Coronary Computed Tomography Angiography for the Diagnosis of Coronary Artery Disease
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Abstract

• **Objective:** To review the current application of coronary computed tomography angiography (CCTA) in the diagnosis of coronary artery disease (CAD).
• **Methods:** Qualitative review of the literature.
• **Results:** CCTA has emerged as a potential noninvasive alternative to both existing noninvasive tests for CAD in some patients and invasive coronary angiography (ICA) in other patients. There have been a large number of small, single-center studies comparing CCTA with ICA for the diagnosis of significant CAD that have reported excellent sensitivity, specificity, and negative predictive value in patient populations with a high prevalence of CAD. These studies often exclude segments or patients who do not have complete visualization of all coronary segments and it can be particularly challenging in patients with significant coronary artery calcification, stent placement, or coronary artery bypass grafts. A few small studies have evaluated the use of CCTA in the diagnosis of chest pain in the emergency department.
• **Conclusion:** To date, there are little data on the role of CCTA in comparison with other noninvasive tests for the diagnosis of CAD, including nuclear perfusion imaging and stress echocardiography. Given the accuracy of CCTA, it may be useful as a strategy to avoid ICA. The high negative predictive value of CCTA suggests great promise in the assessment of low- to moderate-risk patients with acute chest pain, with the potential for rapid patient triage and lower health care costs.

Cardiovascular disease is the leading cause of death in the United States. Over 13 million American adults have coronary heart disease, for which invasive coronary angiography (ICA) represents the gold standard for the diagnosis. More than 14 million inpatient coronary angiograms and 664,000 percutaneous coronary interventions (PCIs) were performed in the United States in 2003 [1]. ICA is associated with a major procedure-related complication rate in 1.7% of patients and a procedure-related mortality rate of 0.1% [2]. Given these risks, the expense, and postprocedure recovery time associated with ICA, there is great interest in the noninvasive diagnosis of coronary artery disease (CAD) using coronary computed tomography angiography (CCTA). Like ICA, this new technique visualizes the artery lumen, but unlike ICA, CCTA also visualizes the vessel wall and can characterize plaque area, volume, and remodeling and can discriminate between calcified and soft plaques (Figure 1 and Figure 2) similar to intravascular ultrasound (IVUS) [3].

There are now established criteria for the appropriate use of CCTA (Table 1) [4], and CCTA is deemed reasonable (Class IIa recommendation) in the evaluation of suspected obstructive CAD in symptomatic patients. Other uses of CCTA include the detection and mapping of coronary artery anomalies (Class IIa recommendation) [5], evaluation of congenital heart disease, preprocedure anatomic mapping, and evaluation of cardiac masses; however, these are beyond the scope of this review.

The detection of CAD on multidetector-row computed tomography (MDCT) has also been shown to have prognostic implications. In 100 patients who underwent MDCT for suspected CAD, the 1-year incidence of cardiac death, acute coronary syndrome (ACS), or revascularization was 30% in patients with any CAD versus 0% in those with normal coronary arteries [6]. A study of 1138 patients who underwent MDCT and a mean follow-up of 15 months found that patients with absent or mild CAD had a 99.7% survival rate, whereas patients with moderate or severe CAD had an 85% survival rate [7].

Recent data suggest that optimal medical management in patients with stable angina and significant ischemic CAD with or without PCI may result in equivalent rates of death, myocardial infarction, or other cardiovascular events [8]. Given the potential shift from PCI to medical management alone in some patients, there may be a greater role for a noninvasive test such as CCTA to diagnose CAD, with potentially less use of diagnostic ICA.
CCTA requires the use of iodinated contrast media, usually administered through an upper extremity intravenous line at 4 to 6 mL/second. Some form of a timing mechanism is used to determine at what time to begin scanning after acquire a single image, and faster gantry rotation has improved this significantly. Faster temporal resolution allows for adequate imaging at higher heart rates and may reduce the need for medications to slow the heart rate. Spatial resolution (in voxels) describes the 3-dimensional image size in any reconstruction plane, which has improved as detectors have become smaller. The best spatial resolution available with 16-slice scanners was $0.5 \times 0.5 \times 0.6$ mm, which improved on 64-slice scanners to $0.4 \times 0.4 \times 0.4$ mm. These voxels are referred to as isometric, which means they are equal in all planes within the 3-dimensional dataset. By comparison, the standard 2-dimensional spatial resolution of ICA is $0.2 \times 0.2$ mm [9].

