Role of Cardiac Multidetector Computed Tomography Beyond Coronary Angiography

Akira Sato, MD; Kazutaka Aonuma, MD, PhD

Cardiac multidetector computed tomography (MDCT) has become a useful noninvasive modality for anatomical imaging of coronary artery disease (CAD). Currently, the main clinical advantage of coronary computed tomography angiography (CCTA) appears to be related to its high negative predictive value at low or intermediate pretest probability for CAD. With the development of technical aspects of MDCT, clinical practice and research are increasingly shifting toward defining the clinical implication of plaque morphology, myocardial perfusion, and patient outcomes. The presence of positive vessel remodeling, low-attenuation plaques, napkin-ring sign, or spotty calcification on CCTA could be useful information on high-risk vulnerable plaques. The napkin-ring sign, especially, showed higher accuracy for the detection of thin-cap fibroatheroma. Recently, it was reported that cardiac 3D single-photon emission tomography/CT fusion imaging, noninvasive fractional flow reserve computed from CT, and integrated CCTA and CT myocardial perfusion were associated with improved diagnostic accuracy for the detection of hemodynamically significant CAD. Furthermore, several randomized, large clinical trials have evaluated the clinical value of CCTA for chest pain triage in the emergency department or long-term reduction in death, myocardial infarction, or hospitalization for unstable angina. In this review we discuss the role of cardiac MDCT beyond coronary angiography, including a comparison with other currently available imaging modalities used to examine atherosclerotic plaque and myocardial perfusion.

Key Words: Multidetector computed tomography; Myocardial perfusion imaging; Vulnerable plaque

Multidetector computed tomography (MDCT) is well established for more precise evaluation of coronary stenosis relative to electron-beam CT.1–3 Multicenter studies have confirmed the accuracy of 64-slice MDCT for directly visualizing and detecting coronary artery stenoses in patients with suspected coronary artery disease (CAD).4–7 Furthermore, dual-source CT (DSCT), 256-slice, and 320-detector scanner were developed to significantly improve scan times, volume coverage, and spatial resolution.8–12 With improvement in the technical aspects of coronary computed tomography angiography (CCTA), clinical practice and research are increasingly shifting toward defining the clinical implication of plaque morphology, myocardial perfusion imaging (MPI), and patient outcomes. In this review, we discuss the role of cardiac MDCT beyond coronary angiography, including a comparison with other currently available imaging modalities used to examine atherosclerotic plaque and myocardial perfusion.

Diagnosis of CAD

Conventional invasive coronary angiography (ICA) has been the gold standard for the diagnosis of CAD and clinical decision making for percutaneous coronary intervention (PCI) for more than a decade. The diagnostic accuracy of 64-slice CCTA for detecting coronary artery stenosis has been compared with ICA. Several studies have demonstrated the ability of CCTA to detect anatomically significant CAD with high negative predictive value (NPV). The CORE 64 study demonstrated that the patient-based diagnostic accuracy of quantitative CCTA for detecting stenoses ≥50% according to ICA revealed an area under the curve (AUC) of 0.93, with sensitivity of 85%, specificity of 90%, positive predictive value (PPV) of 91%, and NPV of 83%.7 The 64-slice CCTA is accurate in identifying coronary stenoses and characterizing disease severity in symptomatic patients who have coronary artery calcium scores (CACS) <600. Given its PPV of 91% and NPV of 83%, 64-slice CCTA cannot replace conventional ICA. The substudy of CORE 64 showed that the AUC for diagnostic accuracy was similar (0.93, 0.92, and 0.93, respectively) for patients with intermediate, high pretest probability for CAD, and known CAD, whereas the NPV was different (0.90, 0.83, and 0.50, respectively). For excluding obstructive CAD, CCTA was less effective in patients with calcium score ≥2600 and high pretest probability for obstructive CAD.13 In the CONFIR M study, the prevalence of observed CAD with either ≥50% diameter stenosis (CAD50) or ≥70% diameter stenosis (CAD70) was substantially lower than predicted by guideline probabilities in the overall population (18% vs. 51% for CAD50, 10% vs.
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Table 1. Studies of Detection of Significant CAD by CT

