TITLE: Multi-Slice Computed Tomography Coronary Angiography for Coronary Artery Disease: A Review of the Clinical Effectiveness and Guidelines

DATE: 25 February 2009

CONTEXT AND POLICY ISSUES:

Coronary artery disease (CAD) manifests as angina, silent ischemia, unstable angina, myocardial infarction, arrhythmias, heart failure, and sudden death. The underlying cause of CAD is atherosclerosis, consisting of plaque formation on the luminal surface of the coronary arteries, which supply blood to the heart muscle. Angina occurs when there is more than 50% stenosis (reduction in cross-sectional area) of the artery.

The standard reference for diagnosis of CAD is still conventional coronary angiography (CA), with the advantage of high spatial and temporal resolution. However, its diagnostic value has been challenged due to its invasiveness and high expenditure by the introduction of multi-slice computed tomography (CT) angiography.

Multi-slice CT angiography is a potential tool for the assessment of CAD. It can provide information about stenosis in coronary arteries and coronary artery by-pass grafts, ventricular size and function, cardiac structure and masses, pulmonary vein anatomy, myocardial perfusion, and coronary artery plaque. The CT scanners have an x-ray source and sensors mounted on opposite sides of a gantry that continuously rotate around the body. The first multi-slice CT scanner had two parallel banks of x-ray detectors to acquire two slices for each gantry rotation was developed in 1991. The advancement of the technology quickly developed scanners with four slices, then 16 slices, and current scanners have up to 64 slices. A prototype of 256-slice detectors is in development. Fast rotation speed of the gantry and thin slice (sub-millimeters) collimation substantially improve temporal and spatial resolution. The multi-slice design shortens data acquisition time to less than 20 seconds. The first dual-source multi-slice CT was recently launched, in which two pairs of x-ray sources and multiple detectors are mounted at 90 degrees to each other.
In performing a scan, contrast media is injected through an intravenous cannula. Beta-blockers may need to be given to slow the heart beat and improve image quality. Contraindications to contrast enhanced CT are renal failure, inability to lie flat, contrast media allergy, and caution in pregnancy. Patients are also excluded for cardiac CT if they have irregular heart beat (atrial fibrillation, frequent ectopic beats), inability to breath-hold, tachycardia or pacing wires, and metallic valves. The dual source scanners, owing to the higher temporal resolution, can permit the scanning of patients with irregular rhythms and reduce the need for beta-blocker administration.

The main drawback with multi-slice CT is the radiation dose. Currently, a non-invasive angiogram receives a dose of 10-15 mSv, which is twice the dose of conventional angiogram. The radiation dose can be reduced by lowering the x-ray power during less important parts of the cardiac cycle (e.g., systole) – termed “dose modulation”. There is evidence suggesting that the radiation dose could be lowered to 5-6 mSv with little impact on diagnostic quality of the scans.

Coronary artery segments are classified according to the American Heart Association classification model, which are used to conduct different levels of analysis when evaluating CT coronary angiography. These segments are as follows: The right coronary artery included segment 1, proximal segment; segment 2, middle segment; segment 3, distal segment; segment 4a, posterior descending coronary artery; and segment 4b, posterolateral artery. The left main coronary artery was segment 5. The left anterior descending coronary artery included segment 6, proximal segment; segment 7, middle segment; segment 8, distal segment; segment 9, first diagonal segment; and segment 10, second diagonal segment. The circumflex branch of the left coronary artery included segment 11, proximal segment; segment 12, first marginal segment; segment 13, middle segment; segment 14, second marginal segment; segment 15, distal segment; and segment 16, intermediate branch.

This report reviews the clinical effectiveness of multi-slice CT coronary angiography for the diagnosis and evaluation of patients with CAD. This report also summarizes key recommendations of current guidelines on the use of multi-slice CT angiography in the diagnosis and evaluation of CAD.

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of multi-slice computed tomography coronary angiography for the diagnosis and evaluation of patients with coronary artery disease?

2. What are the guidelines for the use of multi-slice computed tomography coronary angiography for the diagnosis and evaluation of patients with coronary artery disease?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including OVID Medline, The Cochrane Library (Issue 1, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include articles published between 2002 and January 2009, and are limited to English language publications only. Filters were applied to limit the retrieval to systematic reviews, health technology assessments, meta-analyses, randomized controlled trials, and guidelines.
SUMMARY OF FINDINGS:

Two health technology assessments, systematic reviews and meta-analyses, and three guidelines were identified. No randomized controlled trials were found.

Health technology assessments

The health technology assessment (HTA) report of the Belgian Health Care knowledge Centre (2008) summarized current evidence supporting the use of 64-slice CT angiography as a diagnostic aid in patients suspected for CAD. The HTA was primarily concerned with the diagnostic use of multi-slice CT as an imaging technique for native coronary arteries, by which coronary bypass grafts and intracoronary stents were excluded.

