CTCA for the Detection of \( \geq 50\% \) Stenosis on QCA in the Per-Patient Analysis (95% CI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Included Patients (n = 360)</th>
<th>Excluded Patients (n = 73)</th>
<th>Stable Anginal Syndromes (n = 233)</th>
<th>Unstable Anginal Syndromes (n = 127)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>TP</td>
<td>TN</td>
<td>FP</td>
</tr>
<tr>
<td>Patient-based analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable angina pectoris</td>
<td>68</td>
<td>360</td>
<td>244</td>
<td>73</td>
</tr>
<tr>
<td>Non-ST-segment elevation acute coronary syndrome</td>
<td>63</td>
<td>233</td>
<td>145</td>
<td>56</td>
</tr>
<tr>
<td>Men</td>
<td>76</td>
<td>245</td>
<td>185</td>
<td>38</td>
</tr>
<tr>
<td>Women</td>
<td>51</td>
<td>115</td>
<td>59</td>
<td>35</td>
</tr>
<tr>
<td>Typical angina pectoris</td>
<td>70</td>
<td>151</td>
<td>104</td>
<td>31</td>
</tr>
<tr>
<td>Atypical angina pectoris</td>
<td>50</td>
<td>82</td>
<td>41</td>
<td>25</td>
</tr>
<tr>
<td>Unstable angina pectoris</td>
<td>75</td>
<td>77</td>
<td>57</td>
<td>13</td>
</tr>
<tr>
<td>Non-ST-segment elevated myocardial infarction</td>
<td>84</td>
<td>50</td>
<td>42</td>
<td>4</td>
</tr>
</tbody>
</table>

Values are n (%), unless otherwise indicated. Categories of patients' demographics and characteristics were compared using chi-square tests. Continuous variables were compared with the Mann-Whitney U test. Values of \( p < 0.05 \) are significant. *Mean and standard deviation. †Blood pressure \( \geq 140/90 \) mm Hg or treatment for hypertension. ‡Total cholesterol \( >180 \) mg/dl or treatment for hypercholesterolemia. §Treatment with oral antidiabetic medication or insulin. Median and quartiles.

CIs in both the vessel and segment analyses and their subanalyses (23,24).

Three pairs of observers for different centers conducted the analysis, resulting in 3 intervariabilities, presented as range of intervariability. The data of the 3 intervariabilities were averaged and presented as mean interobserver variability. Intrarobserver agreement of 1 observer in a set of 50 patients is presented using kappa statistics. The statistical analyses were performed using SPSS (version 12.1, SPSS Inc.) and STATA (SE version 8.2, College Station, Texas).

**Results**

Patient characteristics of those included and excluded from the study are shown in Table 3. There were no significant differences between the 2 groups. The prevalence of having

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]

\[ \text{Prevalence of obstructive coronary artery disease} \]

\[ \text{Absence of significant coronary artery disease} \]

\[ \text{1-vessel disease} \]

\[ \text{2-vessel disease} \]

\[ \text{3-vessel disease} \]

\[ \text{Left main coronary artery disease} \]

\[ \text{Calcium score (Agatston score)} \]

\[ \text{Conventional coronary angiography} \]
at least 1 significant coronary stenosis was 68%. Patient demographics of patients presenting with stable or unstable symptoms were comparable, except for a higher prevalence of smokers (p < 0.001) and a higher prevalence and extent of significant CAD (p < 0.01) in patients presenting with unstable anginal syndromes (chi-square test).

Additional beta-blockers before CTCA scanning were administered in 56% (200 of 360) of patients, decreasing the mean heart rate to 59 ± 9 beats/min. The mean scan time was 10.7 ± 1.6 s. One patient needed a short period of observation on the coronary care unit because of a second-degree AV block after beta-blocker administration but recovered completely. In 2 patients, contrast extravasation occurred that resolved without further complications, and 3 patients had mild contrast allergy that was successfully treated with antihistamines.

**Diagnostic performance of 64-slice CTCA: patient-based analysis.** The diagnostic performance of CTCA for detecting significant stenoses on a patient level is detailed in Table 4. Almost all patients with significant CAD on CCA were identified by CTCA (99%, 244 of 246) (Figs. 2 and 3). Two patients with 1-vessel disease were missed. In all patients with left main or 3-vessel disease (100%, 27 of 27), CTCA detected at least 1 significant coronary stenosis, which means...
that in a per-patient analysis all of these patients were correctly identified. Forty-one patients with angiographically nonsignificant disease were incorrectly classified as having significant CAD by CTCA: 49% (20 of 41) of patients were scored as having single-vessel disease, 27% (11 of 41) of patients as having 2-vessel disease, 17% (7 of 41) of patients as having 3-vessel disease, and 7% (3 of 41) as having significant left main CAD (Fig. 4). Sensitivity and specificity between patients who presented with stable versus unstable symptoms were similar.