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Imaging technique</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller et al†</td>
<td>291</td>
<td>64-detector</td>
<td>85</td>
<td>90</td>
<td>91</td>
<td>83</td>
<td>87</td>
</tr>
<tr>
<td>Achenbach et al‡</td>
<td>50</td>
<td>128-detector</td>
<td>92</td>
<td>98</td>
<td>74</td>
<td>99</td>
<td>95</td>
</tr>
<tr>
<td>Dewey et al§</td>
<td>30</td>
<td>320-detector</td>
<td>78</td>
<td>98</td>
<td>75</td>
<td>99</td>
<td>97</td>
</tr>
<tr>
<td>Petcherski et al*</td>
<td>121</td>
<td>256-detector</td>
<td>97</td>
<td>97</td>
<td>75</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>Chao et al**</td>
<td>104</td>
<td>256-detector</td>
<td>94</td>
<td>95</td>
<td>78</td>
<td>99</td>
<td>94</td>
</tr>
<tr>
<td>Li et al**</td>
<td>454</td>
<td>320-detector</td>
<td>87</td>
<td>97</td>
<td>98</td>
<td>83</td>
<td>96</td>
</tr>
<tr>
<td>Westwood et al**</td>
<td>25 studies†</td>
<td>128-detector</td>
<td>87–100</td>
<td>73–98</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Kirili et al‡‡</td>
<td>17</td>
<td>64/320-detector</td>
<td>67.5</td>
<td>90</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Min et al**</td>
<td>252</td>
<td>64-detector</td>
<td>84</td>
<td>42</td>
<td>61</td>
<td>72</td>
<td>64</td>
</tr>
<tr>
<td>Rochitte et al‡‡</td>
<td>381</td>
<td>320-detector</td>
<td>92</td>
<td>51</td>
<td>53</td>
<td>92</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Meta-analysis. CAD, coronary artery disease; CT, computed tomography; CTP, CT perfusion; FFR, fractional flow reserve; PPV, positive predictive value; NPV, negative predictive value; NA, not applicable; SPECT, single-photon emission tomography.

42% for CAD70; P<0.001), driven by pronounced difference in patients with typical angina (29% vs. 86% for CAD50, 19% vs. 71% for CAD70). Determination of the pretest likelihood of angiographically significant CAD based on guideline probabilities greatly overestimated the actual ICA-observed prevalence of disease. More recent studies, performed with DSCT, 256-slice, and 320-detector scanners, confirmed the high NPV of CCTA for exclusion of anatomically significant CAD (Table 1). In a systematic review of the accuracy of DSCT for detection of arterial stenosis in some or all difficult-to-image patients, the pooled, per-patient estimates of sensitivity were 97.7% and 97.7% for patients with arrhythmias and high heart rates, respectively. The corresponding pooled estimates of specificity were 81.7% and 86.3%. The recent guidelines...
demonstrated that PR and LAP observed with CCTA were positively associated with the fibrous cap thickness measured by OCT (76±24 μm in 2-feature-positive plaques, 154±51 μm in 1-feature-positive plaques, and 192±49 μm in 2-feature-negative plaques, P<0.001).

25 Ozaki et al demonstrated that CCTA was able to successfully characterize ruptured plaques as LAP with PR; however, CCTA failed to characterize lesions at risk of intact fibrous cap-ACS, which are often referred to as plaque erosions in ACS patients.

26 We showed that the number of coronary plaques in nonculprit lesions on CCTA images was more significantly observed in acute myocardial infarction (AMI) patients than in stable angina pectoris (SAP) patients.

27 Specifically, noncalcified, mixed, and vulnerable plaques were more significantly observed in AMI patients than in SAP patients. We suggested that all 3 major coronary arteries in patients with AMI were extensively diseased and had multiple vulnerable plaques that could potentially cause another occurrence of ACS. Recently, Puchner et al demonstrated that the presence of high-risk vulnerable plaques [PR, LAP, napkin-ring sign (NRS), or spotty calcification] on CCTA increased the likelihood of ACS, independent of significant CAD and clinical risk assessment (Figure 1). 28 In particular, the presence of NRS showed higher accuracy for the detection of TCFA. NRS had a high PPV for detecting disrupted plaque confirmed by coronary angioscopy.