This HTA reviewed other recent HTA reports, as well as recently published meta-analyses on the diagnostic performance of 64-slice CT in the diagnosis of CAD, and identified key points addressing the clinical effectiveness, safety, organizational issues, and patient issues of multi-slice CT. Key points on cost-effectiveness were not included in this summary.

Clinical effectiveness of multi-slice CT

- In recent international HTA reports, multi-slice CT is not recommended as a substitute for conventional CA for the diagnosis of CAD or in the evaluation of acute chest pain in the emergency department. (p.24)

- Recently published meta-analyses on the diagnostic performance of 64-slice CT in the diagnosis of CAD revealed a good sensitivity and an acceptable specificity, obtained from selected intermediate to high pre-test likelihood populations. (p.26)

- All the trials included in these meta-analyses selected patients that were already scheduled for conventional CA, questioning the external validity of the findings. (p.26)

- The diagnostic performance of multi-slice CT has been tested in trials that enrolled patients selected for conventional CA with a high pre-test likelihood of CAD. A negative likelihood ratio of <0.1 indicates that in these populations multi-slice CT performs very well to rule out obstructive CAD. (p.36)

- It has not been shown that the available trial results can be extrapolated to populations in which the use of multi-slice CT is currently advocated. (p.36)

- Coronary artery calcium load, body mass index, and high or irregular heart rates impose restrictions on the diagnostic performance of multi-slice CT, even with dual source 64-slice CT. (p.36)

- There is an urgent need for evidence on (1) the diagnostic performance of multi-slice CT in the real world clinical practice, (2) its effect on patient outcomes (quality of life, prevention of infarction, prolongation of life) and (3) its cost-effectiveness as compared to diagnostic pathways in which multi-slice CT is not embedded. (p.37)

Safety of multi-slice CT

- The high radiation dose is the most undesirable safety disadvantage of 64-slice CT. The estimated mean effective radiation dose per patient is 15 and 20 mSv and with modulated protocols 7 and 14 mSv for males and females, respectively. (p.40)

- It is unclear whether radiation saving algorithms that are currently under investigation will preserve the diagnostic performance of the test. (p.40)

- Cancer risk induced by multi-slice CT can be substantial, and depends on age and gender. In elderly men, the excess risk of fatal cancer is estimated at 1/5000, whereas in younger women, it can be as high as 1/200. (p.40)
Safety issues are also related to contrast medium administration and the need for beta-blocker pre-medication in many patients. (p.40)

Organizational issues

- The initial investment cost of a multi-slice CT scanner ranges from €850,000 (64-slice CT scanner) to €2 million (scanner with higher number of detectors). Additionally, the cost for software for the coronary applications amounts to 20% of the device cost. The post-processing software is €100,000 and its updating €20,000 per year. The yearly maintenance cost is €100,000. (p.58)

Patient issues

- Diagnostic tests may affect patients in many different ways. Independent of being true or false, both positive and negative test results may induce adverse effects that should be taken into account when considering the submission of a patient to multi-slice CT of the coronary arteries. (p.60)
- Positive and negative likelihood ratios of 64-slice CT for the diagnosis of obstructive CAD in everyday practice are unknown. (p.60)

The Australian HTA (2007) prepared by the Medical Services Advisory Committee assessed the use of multi-slice CT angiography for four clinical indications: 1) evaluation of patients with symptoms consistent with coronary ischemia (including evaluation of coronary by-pass graft patency and coronary artery stent stenosis or patency); 2) exclusion of coronary artery anomaly or fistula; 3) evaluation of coronary arteries in patients with cardiomyopathy; and 4) evaluation of coronary arteries in patients undergoing non-coronary cardiothoracic surgery.

The followings are key points drawn from the assessment in terms of safety and effectiveness of multi-slice CT angiography.

Safety

- Complications may occur from multi-slice CT angiography as a result of the contrast media administered to allow visualization of the coronary arteries.
- There is a risk from radiation exposure.
- Multi-slice CT angiography is safer than conventional CA by avoiding the risks associated with an invasive procedure.

Indication 1 – Evaluation of patients with symptoms consistent with coronary ischemia

- No direct impact of multi-slice CT angiography on patient outcomes available to date.
- A large body of evidence assessed the diagnostic accuracy of multi-slice CT angiography, consistently suggesting an overall good diagnostic performance in assessing coronary arteries in patients with symptoms consistent with coronary ischemia, when compared with conventional CA.
- Limited evidence exists concerning the impact of the multi-slice CT angiography results on patient management.
- No studies comparing diagnostic effectiveness of multi-slice CT angiography with stress imaging tests met the inclusion criteria.
- Due to its consistently proved very high negative predictive value, multi-slice CT angiography is useful in clinical practice to rule out significant CAD.
- The diagnostic performance of multi-slice CT angiography depends on good image quality and the exclusion of severe calcifications. Technical development is rapid and continuous, with consecutive generations of scanners showing improved technical and diagnostic performance.
• More evidence is needed to assess the impact of multi-slice CT angiography on patient clinical management and outcomes.