**Diagnostic performance of 64-slice CTCA: vessel-based analysis.** The diagnostic performance of CTCA for the detection of significant lesions on vessel-based analysis is detailed in Table 5. Significant lesions in the right coronary artery and circumflex coronary artery were more often undetected than lesions in the left anterior descending coronary artery and left main coronary artery. The severity of a lesion was overestimated in 245 nonobstructive vessels (false positives).

**Diagnostic performance of 64-slice CTCA to predict the extent of significant vessel disease.** In 53% (192 of 360) of the patients, CTCA correctly predicted the absence of significant vessel disease and the presence of 1-, 2-, and 3-vessel disease. In 3% (11 of 360), CTCA underrated the extent of disease, and in 44% (157 of 360), it overestimated the extent of disease. The weighted kappa score to predict the extent of vessel disease was moderate (0.47).

The prevalence of 3-vessel disease was 6%. The sensitivity for predicting the presence of significant 3-vessel disease was 90% (95% CI: 68% to 98%), specificity was 77% (95% CI: 72% to 81%), positive predictive value was 19% (95% CI: 12% to 29%), and negative predictive value was 99% (95% CI: 97% to 100%) (Table 6).

**Diagnostic performance of 64-slice CTCA: segment-based analysis.** The diagnostic performance of CTCA for the detection of significant lesions on a segment-based analysis is detailed in Table 7. Overall 5,297 of 6,120 potentially available segments were included for comparison with CCA. Unavailable segments included 628 anatomically absent segments on CCA and 195 segments distal to an occluded coronary segment. All coronary segments were evaluated, also including segments with severe calcifications or poor image quality. Sensitivity decreased with vessel diameter and increased with the presence of calcifications. Specificity decreased with poor image quality and in the presence of severe calcifications.

The severity of 59 significant coronary stenoses was underestimated or missed and classified as nonsignificant by CTCA, and the severity of 471 nonsignificant lesions was overestimated by CTCA. The highest percentage of over-
estimated and underestimated coronary stenoses was clustered around the cutoff value of 50% diameter reduction (Fig. 5). The kappa values for the mean interobserver variability and the intraobserver variability were 0.66 (range 65 to 67) and 0.69, respectively.

Discussion

This prospective, multicenter, multivendor study showed that 64-slice CTCA in intermediate- to high-risk symptomatic patients accurately detects significant CAD and is reliable for ruling out significant CAD. The sensitivity to detect CAD was 99%, and the negative predictive value was 97%. Because of overestimation of the severity of a stenosis, the specificity was moderate (64%) with a positive predictive value of 86%. All patients with 3-vessel disease or left main CAD were detected. The study was performed in 3 independent centers, with different types of 64-slice CT scanners and using different dedicated scan protocols.

The high sensitivity of CTCA for CAD shown in our study is in keeping with the sensitivity of 64-slice CTCA studies performed in single-center studies. The specificity of 64% is, however, lower than results published previously, which ranged from 79% to 100% (4,5,7–15). The main reason for the lower specificity was the rather high rate of false-positive outcomes, which was related to the difficulties in grading the severity of stenosis and the inclusion in the analysis of all available coronary segments regardless of image quality. We included in our analysis segments with poor image quality caused by blurring because of cardiac motion or step artifacts caused by breathing or an irregular heart rate. The precise grading of the severity of a coronary stenosis is hampered in calcified obstructions because of the blooming effect, which overestimates the severity of stenosis. In case of extensive focal calcifications, the visualization of the underlying coronary lumen is obscured. However, we did not exclude these segments from the analysis but tended to grade these lesions as having a significant obstruction.

Our coronary stenosis grading policy, and inclusion of all coronary segments in an intention-to-diagnose approach, is based on the premise that patients with either positive CTA results or nonevaluable segments will undergo CCA. Because the clinical implication is the same, we graded nonevaluable segments as positive, which means that the calculated sensitivity and specificity reflect clinically decision making. Our approach is different from many single-center reports about the diagnostic performance of 64-slice CTCA, in which approximately 6% of all segments were excluded from further analysis because they were considered nonevaluable (4,5,7–15).