CCTA requires the use of the most recent generations of multidetector computed tomography (CT) scanners that are capable of providing a dataset with both high spatial and temporal resolution that is reconstructed in synchrony to simultaneously collected electrocardiogram (ECG) data, essentially suspending cardiac motion. Patients with irregular rhythms cannot undergo CCTA, as ECG and CT data cannot be aligned currently. Helical scanning requires the continuous movement of both the CT gantry and the CT scanning table. With multidetector CT scanners, multiple rows of data are obtained with each 360-degree rotation of the CT gantry. Modern commercially available scanners have detector arrays with up to 64 detector rows, and gantry rotation speeds of under 500 ms.

Spatial and temporal resolutions have increased with newer scanners. Temporal resolution represents the time to acquire a single image, and faster gantry rotation has improved this significantly. Faster temporal resolution allows for adequate imaging at higher heart rates and may reduce the need for medications to slow the heart rate. Spatial resolution (in voxels) describes the 3-dimensional image size in any reconstruction plane, which has improved as detectors have become smaller. The best spatial resolution available with 16-slice scanners was $0.5 \times 0.5 \times 0.6$ mm, which improved on 64-slice scanners to $0.4 \times 0.4 \times 0.4$ mm. These voxels are referred to as isometric, which means they are equal in all planes within the 3-dimensional dataset. By comparison, the standard 2-dimensional spatial resolution of ICA is $0.2 \times 0.2$ mm [9].

CCTA requires the use of iodinated contrast media, usually administered through an upper extremity intravenous line at 4 to 6 mL/second. Some form of a timing mechanism is used to determine at what time to begin scanning after
the start of contrast administration. This most commonly takes the form of a small timing bolus, with 15 mL of contrast administered while images are taken through the aortic root to determine the time to peak enhancement, so that optimum enhancement of the coronary arteries can be achieved. This is particularly important in case of left ventricular dysfunction. Sublingual nitroglycerin is given to dilate the coronary arteries a few minutes prior to the CCTA acquisition, helping to differentiate between normal and diseased segments. Patients with a heart rate over 65 bpm usually receive oral and/or intravenous β blockers prior to CCTA to reduce the heart rate. When the heart rate is over 65 bpm, temporal resolution is inadequate and the images are limited due to motion artifact. Patients who cannot receive β blockers may receive a calcium channel blocker instead. With 64-slice CT scanners, the CCTA acquisition itself requires as few as 5 seconds [10].

After the CCTA has been acquired, the dataset is reconstructed on the CT scanner in both end-diastole, the most motion-free part of the cardiac cycle, and end-systole, the next most motion-free part of the cardiac cycle. The 3-dimensional data are reviewed on a workstation so that each coronary artery can be viewed in its short and long axes, navigating the dataset interactively to view each coronary segment in the best plane for that segment.

More recently, dual-source CCTA has been introduced. This combines two 32-detector arrays and 2 x-ray tubes arranged at 90-degree angles to each other. Therefore, for each 90-degree rotation of the gantry, 180 degrees of image data are collected, resulting in a higher temporal resolution and potentially improved image quality with less motion artifacts. In a preliminary study of dual-source CCTA by Achenbach et al [11] in 14 patients in which no medications were used to control heart rate, 222 of 226 coronary artery segments were free of motion artifacts despite a mean heart rate of 71 bpm and a range from 56 to 90 bpm. It has been suggested that dual-source CT allows motion-free CCTA in patients with a heart rate greater than 65 bpm, but more study is needed to substantiate this.

**Risks of CCTA**

The use of intravenous contrast can be associated with allergic reactions and renal failure. Many protocols exclude patients with renal insufficiency to minimize these risks. There is a significant radiation exposure with CCTA. The effective radiation dose, expressed in millisieverts (mSv), describes the overall risk when accounting for the various involved organs. Younger patients may have a much higher lifetime risk of developing radiation-associated malignancy than older patients, which raises concerns for the use of CCTA in low-risk young populations. Doses associated with various exposures are described in Table 2. Radiation doses have increased with 64-slice scanners compared with 16-slice scanners, as the increasingly thinner slices require higher radiation to maintain adequate signal-to-noise ratios. In women, radiation dose to breast tissue during CCTA is a concern; however, bismuth breast shields can be used to reduce this exposure. Radiation exposure with CCTA and ICA has been projected to convey lifetime mortality risks of 0.07% and 0.02%, respectively. When the other risks associated with ICA are included, the overall lifetime mortality risks of CCTA and ICA have been estimated at 0.07% and 0.13% [12].

