Diagnostic Performance of 64-Multidetector Row Coronary Computed Tomographic Angiography for Evaluation of Coronary Artery Stenosis in Individuals Without Known Coronary Artery Disease: Results From the Prospective Multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) Trial

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Results From the Prospective Multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) Trial

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Objectives The purpose of this study was to evaluate the diagnostic accuracy of electrocardiographically gated 64-multidetector row coronary computed tomographic angiography (CCTA) in individuals without known coronary artery disease (CAD).

Background CCTA is a promising method for detection and exclusion of obstructive coronary artery stenosis. To date, no prospective multicenter trial has evaluated the diagnostic accuracy of 64-multidetector row CCTA in populations with intermediate prevalence of CAD.

Methods We prospectively evaluated subjects with chest pain at 16 sites who were clinically referred for invasive coronary angiography (ICA). CCTAs were scored by consensus of 3 independent blinded readers. The ICAs were evaluated for coronary stenosis based on quantitative coronary angiography (QCA). No subjects were excluded for baseline coronary artery calcium score or body mass index.

Results A total of 230 subjects underwent both CCTA and ICA (59.1% male; mean age: 57 ±10 years). On a patient-based model, the sensitivity, specificity, and positive and negative predictive values to detect ≥50% or ≥70% stenosis were 95%, 83%, 64%, and 99%, respectively, and 94%, 83%, 48%, 99%, respectively. No differences in sensitivity and specificity were noted for nonobese compared with obese subjects or for heart rates ≥65 beats/min compared with >65 beats/min, whereas calcium scores >400 reduced specificity significantly.

Conclusions In this prospective multicenter trial of chest pain patients without known CAD, 64-multidetector row CCTA possesses high diagnostic accuracy for detection of obstructive coronary stenosis at both thresholds of 50% and 70% stenosis. Importantly, the 99% negative predictive value at the patient and vessel level establishes CCTA as an effective noninvasive alternative to ICA to rule out obstructive coronary artery stenosis. (A Study of Computed Tomography [CT] for Evaluation of Coronary Artery Blockages in Typical or Atypical Chest Pain; NCT00348569) (J Am Coll Cardiol 2008;52:1724–32) © 2008 by the American College of Cardiology Foundation

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Coronary computed tomographic angiography (CCTA) has emerged as a promising noninvasive method for the detection and exclusion of obstructive coronary artery disease (CAD) (1). However, widespread clinical applicability of CCTA remains limited, because earlier studies have excluded subjects based on baseline coronary artery calcium (CAC) score or heart rate and have assessed diagnostic performance of CCTA after exclusion of nonevaluable coronary artery segments. In addition, these studies were largely performed in patients with high prevalence (high clinical pre-test likelihood), which can potentially skew the results when applied to other pre-test likelihood groups. Recent studies evaluating the diagnostic performance of newer 64-multidetector (row) computed tomography (MDCT) scanners have shown further potential for an improvement in CCTA diagnostic accuracy and reduction in the number of nonevaluable coronary artery segments compared with older-generation CT scanners (2). However, these studies have been limited to single centers for patients with primarily high prevalence of obstructive coronary artery stenoses. To our knowledge, to date, no prospective multicenter trial for CCTA efficacy in patients without known CAD or with intermediate prevalence of CAD has yet been reported.

The aim of the present prospective blinded multicenter study was to test the ability of current-generation 64-multidetector row CCTA to detect or exclude significant coronary artery stenosis in chest pain subjects without known CAD, using an American Heart Association (AHA) classification of coronary artery segments (3). We assessed the diagnostic performance of 64-multidetector row CCTA on a per-patient and -vessel basis, including all patients and all vessels for final efficacy analysis.

Methods

Patients. The ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) study was designed to prospectively evaluate adult subjects with chest pain who were being clinically referred for nonemergent invasive coronary angiography (ICA). Potential study subjects were screened and enrolled by a site research coordinator if they met both inclusion and exclusion criteria. Study subjects were asked to undergo a research CCTA, as well as data and blood collection as specified by a pre-defined research protocol.