29 Seifarth et al showed that this sign was associated with larger necrotic/lipid core volumes as measured by histology of advanced coronary atherosclerotic plaques. 30 Maurovich-Horvat et al published by the European Society of Cardiology recommend the use of CCTA for patients at low or intermediate pretest probability for CAD in order to avoid unnecessary invasive procedures. 16 Thus, we should take into consideration identifying the patient groups for whom CCTA provides the most value.

Assessment of Coronary Vulnerable Plaque

With the development in the technical aspects of imaging, it is possible to evaluate coronary plaque quality and quantity such as can be done with intravascular ultrasound (IVUS) and optical coherence tomography (OCT). 17-19 A meta-analysis confirmed that CCTA slightly overestimated luminal area, presumably because of partial volume effects that lead to overestimation of the size of very bright structures, whereas plaque area volume, and area stenosis measurements were similar between CT and IVUS. 20

Recently, high-resolution OCT was introduced to clinical practice and can be used to evaluate fibrous cap thickness and lipid content, including for thin-cap fibroatheroma (TCFA). 21 Several studies have examined that the comparisons were CCTA vs. OCT for coronary plaque, and CCTA vs. OCT for TCFA. 18,22,23 Kashiwagi et al revealed that plaques with positive vascular remodeling (PR) and low-attenuation plaques (LAP) had the MDCT morphological features of TCFA observed with OCT, and a ring-like enhancement observed with MDCT was an important sign of TCFA. 18 Motoyama et al showed that the CT characteristics of plaques associated with acute coronary syndrome (ACS) include PR, LAP, and spotty calcification. 24 We demonstrated that PR and LAP observed with CCTA were positively associated with the fibrous cap thickness measured by OCT (76±24 μm in 2-feature-positive plaques, 154±51 μm in 1-feature-positive plaques, and 192±49 μm in 2-feature-negative plaques, P<0.001). 25 Ozaki et al demonstrated that CCTA was able to successfully characterize ruptured plaques as LAP with PR; however, CCTA failed to characterize lesions at risk of intact fibrous cap-ACS, which are often referred to as plaque erosions in ACS patients. 26 We showed that the number of coronary plaques in nonculprit lesions on CCTA images was more significantly observed in acute myocardial infarction (AMI) patients than in stable angina pectoris (SAP) patients. 27 Specifically, noncalcified, mixed, and vulnerable plaques were more significantly observed in AMI patients than in SAP patients. We suggested that all 3 major coronary arteries in patients with AMI were extensively diseased and had multiple vulnerable plaques that could potentially cause another occurrence of ACS. Recently, Puchner et al demonstrated that the presence of high-risk vulnerable plaques [PR, LAP, napkin-ring sign (NRS), or spotty calcification] on CCTA increased the likelihood of ACS, independent of significant CAD and clinical risk assessment (Figure 1). 28 In particular, the presence of NRS showed higher accuracy for the detection of TCFA. NRS had a high PPV for detecting disrupted plaque confirmed by coronary angioscopy. 29 Seifarth et al showed that this sign was associated with larger necrotic/lipid core volumes as measured by histology of advanced coronary atherosclerotic plaques. 30 Maurovich-Horvat et al reported that the NRS, which is considered a CT signature of

<table>
<thead>
<tr>
<th>Table 2. Characteristics of Imaging Modalities for Analysis of Coronary Vulnerable Plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modality</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>MDCT</td>
</tr>
<tr>
<td>IVUS</td>
</tr>
<tr>
<td>OCT</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Angioscopy</td>
</tr>
</tbody>
</table>