The inclusion or exclusion of nonevaluable coronary segments from further analysis on the diagnostic performance of CTCA can have significant effects, as shown in the multicenter CT study reported by Garcia et al. (1). They studied 187 symptomatic patients using 16-slice CT scanners. After exclusion of nonevaluable segments (29% of all available segments), the sensitivity was 75% and the specificity was 77%. Scoring all nonevaluable segments as a positive test result, sensitivity increased to 98% but at the expense of specificity, which decreased to 54%.

The outcome of a negative CTCA scan is important. A recent study showed that conservative management of a patient with a negative CT scan is safe and is associated with an excellent 1-year outcome (25). The presence and extent of both nonobstructive and obstructive CAD as seen on CTCA was shown to predict adverse cardiovascular events in particular in patients with left main and 3-vessel disease (26). In our study we showed that CTCA reliably detected patients with left main or 3-vessel disease, although CTCA overestimated the extent of disease compared with CCA. For clinical decision making, the high number of false-positive CTCA outcomes necessitates further testing with either functional tests or CCA. Alternatively, a functional test could be performed before or in addition to CTCA.

It is time for clinical trials testing the effectiveness and cost-effectiveness of various workup algorithms in a ran-

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Table 5  Diagnostic Performance of 64-Slice CTCA for the Detection of ≥50% Stenosis on QCA in the Per-Vessel Analysis (95% CI)

<table>
<thead>
<tr>
<th>Vessel-based analysis</th>
<th>Prevalence of Disease, %</th>
<th>N</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right coronary artery</td>
<td>26</td>
<td>1,440</td>
<td>354</td>
<td>821</td>
<td>245</td>
<td>20</td>
<td>95 (92-97)</td>
<td>77 (74-80)</td>
<td>59 (55-63)</td>
<td>98 (96-99)</td>
</tr>
<tr>
<td>Left main coronary artery</td>
<td>39</td>
<td>360</td>
<td>132</td>
<td>170</td>
<td>50</td>
<td>8</td>
<td>94 (90-98)</td>
<td>77 (71-82)</td>
<td>73 (66-79)</td>
<td>96 (92-98)</td>
</tr>
<tr>
<td>Left anterior descending coronary artery</td>
<td>2</td>
<td>360</td>
<td>5</td>
<td>338</td>
<td>16</td>
<td>1</td>
<td>83 (50-100)</td>
<td>95 (93-97)</td>
<td>24 (8-44)</td>
<td>100 (99-100)</td>
</tr>
<tr>
<td>Circumflex coronary artery</td>
<td>26</td>
<td>360</td>
<td>84</td>
<td>187</td>
<td>79</td>
<td>10</td>
<td>89 (83-95)</td>
<td>70 (65-76)</td>
<td>52 (45-60)</td>
<td>95 (92-98)</td>
</tr>
</tbody>
</table>

Bias-corrected 95% CIs from a bootstrap analysis are reported for the vessel analyses and the individual vessel analyses. Abbreviations as in Table 4.

Table 6  Performance of CTCA to Predict the Extent of CAD as Seen on CCA

<table>
<thead>
<tr>
<th>Extent of CAD as Seen on CTA</th>
<th>Extent of CAD as Seen on CCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
</tr>
</tbody>
</table>

The weighted kappa = 0.47 and the strength of agreement is considered to be moderate. The left main coronary artery was left out of the analysis. CAD = coronary artery disease; other abbreviations as in Table 2.
domized fashion to see which yield the best outcomes and lowest costs.

**Study limitations.** Our study was performed in pre-selected middle-aged patients referred for CCA who presented with atypical and typical stable angina and unstable angina, which have been shown to fall into categories of patients with intermediate to high pre-test probabilities of having CAD (27). Thus, our study population is neither representative of patients with a low to intermediate probability, for which CTCA is currently recommended (28), nor of unstable patients with ongoing ischemia or with hemodynamic or electrical instability, who require an immediate intervention. A study comparing CTCA with CCA in patients at low to intermediate risk would be difficult to perform because CCA is not always indicated. However, the negative predictive value for low-to-intermediate-risk patients can be estimated using Bayesian revision adjusting the prior probability and is very high. Despite the high sensitivity and lower specificity, our study did not suffer from referral bias. A referral bias occurs when