Individuals were eligible for participation in the ACCURACY trial if they were ≥18 years of age, experienced typical or atypical chest pain, and were being referred for nonemergent ICA. Individuals were excluded from participation in the ACCURACY trial for the following reasons: known allergy to iodinated contrast; baseline renal insufficiency (creatinine ≥1.7 mg/dl); irregular cardiac rhythm; resting heart rate >100 beats/min; resting systolic blood pressure <100 mm Hg; contraindication to beta-blocker, calcium-channel blocker, or nitroglycerin; pregnancy; and known history of CAD (prior myocardial infarction, percutaneous transluminal coronary angioplasty or intracoronary stent, or coronary artery bypass surgery). Importantly, patients were not excluded for an elevated CAC score or body mass index.

The study was performed at 16 centers in the U.S. (Online Appendix). Before the study commenced, each Institutional Review Board had reviewed and approved the study protocol and patient safety monitoring plan. Protocols associated with patient enrollment, safety analysis, image acquisition, image interpretation, and statistical analysis were developed by a Steering Committee. GE Healthcare (Milwaukee, Wisconsin) performed study monitoring, data management, and quality control. Adverse and serious adverse events were determined for follow-up by a Data and Safety Monitoring Board.

Sample size. Estimation of sample sizes using a binary end point for each subject (e.g., agreement between CCTA and ICA, whether sensitivity or specificity) gave a conservative estimate of the required sample size. Based on historical data, we assumed values for sensitivity and specificity of 0.88 (standard deviation: 0.045) at the patient level, which required a minimum of 173 subjects to reject the null hypothesis that either sensitivity or specificity is ≤0.80 in favor of the alternative >0.80.

CCTA image acquisition. Study subjects underwent CCTA before conventional ICA. All CCTA scans were performed with a 64-multidetector row Lightspeed VCT scanner (GE Healthcare). All patients were in normal sinus rhythm at the time of the CCTA scan. Individuals presenting with baseline heart rates >65 beats/min were administered oral beta-blocker therapy as the preferred method for slowing down the heart rate. Intravenous administration was allowed in the protocol, using metoprolol at 5 mg increments to a total possible dose of 25 mg to achieve a resting heart rate <65 beats/min. All patients eligible for CCTA were scanned, whether or not the goal of a heart rate <65 beats/min was achieved.

Following a scout radiograph of the chest (anteroposterior and lateral), a timing bolus (using 10 to 20 ml contrast) was performed to detect time to optimal contrast opacification in the axial image at a level immediately superior to...
the ostium of the left main artery. Nitroglycerine 0.4 mg sublingually was administered immediately before contrast injection. During CCTA acquisition, 80-ml iodinated contrast (Visipaque, GE Healthcare, Buckinghamshire, United Kingdom) was injected using a triple-phase contrast protocol: 60-ml iodixanol, followed by 40 ml of a 50:50 mixture of iodixanol and saline, followed by a 50-ml saline flush. Retrospective electrocardiogram-gated helical contrast-enhanced CCTA was performed, with scan initiation 20 mm above the level of the left main artery to 20 mm below the inferior myocardial apex. The scan parameters were 64 × 0.625 mm collimation, tube voltage 120 mV, and effective mA 350 to 780 mA. Radiation reduction algorithms using electrocardiography modulation were used, which reduce radiation exposure (mA) during systole and end-diastole. After scan completion, multiphasic reconstruction of the CCTA scans was performed, with reconstructed images from 70% to 80% by 5% increments and 5% to 95% by 10% increments.