IVUS, intravascular ultrasound; MDCT, multidetector computed tomography; OCT, optical coherence tomography; TCFA, thin-cap fibroatheroma.
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CCTA with stress nuclear MPI for all unevaleuable arteries on CCTA. Motoyama et al evaluated the role of combined evaluation of MPI by SPECT and CCTA for risk stratification of CAD. Their cardiac event rates were significantly different between high-risk plaque (PR and/or LAP)(+) and (−) (16.1% vs. 2.7%, P=0.0013). High-risk plaque on CCTA was an independent predictor of acute coronary events, as was stenosis (+)

Table 3. Studies of Coronary Plaque Characteristics on MDCT and SF Phenomenon/Cardiac Troponin T Elevation

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>Event rate (%)</th>
<th>Minimum CT value (HU)</th>
<th>Positive remodeling index</th>
<th>Calcification</th>
<th>Ring-like appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakazawa et al</td>
<td>51</td>
<td>TNF 17.6</td>
<td>67.0±10.1</td>
<td>NA</td>
<td>NA</td>
<td>55.6%</td>
</tr>
<tr>
<td>Uetani et al</td>
<td>189</td>
<td>PMI 31.2</td>
<td>&lt;50</td>
<td>1.10±0.21</td>
<td>37.7%</td>
<td>NA</td>
</tr>
<tr>
<td>Watabe et al</td>
<td>107</td>
<td>TNF 7.5, PMI 33.6</td>
<td>43 (26.5–75.7)*</td>
<td>1.20±0.18</td>
<td>Spotty (50%)</td>
<td>31%</td>
</tr>
<tr>
<td>Kodama et al</td>
<td>40</td>
<td>SF 50</td>
<td>23.5 (9.5–40)*</td>
<td>1.5 (1.3–1.8)*</td>
<td>CPC (63%)</td>
<td>10%</td>
</tr>
<tr>
<td>Nishio et al</td>
<td>55</td>
<td>SF 20</td>
<td>&lt;40</td>
<td>&gt;1.05</td>
<td>NA</td>
<td>36%</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD except as noted. *Median and interquartile range. CPC, circumferential plaque calcification; HU, Hounsfield units; PMI, post-procedural myocardial injury; SF, slow-flow; TNF, transient no-reflow. Other abbreviations as in Tables 1,2.

Prediction of Slow-Flow Phenomenon/Cardiac Troponin T Elevation After PCI

The slow-flow, no re-flow phenomenon, or periprocedural myocardial injury (PMI), after PCI has been associated with distal embolization, especially of plaque debris, and with unfavorable clinical outcomes. Therefore, determining the pre-PCI plaque composition on MDCT may have an effect on these complications of PCI. Nakagawa et al reported that patients who experienced transient no-reflow during PCI had lower plaque CT density values in culprit lesions. Uetani et al demonstrated that PMI was associated with the volume and fraction of LAP by MDCT. We demonstrated that a CT attenuation value <55 Hounsfield units, PR (remodeling index >1.05) and spotty calcification were significant predictors of PMI; the presence of all 3 CT characteristics showed a high PPV of 94%, and their absence showed a high NPV of 90%. Kodama et al demonstrated that CCTA-verified circumferential plaque calcification with LAP and PR were determinants of slow-flow phenomenon during PCI. Nishio et al showed that finding both LAP and PR on MDCT was highly sensitive for predicting plaque debris embolization. These findings suggest that it would be worthwhile identifying vulnerable plaques by MDCT before PCI (Table 3). If the lesion has the characteristics of high-risk vulnerable plaques, a plan for preventing complications can be made before the PCI procedure.

Comparison of CCTA and Nuclear MPI

Stress nuclear MPI using single-photon emission tomography (SPECT) is an established method for assessing the functional significance of coronary stenosis and risk stratification. Although CCTA demonstrates “anatomic” stenosis and SPECT reflects “physiologic” stenosis, disagreement between CCTA ≥50% stenosis and reversible MPI defects is common. It is logically proposed that the combination of these 2 noninvasive imaging techniques would enable better evaluation of CAD and prognostic outcomes. We demonstrated that combined CCTA and stress nuclear MPI provided improved diagnostic accuracy for the noninvasive detection of CAD in comparison with 64-slice CCTA alone. The sensitivity, specificity, PPV and NPV were 95%, 80%, 69%, and 97%, respectively, for CCTA alone and 94%, 92%, 85%, 97%, respectively, for CCTA with stress nuclear MPI for all unevaleuable arteries on CCTA. Motoyama et al evaluated the role of combined evaluation of MPI by SPECT and CCTA for risk stratification of CAD. Their cardiac event rates were significantly different between high-risk plaque (PR and/or LAP)(+) and (−) (16.1% vs. 2.7%, P=0.0013). High-risk plaque on CCTA was an independent predictor of acute coronary events, as was stenosis (+)