### Table 7

<table>
<thead>
<tr>
<th>Prevalence of Disease, %</th>
<th>N</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segment-based analysis</td>
<td>9</td>
<td>5,297</td>
<td>422</td>
<td>4,345</td>
<td>471</td>
<td>59</td>
<td>88 (85–91)</td>
<td>90 (89–92)</td>
<td>47 (44–51)</td>
</tr>
<tr>
<td>Diameter, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>10</td>
<td>4,531</td>
<td>407</td>
<td>3,655</td>
<td>419</td>
<td>50</td>
<td>89 (86–92)</td>
<td>90 (88–91)</td>
<td>49 (45–53)</td>
</tr>
<tr>
<td>1.5–2</td>
<td>3</td>
<td>449</td>
<td>10</td>
<td>396</td>
<td>40</td>
<td>3</td>
<td>77 (54–100)</td>
<td>91 (88–94)</td>
<td>20 (10–32)</td>
</tr>
<tr>
<td>≤1.5</td>
<td>3</td>
<td>317</td>
<td>5</td>
<td>294</td>
<td>12</td>
<td>6</td>
<td>45 (10–75)</td>
<td>96 (94–98)</td>
<td>29 (7–58)</td>
</tr>
<tr>
<td>Image quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>9</td>
<td>3,710</td>
<td>282</td>
<td>3,188</td>
<td>206</td>
<td>34</td>
<td>89 (85–93)</td>
<td>94 (93–95)</td>
<td>58 (53–62)</td>
</tr>
<tr>
<td>Moderate</td>
<td>11</td>
<td>851</td>
<td>78</td>
<td>641</td>
<td>117</td>
<td>15</td>
<td>84 (76–91)</td>
<td>85 (82–88)</td>
<td>40 (33–47)</td>
</tr>
<tr>
<td>Poor</td>
<td>10</td>
<td>736</td>
<td>62</td>
<td>516</td>
<td>148</td>
<td>10</td>
<td>86 (78–94)</td>
<td>78 (74–82)</td>
<td>30 (24–36)</td>
</tr>
<tr>
<td>Calcium</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>5</td>
<td>3,640</td>
<td>128</td>
<td>3,367</td>
<td>108</td>
<td>37</td>
<td>78 (71–84)</td>
<td>97 (96–98)</td>
<td>54 (48–60)</td>
</tr>
<tr>
<td>Moderate</td>
<td>17</td>
<td>1,235</td>
<td>192</td>
<td>829</td>
<td>197</td>
<td>17</td>
<td>92 (88–95)</td>
<td>81 (78–84)</td>
<td>49 (44–55)</td>
</tr>
<tr>
<td>High</td>
<td>25</td>
<td>422</td>
<td>102</td>
<td>149</td>
<td>166</td>
<td>5</td>
<td>95 (91–99)</td>
<td>47 (41–54)</td>
<td>38 (32–44)</td>
</tr>
</tbody>
</table>

Bias-corrected 95% computed tomography scans from a bootstrap analysis are reported for the segment analyses and their subanalyses.

Abbreviations as in Table 4.

### Figure 5

**Diagnostic Performance of CTCA Per Segmental Analysis Categorized by Diameter Stenoses on QCA**

In the graph, the diagnostic performance of CTCA is shown according to various diameter stenoses as measured by QCA in a per-segment analysis. The absolute number of segments per stenosis category is shown in the table. The highest frequency of overestimated (FP) and underestimated (FN) coronary stenoses by CTCA was clustered around the cutoff value of 50% diameter reduction (significant coronary stenosis). FN = false-negative; FP = false-positive; TN = true-negative; TP = true-positive; other abbreviations as in Figure 1.
patients are selected for referral to the reference test based on the results of the index test. In our study all patients underwent the reference test, CCA, irrespective of the results of the index test, CTCA. Ideally, a consecutive series of patients who are referred for CTCA, and not CCA, needs to be considered in which all patients should undergo CCA regardless of CTCA results.

The high radiation exposure, with an estimated effective dose of 15 to 18 mSv, is of concern. In this study we did not use prospective electrocardiogram-triggered X-ray tube modulation to reduce the radiation dose because the first-generation 64-slice multidetector CT systems were equipped with nonflexible tube current modulation ability. We were concerned that the use of this mode would increase the number of coronary segments with poor image quality because the technique limits the ability to reconstruct images in all coronary phases and may cause motion artifacts.

Conclusions

Among patients in whom a decision had already been made to obtain CCA, we found that 64-slice CTCA was reliable for ruling out significant CAD in patients with stable and unstable anginal syndromes. A positive 64-slice CTCA scan can often overestimates the severity of atherosclerotic obstructions and requires further testing to guide patient management.

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REFERENCES


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