There are methods to significantly reduce the radiation dose, the most widespread of which is dose modulation or ECG pulsing. During the part of the R-R interval when data are not used to evaluate the coronary arteries, the mA (milliamperes) is reduced, ramping up at the part of the R-R interval when data are collected, resulting in a higher temporal resolution and potentially improved image quality with less motion artifacts. In 64-slice scanners, as the increasingly thinner slices require higher radiation to maintain adequate signal-to-noise ratios. In women, radiation dose to breast tissue during CCTA is a concern; however, bismuth breast shields can be used to reduce this exposure. Radiation exposure with CCTA and ICA has been projected to convey lifetime mortality risks of 0.07% and 0.02%, respectively. When the other risks associated with ICA are included, the overall lifetime mortality risks of CCTA and ICA have been estimated at 0.07% and 0.13% [12].

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<table>
<thead>
<tr>
<th>Use</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Evaluation of chest pain syndromes</td>
<td>Intermediate pretest probability of CAD and ECG uninterpretable or unable to exercise</td>
</tr>
<tr>
<td>Evaluation of intracardiac structures</td>
<td>Evaluation of suspected coronary anomalies</td>
</tr>
<tr>
<td>Acute chest pain</td>
<td>Intermediate pretest probability of CAD and no ECG changes and serial enzymes negative</td>
</tr>
<tr>
<td>Asymptomatic detection of CAD</td>
<td>None</td>
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<tr>
<td>Asymptomatic risk assessment</td>
<td>None</td>
</tr>
<tr>
<td>Preoperative evaluation for noncardiac surgery</td>
<td>Assessment of complex congenital heart disease</td>
</tr>
<tr>
<td>Morphology</td>
<td>Evaluation of coronary arteries in patients with new-onset heart failure</td>
</tr>
<tr>
<td>Suspected aortic or pulmonary disease</td>
<td>Evaluation of suspected aortic dissection, thoracic aortic aneurysm, or pulmonary embolism</td>
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Table 2. Radiation Dose Associated with Various Radiation Exposures

<table>
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<tr>
<th>Exposure</th>
<th>Total Effective Dose, mSv</th>
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<tr>
<td>Mean background radiation in 1 year (United States)</td>
<td>3.0</td>
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<tr>
<td>Two-view chest radiograph</td>
<td>0.08</td>
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<tr>
<td>Air travel per 1000 miles</td>
<td>0.01</td>
</tr>
<tr>
<td>Tc-99m sestamibi stress test</td>
<td>12.0–17.5</td>
</tr>
<tr>
<td>EBCT coronary calcium scoring</td>
<td>1.0–1.3</td>
</tr>
<tr>
<td>16-Slice CCTA without ECG pulsing</td>
<td>7.9–1.63</td>
</tr>
<tr>
<td>16-Slice CCTA with ECG pulsing</td>
<td>4.0–8.7</td>
</tr>
<tr>
<td>64-Slice CCTA without ECG pulsing</td>
<td>9.6–21.4</td>
</tr>
<tr>
<td>64-Slice CCTA with ECG pulsing</td>
<td>4.8–14.0</td>
</tr>
<tr>
<td>Invasive diagnostic coronary angiography</td>
<td>5.6</td>
</tr>
</tbody>
</table>


interval used to visualize the coronary arteries. In 1 study, ECG pulsing reduced the mean dose estimate of 64-slice CCTA from 14.8 mSv to 9.4 mSv [13]. Newer techniques to reduce doses include the use of prospective triggering, in which data are only collected at a prospectively set part of the R-R interval, with no radiation exposure during the rest of the R-R interval; this has demonstrated promise with doses as little as 1 to 3 mSv [14].