Figure 2. Matched hybrid finding on single-photon emission computed tomography/computed tomography. The posterior (A) and anterior (B) views of ischemia of the apex (arrowheads) in a territory subtended by a stenotic left anterior descending coronary artery (arrow) as further documented in the multiplanar coronary computed tomography angiography reconstruction (C). Reprinted with permission from Pazhenkotti AP, et al.
with a summed difference score >0, and high-risk plaque had increased prognostic value over stenosis and abnormal MPI findings. Clinical outcomes, resource utilization, and subsequent patient management after CCTA vs. MPI in SAP and CAD patients have not been examined. In a pilot randomized controlled trial, patients with stable CAD undergoing CCTA and MPI experienced comparable improvements in near-term angina-related quality of life. Compared with MPI, the CCTA evaluation was associated with more aggressive medical therapy, increased coronary revascularization, lower total costs, and lower effective radiation dose. Hachamovitch et al assessed the 90-day post-test rates of catheterization and medication changes in a prospective registry of 1,703 patients without a history of CAD and an intermediate-to-high likelihood of CAD undergoing cardiac SPECT, positron emission tomography (PET), or 64-slice CCTA. Among patients with the most severe test result findings, 38–61% were not referred to catheterization, 20–30% were not receiving aspirin, 35–44% were not receiving a β-blocker, and 20–25% were not receiving a lipid-lowering agent at 90 days after the index test. Patients were more likely to undergo cardiac catheterization after CCTA than after SPECT or PET with normal/nonobstructive and mildly abnormal findings. Economic outcomes of testing are particularly important in light of rising medical care costs. The 2-year costs were significantly lower after using SPECT (US$3,965) rather than CCTA ($4,909) or PET ($6,647) in an evaluation of suspected CAD. SPECT was economically attractive compared with PET, whereas CCTA was associated with higher costs and no significant difference in mortality compared with SPECT.

CCTA has paved the way for purely noninvasive SPECT/CT hybrid imaging, directly relating individual myocardial perfusion territories to the subtending coronary artery. Cardiac 3D SPECT/CT fusion imaging can provide additional information about hemodynamic relevance and facilitate lesion interpretation by allowing exact allocation of perfusion defects to the subtending coronary artery. Pazhenkotti et al demonstrated the effect of hybrid SPECT/CT imaging in 318 consecutive patients. Referral to revascularization was higher for patients with matched abnormalities (41%), compared with those with unmatched abnormalities (11%) or those with normal studies (9%).

In low-to-intermediate likelihood patients, CCTA may well be the best initial test because of its high NPV; however, in intermediate-to-high probability patients, CCTA’s low PPV may result in unnecessary radiation exposure, and stress nuclear MPI might be a better first-line test. From the present study, we cannot definitely conclude which is the better first-line test, and we acknowledge that further head-to-head comparisons of the 2 modalities are required.

Fractional Flow Reserve (FFR), CT MPI and Delayed Enhancement (DE) Recently, the addition of physiologic measures of coronary flow by FFR to anatomic-based stenosis severity by ICA to guide decisions on coronary revascularization has improved event-free survival. Moreover, a novel noninvasive FFR measurement based on CCTA and computational fluid dynamics has been developed in clinical practice. Min et al demonstrated that use of noninvasive FFRCT plus CT for stable patients with suspected CAD was associated with improved diagnostic accuracy and discrimination vs. CT alone for the diagnosis of hemodynamically significant CAD when FFR determined at the time of ICA was the reference standard. Economic outcomes of testing are particularly important in light of rising medical care costs. The 2-year costs were significantly lower after using SPECT ($3,965) rather than CCTA ($4,909) or PET ($6,647) in an evaluation of suspected CAD. SPECT was economically attractive compared with PET, whereas CCTA was associated with higher costs and no significant difference in mortality compared with SPECT.