**CCTA interpretation.** The CCTA images were interpreted separately by 3 readers (M.J.B., D.D., and J.K.M.) blinded to all patient characteristics and ICA results. All CCTA images were evaluated on a 3-dimensional image analysis workstation (GE Advantage Workstation, GE Healthcare, Milwaukee, Wisconsin). The CCTA readers were permitted to use any or all of the available post-processing image reconstruction algorithms, including 2-dimensional axial and 3-dimensional maximal intensity projection, multiplanar reformat, cross-sectional analysis, and volume-rendered technique. Coronary arteries were scored using a 15-segment AHA coronary artery classification, as previously described (3). An overall assessment of image quality and coronary supply dominance was performed on the subject level (4,5). For each coronary segment, readers assessed whether coronary segments were evaluable. For any coronary artery segments considered to be nonevaluable, stenosis severity was assigned based on the outcome of the most adjacent proximal and identifiable segment, as previously described (6). A semiquantitative scale was used by the CCTA readers to grade extent of luminal stenosis as a percentage of the vessel diameter using visual estimations. Stenosis severity was recorded in the following manner: no stenosis; 1% to 29% stenosis; 30% to 49% stenosis; 50% to 69% stenosis; 70% to 99% stenosis; and 100% stenosis. For coronary artery segments considered to have 100% stenosis by CCTA, all segments distal to the occlusion were excluded from analysis (Fig. 1).

The degree of coronary artery stenosis identified by CCTA was assigned based upon a consensus of ≥2 of the 3 blinded CCTA readers who identified narrowing of the coronary artery lumen at a threshold of 50% or 70% stenosis. Consensus was achieved on a per-patient and per-vessel level. Consensus was obtained in all but 3 cases.

**ICA image acquisition and interpretation.** Selective ICA was performed by standard transfemoral arterial catheterization. A minimum of 8 projections were obtained (minimum of 5 views for the left coronary artery system and minimum of 3 views for the right coronary artery system). Because of differences in cardiac position, angles of projection for ICA differed slightly among study subjects. All ICA images were interpreted by an independent ICA reader (J.G.J.) blinded to all patient characteristics and CCTA results. The ICAs were quantitatively evaluated for coronary artery stenosis with quantitative coronary angiog-
raphy (QCA) software (CAAS, Pie Medical Imaging, Maastricht, the Netherlands). Any segment deemed visually to have >15% stenosis was quantified. Coronary artery segments by QCA were also evaluated using a 15-segment AHA coronary tree model and were judged as having significant stenosis at 2 levels (i.e., if ≥50% or ≥70% luminal narrowing of the coronary artery diameter was present).

Data analysis. In all analyses, all patients and all vessels were included. Analyses were performed separately for 2 distinct conditions—≥50% and ≥70% luminal diameter narrowing—that defined obstructive coronary artery stenosis. For the patient-based analysis, a true-positive was defined as the presence of ≥1 coronary artery segment considered to have an obstructive stenosis by both CCTA and ICA, irrespective of location. For the vessel-based analysis, a true-positive was defined as the presence of ≥1 coronary artery segment considered to have an obstructive stenosis by both CCTA and ICA in a single arterial system. Four arterial systems were predefined and consisted of the: 1) left main artery; 2) left anterior descending artery inclusive of diagonal branches; 3) left circumflex artery inclusive of obtuse marginal and left-sided posterolateral branches; and 4) right coronary artery inclusive of posterior descending artery and right-sided posterolateral branches. Ramus intermediate arteries were considered to be the first obtuse marginal branch for per-vessel analyses.

Statistical analysis. Categorical variables are presented as frequency and percentage, continuous variables as mean ± SD. The area under the receiver operating characteristic curve (AUC) was calculated for CCTA to identify obstructive coronary artery stenosis at either 50% or 70% threshold. All statistical analyses were performed using SAS Proprietary Software, version 9.1 (SAS Institute, Cary, North Carolina).

Results

Patient characteristics. There were 245 subjects initially enrolled into the study. Fifteen subjects did not complete either CCTA or ICA (withdraw after CCTA and did not undergo ICA or opted out of the CCTA and only underwent ICA) and were therefore excluded from the final efficacy analyses. Of the patient study cohort, 147 patients underwent stress testing by a range of different tests, including exercise treadmill testing (n = 17), exercise echocardiogram stress testing (n = 28), exercise nuclear stress testing (n = 96), pharmacological echocardiographic stress testing (n = 2), and pharmacological nuclear stress testing (n = 4). The remainder of the test cohort was referred on the basis of symptoms and/or testing not performed at the primary site.