Accuracy

While early CCTA studies showed very good to excellent sensitivity and specificity using 4-, 8-, and 16-detector CT scanners, studies often excluded a substantial number of patients, arteries, or segments from the analysis due to artifacts or insufficient contrast opacification of the coronary arteries. A meta-analysis evaluated 28 studies using 4-, 8-, or 16-slice CCTA compared with ICA as the reference standard. There were 617 patients enrolled in 4-slice CT studies, 50 patients in 8-slice studies, and 872 patients in 16-slice CT studies. Data were pooled to provide average sensitivity and specificity for detecting significant CAD, defined as greater than 50% diameter stenosis. Using segment-based analysis, average sensitivity was 83% with 4-slice scanners and 88% with 16-slice scanners, and average specificity was 93% and 97%, respectively. With 4-slice CCTA, 78% of segments were deemed adequate for evaluation, while 91% of segments were evaluable with 16-slice CCTA. Since nonevaluable segments were excluded from analysis, measures of accuracy may be overestimated. Sensitivity was better in the proximal and mid-artery segments, and lower in distal segments. In addition, many studies excluded small vessel segments with diameters less than 1.5 or 2.0 mm. Analysis by patient resulted in an identical mean sensitivity of 95% and specificity of 84% for both 4- and 16-slice CCTA [15].

A more recent meta-analysis evaluated 47 studies that compared CCTA and ICA in patients scheduled for ICA. There were 20 studies that used 4-slice CCTA, 1 study with 8-slice CCTA, 19 studies with 16-slice CCTA, and 7 studies with 64-slice CCTA. Assessable segments with CCTA increased significantly with 64-slice CCTA compared with 4- and 16-slice CCTA (P < 0.05), with pooled assessable segments observed in 74% of segments with 4-slice CCTA, 92% of segments with 16-slice CCTA, and 97% of segments with 64-slice CCTA. Pooled sensitivity and specificity for the detection of CAD was 76% and 93% with 4-slice CCTA, 82% and 95% with 16-slice CCTA, and 92% and 94% with 64-slice CCTA, respectively. This suggests that 64-detector CCTA has significant better diagnostic accuracy compared with earlier scanners. The mean prevalence of significant CAD in this study was 74%, indicating a very high pretest probability of disease. The reliable exclusion of significant CAD in these studies finds a high negative predictive value in this population. While it is expected that the high negative predictive value would also be present in low- or intermediate-risk patient cohorts, it is also likely that the positive predictive value would decrease [16].

Imaging Coronary Artery Stenosis with 64-Slice CCTA

There are now many published studies that have compared 64-slice CCTA with ICA (Table 3), which generally find excellent sensitivity and specificity for the detection of significant CAD (generally defined as a stenosis ≥50%). Patients were recruited for CCTA from the pool of patients who were already scheduled to undergo ICA. Hence, the prevalence of significant disease is higher than it would be in a screening population or a population of patients who may be undergoing other noninvasive tests such as stress echocardiography or radionuclide imaging for suspected CAD.

It is important to note exclusions from these investigations. Many studies excluded segments, arteries, or patients that were inadequately visualized on CCTA from the subsequent analysis, which likely overestimates its accuracy. Smaller arteries, particularly those less than 1.5 mm in diameter, are more difficult to visualize with CCTA than the larger proximal segments. For this reason, some published studies have excluded all segments less than 1.5 mm in diameter. For example, Leschka et al [19] excluded all segments under 1.5 mm, but reported no nonanalyzable...
segments. Raff et al [28] did not exclude segments based on size, but excluded 17% of segments from the segment-based analysis because of inadequate visualization, predominantly due to either calcification or motion artifact. Leber et al [18] excluded 4 of 59 patients from their analysis because of inadequate studies. Patients with stents were included, but 13 segments with stents were excluded from the segment-based analysis, and all patients with stents were excluded from the patient-based analysis, resulting in the inclusion of only 45 of 59 patients. This study stratified lesions by stenosis severity. In the stent-based analysis, there was a 79% sensitivity for the detection of a stenosis less than 50%, 73% for a stenosis greater than 50%, and 80% for a stenosis greater than 75%; specificity was reported as 97%. Analysis by patient found a sensitivity of 88% for detecting a stenosis greater than 50%, and an 85% specificity for excluding a stenosis greater than 75%. IVUS was performed in 32 vessels from 18 patients, with 46 of 55 plaques (84% sensitivity for detection of any plaque) and 39 of 43 disease-free segments correctly identified on CCTA (91% specificity). Compared with IVUS, CCTA significantly underestimated lesion stenosis (50.4% vs. 41.1%; P < 0.001). CCTA also overestimated the lumen area and underestimated the plaque area, which was attributed to partial volume effects at the lumen-plaque border secondary to overlapping attenuation values [18].