Figure 3. Procedure for computation of CT-derived computed fractional flow reserve (FFRCT). CTA, computed tomography angiography. Reprinted with permission from Koo BK.
because computation of \( \text{FFR}_{\text{CT}} \) requires a supercomputer.

The CORE 320 study compared the combination of CT perfusion (CTP) and coronary artery assessment with SPECT imaging and conventional ICA. \(^5\) The patient-based diagnostic accuracy defined by the AUC of integrated CCTA-CTP for detecting or excluding flow-limiting CAD was 0.87. In patients without prior MI, the AUC was 0.90 and in patients without prior CAD the AUC for combined CCTA-CTP was 0.93. For the combination of CCTA stenosis ≥50% stenosis and CTP perfusion deficit, the sensitivity, specificity, PPV, and NPV were 80%, 74%, 65%, and 86%, respectively. For flow-limiting disease defined by ICA-SPECT/MI, the accuracy of CCTA was significantly increased by the addition of CTP at both the patient and vessel levels.

Myocardial DE on MDCT enables the accurate evaluation of infarct size and has comparable results as an alternative technique to MRI in AMI. \(^5\)

We previously showed that contrast DE patterns might be reliably useful in predicting functional recovery of the post-ischemic myocardium and LV remodeling, \(^6\) and the size of the myo-

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**Table 4. Studies Reporting CT Analysis of Clinical Outcomes**

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>No. of CT detector rows</th>
<th>Follow-up (months)</th>
<th>Endpoint</th>
<th>Event rate (%)</th>
<th>CCTA result</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min et al(^6^7)</td>
<td>1,127</td>
<td>64</td>
<td>All-cause death</td>
<td>3.5</td>
<td>Moderate or severe CS</td>
<td>1.05 (1.02–1.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Any left main stenosis</td>
<td>2.65 (1.37–5.12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SSC</td>
<td>1.52 (1.09–2.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SIS</td>
<td>1.16 (1.05–1.28)</td>
</tr>
<tr>
<td>Ostrom et al(^6^8)</td>
<td>2,538</td>
<td>64</td>
<td>All-cause death</td>
<td>3.4</td>
<td>Any CAD</td>
<td>2.51 (1.47–4.25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7.1</td>
<td>1.82 (1.45–2.3)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11.3</td>
<td>2.31 (1.86–2.89)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
<td>2.59 (1.99–3.68)</td>
</tr>
<tr>
<td>Hadamitzky et al(^6^9)</td>
<td>1,584</td>
<td>16/64</td>
<td>(61–75)* Composite of death/ nonfatal MI</td>
<td>3.9</td>
<td>CAD severity</td>
<td>C-index 0.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total plaque score</td>
<td>C-index 0.66</td>
</tr>
<tr>
<td>Cho et al(^7^1)</td>
<td>7,590</td>
<td>≥64</td>
<td>(18–35)* All-cause death</td>
<td>1.8</td>
<td>Obstructive CAD</td>
<td>1.70 (1.20–2.41)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2-VD</td>
<td>2.20 (1.19–4.16)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3-VD or left main CAD</td>
<td>2.91 (1.55–5.47)</td>
</tr>
<tr>
<td>Muhlestein et al(^7^4)</td>
<td>Total 900</td>
<td>64</td>
<td>48±20 Composite of all-mortality/nonfatal MI/unstable angina</td>
<td>CCTA 6.2 Control 7.6</td>
<td>CAG: 13.3% vs. 5.1% PCI: 6.0% vs. 1.8%</td>
<td>0.80 (0.49–1.32)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CABG: 2.9% vs. 1.3%</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean±SD except as noted. *Median and interquartile range. CABG, coronary artery bypass graft surgery; CAG, coronary angiography; CCTA, coronary CT angiography; CI, confidence interval; CS, coronary stenosis; PCI, percutaneous coronary intervention; SSC, segment stenosis score; SIS, segment involvement score; VD, vessel disease. Other abbreviations as in Table 1.
cardiac contrast DE might be a very early predictive marker for future clinical cardiac events in patients with AMI (Figure 4). Amanieu et al reported that the presence of a hypoenhanced area had high specificity for the prediction of microvascular obstruction on DE-MRI. Recently, Kurobe et al demonstrated that targeted spatial-frequency filtration with image averaging can significantly improve the image quality of DE CT and considerably enhances interobserver reproducibility of infarct sizing in comparison with conventional half-scan reconstruction. However, the clinical utility of myocardial DE on MDCT is currently limited because of relatively poor contrast-to-noise ratio and artifacts. CTP was not superior to nuclear MPI for assessment of myocardial viability. A preliminary study of delayed plaque enhancement by CCTA demonstrated that serial CT acquisitions at a short imaging interval following contrast injection should allow analysis of plaque enhancement as a marker of intraplaque neovascularization.