One subject experienced a coronary artery dissection at the time of ICA involving 2 coronary artery segments (proximal right coronary artery, mid-right coronary artery). For this patient, efficacy analyses were performed based upon a total of 13 rather than 15 coronary segments, excluding comparison of these 2 dissected segments from the ICA and CCTA. Patient-level data were available for efficacy analysis for 230 subjects (mean age: 57 ± 10 years; 59.1% male) (Table 1). The mean inter-test interval between CCTA and ICA was 5.9 ± 4.3 days.

Patient-based evaluation. The CCTA test characteristics and performance for patient-based evaluation are listed in Table 2. There were 57 (24.8%) and 32 (13.9%) subjects found to have ≥50% or ≥70% stenosis, respectively, by QCA (Figs. 1 and 2). Discordance—specifically, the first reader scoring a subject’s examination nonevaluable, a second reader scoring an examination without obstructive stenosis, and a third reader scoring an examination with obstructive coronary stenosis—occurred for 3 subjects (1.3%), which were not included in the patient-level efficacy analysis. Among the 55 patients with ≥50% stenosis by QCA, 52 were correctly identified as having ≥50% stenosis by CCTA. Among the 31 patients with ≥70% stenosis by QCA, 29 were correctly identified as having ≥70% stenosis by CCTA. The AUC for identification of patients with ≥50% coronary artery stenosis by QCA was 0.96 (95% CI: 0.94 to 0.98). Applying CCTA stenosis thresholds to identify ≥70% stenosis by QCA resulted in a similarly high AUC of 0.95 (95% CI: 0.92 to 0.97) (Fig. 3). Sensitivity at both the 50% and 70% thresholds of disease was 95% and 94%, respectively, specificity was 83%, and negative predictive value (NPV) was 99% (Table 2). Given the low to intermediate prevalence of disease, positive predictive value (PPV) was low (64% and 48% for 50% and 70% thresholds of disease, respectively). Adding in the 3 unevaluable (due to lack of agreement) patients, the results remained statistically

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline Demographics of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>57 ± 10</td>
</tr>
<tr>
<td>Male gender</td>
<td>136 (59%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>202 (87.8%)</td>
</tr>
<tr>
<td>African American</td>
<td>13 (5.7%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8 (3.5%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (3.1%)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 ± 11 (140–198)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>93 ± 21 (49–174)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>31.4 ± 6.2 (16.8–50.5)</td>
</tr>
<tr>
<td>Heart rate (beats/min)*</td>
<td>60 ± 12</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.0 ± 0.2</td>
</tr>
<tr>
<td>Agatston coronary artery calcium score</td>
<td>284 ± 538</td>
</tr>
<tr>
<td>Diabetes</td>
<td>55 (23.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>154 (67.0%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>157 (68.3%)</td>
</tr>
<tr>
<td>Family history of coronary artery disease*</td>
<td>169 (73.5%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>128 (55.7%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>90 (39.1%)</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>78 (33.9%)</td>
</tr>
</tbody>
</table>

Values are n (%) or mean ± SD (95% confidence interval). *At the time of coronary computed tomographic angiography.
similar (at 50% threshold: sensitivity 94.7%, specificity 82.1%, PPV 64.2%, and NPV 99.3%; at 70% threshold: sensitivity 93.8%, specificity 81.8%, PPV 47.6%, and NPV 98.8%).