Fine et al [33] compared 66 patients undergoing CCTA and ICA, and after excluding segments smaller than 1.5 mm reported uninterpretable CCTA studies in 6% of patients. After these were also excluded, analysis by artery yielded 95% sensitivity, 96% specificity, 97% positive predictive value, and 92% negative predictive value for identifying stenosis greater than 50% [33]. Muhlenbruch et al [23] defined significant stenosis as at least 70% and had a lower patient-based specificity and negative predictive value than studies that used a 50% cutoff.

Calcification is known to contribute to both overestimation of stenosis and nonanalyzable segments. For example, Ong et al [25] reported that more segments were interpretable with a lower calcium score (94% vs. 87%) in a comparison of CCTA and ICA in which 68 patients had an Agatston score equivalent of less than 142, and 66 patients had a higher score. Raff et al [28] also compared the diagnostic accuracy of CCTA in patients stratified by calcium score. Patient-based sensitivity and specificity for a low score (Agatston score up to 100) were 94% and 95%, for a moderate score (101–400) were 100% and 88%, and for a high score (> 401) were 93% and 67%, respectively. This suggests a significantly decreased specificity with increased coronary artery calcification [28].

For this reason, some have suggested that a calcium score threshold should be used above which CCTA is less useful. However, other variables, such as the size and distribution of calcified plaques, should be considered. A calcium score of 400 could mean many tiny calcified plaques or fewer larger plaques, the latter creating more of a challenge to CCTA accuracy than the former. If calcium scoring is being done as part of a CCTA examination, it is also not operationally practical to process the examination data and generate the calcium score before deciding to do the CCTA acquisition.

**Evaluation of Coronary Stents**

The evaluation of in-stent stenosis is challenging, as metal causes variable degrees of blooming artifact (Figure 3). There is a significant variability in the ability of CCTA to evaluate in-stent restenosis, which may related to variables such as stent type, size, and composition, scan protocol, and the positional relationship of the stent to the scanner axis. For example, in an in vitro comparison of 68 different stents with 64-slice CCTA, in which all the stents were placed in the same orientation and imaged perpendicular to the stent axis, the visible lumen diameter ranged from 3% to 73% even when using a sharp reconstruction algorithm and a high-resolution dedicated kernel. In this study, 58 of the 68 stents had a lumen visibility of at least 50%, while only 10 stents had a lumen visibility of at least 66% [34]. This confirms not only the difficulty of evaluating the coronary artery lumen within stented segments but also in comparing studies of populations with different types of stents. In another study, 64-slice CCTA was used to evaluate in-stent dimensions of 4 different stents expanded to 3.0 mm diameter in vitro, with IVUS as the reference standard. While the IVUS-measured diameter ranged from 2.8 to 3.0 mm, the diameter measured on CCTA ranged from 1.7 to 1.9 mm, with CCTA underestimating in-stent lumen diameter for all stent types [35].

Several studies of 64-detector CCTA have included patients with stents. Leber et al [18] excluded segments and patients with stents from the primary analyses and reported an analysis of the 13 stented segments separately. Only 7 of the stents were correctly evaluated by CCTA; 2 of 4 stents with restenosis were correctly identified, while 4 of 9 stents without restenosis were reported as having restenosis. Other studies have included segments with stents in the primary analyses (Table 3). Schuijf et al [32] evaluated 61 patients with stents in 44 segments, reporting that all 3 in-stent stenoses and all 41 stents without significant stenosis were correctly identified. The study by Ehara et al [30] included a subanalysis of 67 stents in 39 patients. After excluding 9 stents with poor image quality, they reported a sensitivity, specificity, positive predictive value, and negative predictive value of 93%, 96%, 87%, and 98%, respectively. Nikolaou et al [31] included 15 patients with a total of 24 stents, of which 22 were interpretable with CCTA. Of these 22, CCTA made the correct diagnosis of significant stenosis in 11 stents, with 1 false-negative and 10 false-positive CCTA results. When
these stents were assessed for patency only, the correct diagnosis was made in 20 of 22 stents.