Prognostic Value of CCTA

The ability to rule out significant CAD in symptomatic patients with a low pretest likelihood of disease makes CT a useful tool for diagnosing the many patients with acute chest pain who are often at a low risk of actual ACS. Recently, several randomized large trials have evaluated the clinical value of CCTA for chest pain triage in the emergency department. Litt et al demonstrated that patients in the CCTA group had a higher rate of discharge from the emergency department (49.6% vs. 22.7%), a shorter length of stay (median, 18.0 h vs. 24.4 h; P<0.001), and a higher rate of detection of CAD (9.0% vs. 3.5%), as compared with patients receiving traditional care. Hoffmann et al demonstrated that after early CCTA, as compared with standard evaluation, the mean length of stay in the hospital was reduced by 7.6 h (P<0.001) and more patients were discharged directly from the emergency department (47% vs. 12%, P<0.001). No patient with negative findings on CT experienced AMI, and only 23 MI occurred in the entire patient cohort. The use of CCTA has been advocated as a potentially valuable atherosclerotic imaging tool for risk stratification. Several studies have explored the prognostic value of CCTA, primarily limited to symptomatic populations. Hadamitzky et al reported new data on CCTA that predicted both death and MI, as well as the need for subsequent revascularizations out to 5 years. CCTA imaging may be a valuable tool for assessment of long-term prognosis in patients with suspected CAD (Table 4). Atherosclerosis imaging such as CACS or carotid intima-media thickness for individuals without chest pain has been advocated recently by professional consensus guidelines. CACS has been demonstrated to improve risk re-stratification above and beyond global risk scores that combine traditional CAD risk factors. However, in the CONFIRM registry, the additional risk-predictive advantage of CCTA was not clinically meaningful compared with a risk model based on CACS. Recently, the FACTOR-64 randomized trial evaluated whether routine CCTA screening of asymptomatic patients with diabetes could beneficially influence clinical outcomes and risk factor control. Overall, annual event rates in both the control and intervention groups were low (<2%), and outcomes (death, MI, or unstable angina) did not differ significantly between the CCTA and no CCTA groups after a mean of 4 years of follow-up. At present, these findings do not support CCTA screening for risk assessment of individuals without chest pain.

Conclusions

Current guidelines encourage the use of CCTA as the first-line imaging modality for the diagnosis of patients with low and intermediate likelihood for CAD. CCTA could also provide useful information on high-risk vulnerable plaques, such as PR, LAP, NRS, or spotty calcification. With further improvements in CT technology, CCTA could become useful for accurate detection of coronary plaque in clinical practice. Assessment of both coronary stenosis and perfusion has great potential application in further advancing the evaluation of patients with CAD. Further large studies will be needed to confirm that an integrated, multi-modality imaging approach will become the gold standard for noninvasive evaluation in the clinical examination of coronary plaque morphology, myocardial perfusion, and outcome.

Source of Funding

None.

Disclosures

No author has a real or perceived conflict of interest.

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