**Vessel-based evaluation.** The CCTA test characteristics and performance for vessel-based evaluation are listed in Table 3. For the vessel-based evaluation, 3 vessels were not evaluable by QCA and 7 vessels were scored discordantly by CCTA readers, resulting in 910 vessels in 229 patients. In total, 89 (9.7%) and 39 (4.3%) vessels reached the 50% or 70% stenosis threshold, respectively, by QCA. Among the 89 vessels with $\geq 50\%$ stenosis by QCA, 73 vessels were correctly identified as having $\geq 50\%$ stenosis by CCTA. Among the 39 vessels with $\geq 70\%$ stenosis by QCA, 32 were correctly identified as having $\geq 70\%$ stenosis by CCTA. For both 50% and 70% stenosis thresholds, sensitivity was 84%, specificity was 90% and 92%, respectively, and NPV was 99% (Table 3).

**Calcium score.** We examined diagnostic performance of CCTA based on baseline CAC score, stratified by $\leq 400$ versus $> 400$ Agatston units. Stratifying the diagnostic test performance characteristics of CCTA by these CAC score thresholds resulted in no change in diagnostic sensitivity but a reduction in specificity. The patient-based sensitivity for the presence of $\geq 50\%$ stenosis for patients with calcium scores $\leq 400$ versus $> 400$ or $\leq 600$ versus $> 600$ Agatston units was 95.8% versus 93.6% ($p = 0.71$) and 96.9% versus 91.3% ($p = 0.37$), respectively. The specificity of CCTA-diagnosed obstructive disease at the 50% stenosis threshold was reduced in patients with coronary artery calcium scores.

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**Table 2** Patient-Based Analysis

<table>
<thead>
<tr>
<th>Estimate, %</th>
<th>95% CI, %</th>
<th>Subjects in Group, n</th>
<th>Subjects Correct by CCTA, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 50%$ stenosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>95</td>
<td>85–99</td>
<td>55</td>
</tr>
<tr>
<td>Specificity</td>
<td>83</td>
<td>76–88</td>
<td>172</td>
</tr>
<tr>
<td>PPV</td>
<td>64</td>
<td>53–75</td>
<td>81</td>
</tr>
<tr>
<td>NPV</td>
<td>99</td>
<td>96–100</td>
<td>143</td>
</tr>
<tr>
<td>$\geq 70%$ stenosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>94</td>
<td>79–99</td>
<td>31</td>
</tr>
<tr>
<td>Specificity</td>
<td>83</td>
<td>77–88</td>
<td>196</td>
</tr>
<tr>
<td>PPV</td>
<td>48</td>
<td>35–62</td>
<td>60</td>
</tr>
<tr>
<td>NPV</td>
<td>99</td>
<td>96–100</td>
<td>164</td>
</tr>
</tbody>
</table>

CCTA = coronary computed tomographic angiography; CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value.

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**Figure 2** Computed Tomographic Angiogram Demonstrating Obstructive Disease of the Left Circumflex Artery With Quantitative Angiography Correlation

(A) Right anterior oblique orientation of the left circumflex artery with quantitative coronary angiography. (B) Curved multiplanar reformation and short-axis cross-sectional view (inset) of the left circumflex artery demonstrating obstructive coronary artery stenosis. (C) Multiplanar reformation and short-axis cross-sectional view (inset) of the left circumflex artery demonstrating obstructive coronary artery stenosis. Arrows indicate significant stenosis present on the computed tomographic angiogram and corresponding invasive angiogram.
≤400 versus >400 Agatston units (86.3% vs. 52.6%; p = 0.0003).

**Body mass index and heart rate.** Diagnostic performance of CCTA was examined in nonobese versus obese study participants, stratified by body mass index ≤30 kg/m² or >30 kg/m². For CCTA detection of ≥50% coronary artery stenosis at the patient level in nonobese versus obese subjects, sensitivity was 94.4% and 94.7% (p = 0.96), respectively, and specificity was 76.4% and 87.0% for ≤30 kg/m² or >30 kg/m², respectively (p = 0.07).

Diagnostic performance of CCTA for detection of ≥50% coronary artery stenosis at the patient level did not differ in individuals with heart rates ≤65 beats/min versus >65 beats/min, with a diagnostic sensitivity of 92.9% versus 100%, respectively, and a diagnostic specificity of 82.3% versus 82.8%, respectively (p > 0.35 for both comparisons).