In a study of left main stent patency on 16- and 64-slice CCTA, 70 of 74 patients had adequate scans, from which CCTA correctly identified all 10 patients with in-stent restenosis, with false-positive results in 5 patients. In the 50 patients with quantitative IVUS and CCTA data, there was good correlation between IVUS and CCTA in the assessment of stent diameter ($r = 0.78$) [36].

**Evaluation of Bypass Grafts**

Many studies have evaluated graft patency and distal graft anastomoses with CCTA (Figure 4). For example, in a study by Anders et al [37] using 16-slice CCTA to evaluate 32 patients with 94 bypass grafts, the sensitivity was 100% and specificity was 98% for identifying a stenosis of 50% or more among the interpretable grafts. However, many grafts were uninterpretable; when all patients with at least 1 uninterpretable graft or anastomosis were included in the analysis, only 25% could be excluded from having significant graft disease [37]. In a study of 16-slice CCTA by Chiurlia et al [38] of 52 patients with 166 bypass grafts, only 1 graft was excluded because of significant clip artifacts. The sensitivity and specificity for detecting high-grade stenosis with CCTA were 96% and 100%, respectively, and were both 100% for detecting complete occlusion [38]. Schlosser et al [39] evaluated 48 patients with 131 bypass grafts using 16-detector CCTA and reported that while the sensitivity and specificity for graft patency were 96% and 95%, only 74% of distal anastomoses could be visualized. When the analysis was done with the nonvisualized distal anastomoses assumed stenotic, the sensitivity remained at 96%, but the specificity decreased to 68%.

Another study examined 52 patients with 45 arterial and 64 venous bypass grafts undergoing scheduled ICA with 64-slice CCTA. The presence or absence of significant CAD was correctly identified in all arterial grafts (10 had significant stenosis). For the vein grafts, CCTA correctly identified all 39 with significant stenosis, and 24 of 25 without significant stenosis. This resulted in an overall sensitivity of 100%
Table 3. continued

<table>
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<tr>
<th>Excluded, %</th>
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<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
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and a specificity of 98% for the detection of significant graft disease [40]. Another study retrospectively compared 31 patients with a total of 23 arterial bypasses and 73 venous bypasses undergoing ICA with 64-slice CCTA. ICA was not able to evaluate 1 arterial graft and 2 venous grafts, both of which were well-visualized by CCTA but not included in the analysis given the missing reference standard. The distal anastomoses were not well visualized with CCTA in 3 of the 51 patent grafts and classified as stenotic for the analysis. Of the 22 arterial grafts seen with ICA, 5 of 6 were correctly identified with significant stenosis using CCTA, and 12 of 16 were correctly identified without significant stenosis. Of the 71 venous grafts visualized with ICA, all 40 grafts with significant stenosis were correctly identified, while 30 of 31 without significant stenosis were correctly identified. Analysis by patient found 100% sensitivity with CCTA in detecting the 24 patients with significant stenosis, and 5 of the 7 patients without significant disease were correctly identified [41].

Ropers et al [42] used 64-detector CCTA in 50 patients with 138 grafts, including only segments and grafts larger than 1.5 mm in diameter. All grafts were correctly identified as patent or occluded. Among patent grafts, the sensitivity and specificity for the detection for a stenosis of at least 50% were 100% and 94%, respectively.

**CCTA in the Emergency Department**

The high negative predictive value of CCTA has led to considerable interest in using CCTA in the emergency department setting as a possible way to safely discharge home
the majority of chest pain patients who are not having an ACS, saving time and cost. This interest has been fueled by several recent studies. Hoffman et al [43] performed 64-slice CCTA in 103 patients with acute chest pain and suspected ACS who had a negative initial ECG and cardiac markers. These patients had CCTA in addition to usual care, and the CCTA results were not revealed at the time of the initial emergency department visit. Fourteen of the 103 patients had a confirmed ACS based on standard clinical care with serial ECGs, cardiac markers, and stress testing or cardiac catheterization in most patients. CCTA correctly excluded an ACS in all patients based on the absence of significant stenosis or plaque. The absence of a significant stenosis predicted the absence of an ACS with a sensitivity of 100%, specificity of 82%, positive predictive value of 46%, and most importantly a negative predictive value of 100%.

Goldstein et al [44] performed a randomized clinical trial of usual care (including stress nuclear perfusion scintigraphy) versus 64-slice CCTA in 197 low-risk emergency department patients with chest pain and negative ECGs and cardiac enzymes after 4 hours. Among the 461 patients screened, 10% declined consent, and 46% were excluded from the study predominantly because of pulmonary disease that precluded the use of β blockers, potential contrast allergy, known CAD, or atrial fibrillation. Of the 99 patients in the CCTA arm, 67 had normal coronary arteries or a stenosis of 25% or less and a calcium score of less than 100 Agatston units and were eligible for immediate discharge home. Eight patients with greater than 70% stenosis on CCTA were referred for ICA, and 24 patients were sent for a nuclear stress test either because they did not fit into the 2 aforementioned groups or at least 1 major coronary segment was not interpretable. Compared with the usual care group, patients in the CCTA arm had a significantly lower time to establish or exclude significant CAD (3.4 vs. 15 hours; P < 0.001) and lower cost of care ($1586 vs. $1872; P < 0.001). After 6 months of follow-up, there were no cases of ACS or death in either group, although this study was underpowered to detect a difference in coronary event rates [44].

Lastly, Gallagher et al [45] compared nuclear stress testing and CCTA in 92 low-risk patients presenting to the emergency department with chest pain. Patients with stenosis greater than 50% on CCTA, a calcium score greater than 400, or a reversible perfusion defect on nuclear stress testing were considered for ICA. After 7 patients were excluded for an uninterpretable CCTA in at least 1 major segment, CCTA was not significantly more or less accurate than nuclear stress testing in the detection of an ACS, significant CAD stenosis on catheterization, or an adverse event within 30 days (CCTA sensitivity, 86% and specificity, 92%; nuclear stress sensitivity, 71% and specificity, 90%). However, the confidence intervals around these test characteristics were very wide, due to the small number of cardiac events. For the 66 patients with both a negative CCTA and a negative perfusion study, the negative predictive value of the combined test combination was 100%, whereas for the 6 patients with a positive CCTA and positive perfusion study, only 4 of 6 had a confirmed ACS [45]. Obvious limitations for this study are the lack of ICA in all patients with abnormal noninvasive testing and the lack of power to detect significant outcome differences in this low-risk population.

Limitations of Current CCTA Studies
There are several limitations in the literature currently available to evaluate CCTA. Although there are now many published single-center studies that show excellent diagnostic accuracy for the detection of significant CAD, the studied populations in each series have been small. In all studies evaluating the accuracy of CCTA in which ICA has been used as the reference standard, the prevalence of disease has been very high, as patients were recruited from those already scheduled to undergo ICA for clinical reasons. There are no studies of how CCTA performs in populations with a lower prevalence of disease, such as the population of patients that undergo myocardial perfusion scintigraphy for suspected CAD or asymptomatic high-risk screening populations, which may alter the high sensitivities and specificities reported to date. In addition, current studies frequently use readers with extensive experience in cardiac imaging, and the reported results often represent a consensus of readers.

It is unclear how CCTA compares with other noninvasive tests for CAD, such as exercise treadmill tests, stress echocardiography, or myocardial perfusion scintigraphy. For example, a recent study found that 64-slice CCTA lesions did not predict perfusion deficits on gated-SPECT [46]. Although most CCTA studies define significant lesions as those with at least 50% stenosis, severe reductions in coronary flow reserve typically occur at a stenosis of 70% or greater, emphasizing that CCTA cannot predict the functional relevance of detected CAD.

CCTA appears to be accurate for detecting bypass graft patency but not for evaluating distal anastomoses. Caution should be used when evaluating stents, as there is great variability in the accuracy of evaluating in-stent restenosis.

Conclusion
CCTA provides noninvasive imaging of the coronary arteries, which may be an alternative for ICA in some patients. CCTA has a high sensitivity and specificity in for detection of significant CAD, and newer scanners have resulted in improved temporal and spatial resolution as well as fewer poorly visualized segments. CCTA has potential advantages over ICA with its noninvasive nature and its ability to visualize the plaque
and wall in addition to the lumen visible with ICA, although ICA still has higher spatial resolution, is associated with less radiation exposure, and is better able to quantify stenosis. The use of CCTA in low-risk patients with chest pain has great promise for rapid patient triage as well as decreasing health care costs. Additional studies are needed to determine the best roles for CCTA in the evaluation of patients with chest pain.

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