**Discussion**

These results of the ACCURACY trial represent the first prospective blinded multicenter study evaluating the diagnostic performance of 64-multidetector row CCTA compared with QCA in chest pain subjects without known CAD being clinically referred for nonemergent ICA. The present data demonstrate high diagnostic performance of 64-multidetector row CCTA for detection of obstructive coronary artery stenosis at both 50% and 70% stenosis thresholds. Of equal importance, the 99% NPV of CCTA at the patient and vessel levels establishes it as a highly effective noninvasive alternative to ICA for the exclusion of obstructive coronary artery stenosis. The specificity of CAD obstruction detection in this study was 83% (at both 50% and 70% stenosis thresholds). This specificity is on par with other noninvasive imaging modalities (e.g., stress echocardiogram, stress nuclear), whereas the diagnostic sensitivity and NPV are higher (7). These results are in keeping with

![Figure 3](image_url)
earlier single-center studies in which CCTA demonstrated higher diagnostic performance for obstructive coronary artery stenosis detection compared with myocardial perfusion imaging (8,9).

To date, only one other multicenter trial, using former-generation 16-multidetector row CCTA, has been reported evaluating CCTA accuracy (10). In that study, the diagnostic performance of 16-multidetector row CCTA was inferior to that which had been previously reported in single-center studies, primarily due to high rates of false positivity and coronary artery segment nonevaluability. That study used a cutoff of ≥50% stenosis in a major epicardial vessel to define significant CAD.

In contrast, the present study used newer-generation 64-multidetector row CCTA for evaluation of CCTA diagnostic performance. Compared with 16-row CCTA, 64-MDCT studies represent a significant improvement in diagnostic accuracy and evaluable segments. New-generation 64-MDCT systems permit the acquisition of cardiac studies in <10 s, allowing faster contrast injection rates and lower contrast volume requirements, and reducing the number of artifacts related to inadequate breath-holding and heart rate variability. An earlier meta-analysis of individual 64-MDCT studies demonstrated a sensitivity of 96% and specificity of 73% (1). The present multicenter study with blinded readers for both CTA (3 readers) and invasive angiography (QCA), demonstrates very similar numbers, with higher per-patient specificity. In addition, the present study evaluated CCTA diagnostic accuracy at QCA stenosis at 2 thresholds: ≥50% stenosis, similar to that which has been studied in earlier CCTA studies; and ≥70%, in keeping with "real-world" practice in which a ≥70% stenosis may be a more useful clinical discriminator for obstructive CAD. Use of both thresholds for significant stenosis resulted in nearly identical results, affirming the utility of CCTA to identify disease at both the 50% and 70% stenosis thresholds. The receiver-operating characteristic curve in Figure 3 shows the degree to which we predict disease/no disease of 70% stenosis by invasive angiography. Because CCTA tends to overpredict stenosis, all stenoses of ≥70% on invasive angiography were identified at the >50% cut-point for CCTA.

Although PPV and NPV are generally well-accepted measures of diagnostic test performance, their values may be affected by disease prevalence within specific study populations. In contrast, likelihood ratios are measures of diagnostic test characteristics that simultaneously incorporate sensitivity and specificity, and are considered to be generally unaffected by the prevalence of disease. In the present study, the positive and negative likelihood ratios were 5.56 and 0.06, respectively, at the 50% threshold and 5.53 and 0.07, respectively, at the 70% threshold, indicating the high magnitude of power of CCTA to substantially alter pre-test probabilities, particularly for negative CCTAs. The calculated odds ratios of CCTA within the present study cohort were high (92.7 and 79.0 at the 50% and 70% thresholds, respectively) and further demonstrate the strong ability of a positive CCTA to identify subjects with obstructive coronary artery stenosis compared with those with a negative CCTA.

Due to the limited temporal resolution of MDCT scanners, significant coronary artery motion that occurs at higher heart rates or during irregular heart rhythms may render certain coronary artery segments difficult to evaluate. Earlier studies have generally excluded these nonevaluable coronary artery segments from final accuracy analyses (1,11,12). Although the number of coronary artery segments considered nonevaluable has decreased with use of 64-multidetector row CCTA compared with older-generation MDCT scanners, critics have contended that exclusion of nonevaluable segments falsely elevates the diagnostic performance of CCTA (2). In the present study, overall CCTA diagnostic performance was based upon the totality of all coronary artery segments, with no segments being excluded from analysis due to nonevaluability. The CCTA readers performed systematic evaluation of scans in multiple cardiac phases and used an assortment of 3-dimensional post-processing algorithms (maximal intensity projection, multiplanar reformat, volume-rendered technique, cross-section) for optimal visualization of coronary arteries, thereby improving the likelihood of segment evaluability. The data demonstrated that inclusion of all coronary segments for efficacy analyses of CCTA scans performed in a careful manner results in excellent diagnostic accuracy.

In the previously reported 16-row CCTA multicenter trial, as well as numerous single-center studies using 16- and 64-row CCTA, study subjects were routinely excluded based on baseline elevated CAC scores. Historically, CCTA diagnostic accuracy has been adversely affected by inclusion of individuals with high CAC scores, and many earlier studies simply elected to exclude them (1,11,12). Importantly, no subject in the present study was excluded for baseline CAC, and overall diagnostic performance remained high.

Given the limited spatial resolution of MDCT scanners, the diagnostic accuracy of CCTA has been commonly reported in the context of vessels of diameters ≥1.5 or ≥2.0 mm. Inclusion of smaller vessels of <2 mm diameter has generally unfavorably affected CCTA performance, and earlier studies have simply elected to ignore them (1,11,12). The high diagnostic accuracy of 64-multidetector row CCTA in the present analysis included all vessels, irrespective of size, for final efficacy analyses.

The average body mass index of our study population was 31.4 ± 6.2 kg/m², indicating a generally obese population (13). Because earlier investigations have reported decreased accuracy for CCTA in obese individuals, the present results indicate that proper use of current-generation 64-multidetector row scanners in obese subjects can still yield highly accurate results (12).

Earlier studies evaluating CCTA accuracy have been performed primarily in academic centers with expertise in
performance and interpretation of CCTA. Therefore, whether the results thus far reported represent performance generalizable to other academic or nonacademic centers has to date been unknown. The present study enrolled subjects from predominantly nonacademic (private) centers: 83% of the subjects were recruited by nonacademic centers versus only 17% from academic centers. Therefore, with adequate training, any imaging center can perform CCTA procedures with high quality. Interpretation of CCTAs was performed by 2 readers from academic centers and 1 reader from a nonacademic center. Despite the diversity in enrolling centers and CCTA interpreters, diagnostic performance of 64-multidetector row CCTA remained high, thus establishing it as a highly effective diagnostic modality in a variety of settings.

Importantly, 1 iatrogenic coronary artery dissection occurred in a study subject undergoing ICA. Although the risk of adverse events for ICA is generally considered to be low, significant and potentially life-threatening complications can arise, including not only coronary artery dissection, but also arrhythmia, stroke, hemorrhage, myocardial infarction, and death (14). This single event during the ICA procedure in the present study confirms the low incidence of such complications, while at the same time highlighting the enhanced risk of potential complications of ICA compared with a noninvasive alternative.

Subjects within the present study possessed a prevalence of obstructive coronary artery stenosis at the ≥50% threshold of only 25%, despite clinical indications for nonemergent ICA, uniformity of chest pain, and high prevalence of established cardiac risk factors. This intermediate prevalence of obstructive coronary artery stenosis, identified by CCTA and confirmed by ICA, underscores the common scenario in which patients with clinical indications for ICA fail to have clinically significant anatomic disease (15).

Recently published appropriateness criteria addressing the clinical use of CCTA have suggested that its greatest potential utility may be for the intermediate-risk patient with chest pain syndrome or acute chest pain (16). Similarly, the AHA scientific statement on CT angiography states, “CT coronary angiography is reasonable for the assessment of obstructive disease in symptomatic patients (Class IIa)” (7). Considering these recommendations, it should be noted that most of the earlier studies evaluating the diagnostic accuracy of CCTA were performed with patients with a generally high prevalence of obstructive coronary artery stenosis. Because disease prevalence may directly impact the characteristics and performance of a diagnostic test, CCTA requires efficacy assessment in patient populations with intermediate disease prevalence if it is to be successfully used in this population. The prevalence of obstructive coronary artery stenosis at the 50% threshold in the present study was only 24.8%, a prevalence that is less than half of that which had been reported in earlier pooled analyses (11). The present data expand the current base of CCTA diagnostic accuracy beyond high disease prevalence populations to symptomatic subjects with intermediate disease prevalence, and affirm CCTA’s potential diagnostic efficacy in intermediate-risk patients with chest pain syndrome or acute chest pain. The results demonstrate that in symptomatic patients, a negative (including nonobstructive disease) CCTA can noninvasively exclude angiographic disease, with post-test probabilities for patient- or vessel-specific disease approaching 1%. For example, a 57-year-old man with a pre-test probability of 25% and no obstructive disease on CT angiography has a post-test probability of 0.99.

**Study limitations.** We enrolled subjects in outpatient settings without known CAD who were being referred for nonemergent conventional coronary angiography. Therefore, whether these results can be extrapolated to individuals with known CAD or to other settings (e.g., emergency department) requires further study. Furthermore, only 1 blinded reader interpreted the ICAs. Nevertheless, the reference standard used in the present study was QCA rather than semiquantitative assessment of luminal diameter stenosis by ICA, a technique more prone to interobserver variability (17,18). We elected to implement tube current modulation to reduce radiation dose. Tube current modulation, however, limits the ability to interpret the coronary anatomy in cardiac phases other than the modulated phase and may result in artifacts in patients with irregular heart rates. Finally, no interpreting format was pre-specified for the CCTA readers, who used a variety of interpretative 3-dimensional post-processing algorithms, which precludes definitive comparison of 1 CCTA interpretation technique to another (19).

The benefit of this study is that it is a multicenter investigation using established methods widely used by practitioners and under less than ideal conditions (variable heart rates, obesity, high CAC scores, and dose modulation) that mimic current clinical practice. Despite these limitations, the performance of 64-MDCT was quite good. The analysis methods focused on the diagnostic accuracy of determining obstructive disease, not on establishing the value in defining atherosclerotic plaque burden. CCTA is clearly not as accurate as angiography in finding obstructive CAD (the findings of multiple studies put the PPV at ~60%). However, this study, as well as earlier single-center evaluations, demonstrate that CCTA provides a valuable NPV as well as a nearly 100% PPV for presence of atherosclerotic plaque. The high NPV for obstructive disease and the high PPV for atherosclerotic plaque makes CCTA unique in evaluating patients in which the suspicion for “obstructive” is intermediate.

**Conclusions**

The present results of the ACCURACY trial provide the first prospective multicenter data evaluating the diagnostic performance of current-generation 64-multidetector row CCTA compared with QCA in symptomatic individuals without known CAD with intermediate disease prevalence.
REFERENCES


CCTA demonstrates high accuracy for detection of obstructive coronary artery stenosis. Importantly, the high NPV (99%) firmly establishes CCTA as an effective non-invasive method to rule out obstructive coronary artery stenosis.

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Key Words: computed tomography • coronary artery disease • angiography.

APPENDIX

For a complete list of investigators, please see the online version of this article.
Diagnostic Performance of 64-Multidetector Row Coronary Computed Tomographic Angiography for Evaluation of Coronary Artery Stenosis in Individuals Without Known Coronary Artery Disease: Results From the Prospective Multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) Trial

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