• At the present time, there is not enough evidence to support replacement of CA by multi-slice CT angiography. CA is still the gold standard but multi-slice CT angiography is a viable alternative in selected patient subgroups.

Indication 2 – Exclusion of coronary anomaly and fistula

• No studies meeting the inclusion criteria were found.

• A number of case reports suggest that the multi-slice CT angiography is increasingly used in clinical practice for this particular indication.

Indication 3 – Evaluation of coronary arteries in patients with cardiomyopathy

• No literature was identified

Indication 4 – Evaluation of coronary arteries in patients undergoing non-coronary cardiothoracic surgery

• Limited but good quality evidence suggests that multi-slice CT angiography has the ability to rule out CAD in patients awaiting valve surgery. (p.162 -163)\textsuperscript{12}

Systematic reviews and meta-analyses

Mowatt \textit{et al}. (2008)\textsuperscript{13} assessed the clinical effectiveness, in different patient groups, of the use of 64-slice or higher CT angiography, instead of invasive CA, for diagnosing people with suspected CAD and assessing people with known CAD. Forty-one diagnostic accuracy studies (21 full-text papers and 20 abstracts) and five prognostic studies (one full-text paper and four abstracts) were included. Over 2500 and 1700 people were enrolled in the diagnostic and prognostic studies, respectively. The overall quality of the full-text diagnostic accuracy studies was reasonably good as measured by the modified QUADAS checklist.

Table 1 summarizes the pooled estimates of the diagnostic accuracy of 64-slice CT angiography for detection of CAD with respect to different levels of analysis. The reference standards were either invasive CA or long-term follow-up participants. The cut-off for a positive result was ≥50\% stenosis. There was no evidence of substantial statistical heterogeneity in terms of sensitivity or specificity in patient-level analysis, left main artery analysis, and coronary artery bypass graft (CABG) analysis. There was evidence of substantial statistical heterogeneity across the studies in terms of sensitivity or specificity for segment-level analysis, left anterior descending (LAD) artery analysis, and left circumflex (LCX) artery analysis. There was evidence of substantial statistical heterogeneity across the studies in terms of sensitivity but not specificity for proximal LAD artery analysis and right coronary artery (RCA) analysis. For stents or stented segment analysis, there was no evidence of substantial heterogeneity in terms of sensitivity, but there was in terms of specificity.
Table 1: Pooled estimates of the diagnostic accuracy of 64-slice CT angiography

<table>
<thead>
<tr>
<th>Levels of analysis</th>
<th>No of included studies (No of patients)</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>Median PPV, % (range)</th>
<th>Median NPV, % (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-level</td>
<td>18 studies (N= 1176)</td>
<td>99 (97 to 99)</td>
<td>89 (83 to 94)</td>
<td>93 (64 to 100)</td>
<td>100 (86 to 100)</td>
</tr>
<tr>
<td>Segment-level</td>
<td>17 studies (N= 1078)</td>
<td>90 (85 to 94)</td>
<td>97 (95 to 98)</td>
<td>76 (44 to 93)</td>
<td>99 (95 to 100)</td>
</tr>
<tr>
<td>Left main artery</td>
<td>5 studies (N= 408)</td>
<td>95 (84 to 99)</td>
<td>100 (99 to 100)</td>
<td>100 (99 to 100)</td>
<td>100 (all 100)</td>
</tr>
<tr>
<td>LAD artery</td>
<td>7 studies (N= 511)</td>
<td>92 (83 to 97)</td>
<td>96 (91 to 98)</td>
<td>86 (63 to 100)</td>
<td>98 (95 to 100)</td>
</tr>
<tr>
<td>Proximal LAD artery</td>
<td>5 studies (N= 369)</td>
<td>97 (87 to 99)</td>
<td>97 (90 to 99)</td>
<td>95 (85 to 100)</td>
<td>98 (90 to 100)</td>
</tr>
<tr>
<td>LCX artery</td>
<td>7 studies (N= 511)</td>
<td>85 (69 to 94)</td>
<td>96 (92 to 99)</td>
<td>81 (56 to 100)</td>
<td>98 (93 to 100)</td>
</tr>
<tr>
<td>RCA</td>
<td>7 studies (N= 511)</td>
<td>87 (77 to 95)</td>
<td>97 (92 to 98)</td>
<td>82 (74 to 91)</td>
<td>98 (94 to 100)</td>
</tr>
<tr>
<td>Stents or stented segment</td>
<td>6 studies (N= 319)</td>
<td>89 (68 to 97)</td>
<td>94 (83 to 98)</td>
<td>77 (33 to 100)</td>
<td>96 (71 to 100)</td>
</tr>
<tr>
<td>CABG</td>
<td>4 studies (N= 543)</td>
<td>99 (95 to 100)</td>
<td>96 (86 to 99)</td>
<td>93 (90 to 95)</td>
<td>99 (98 to 100)</td>
</tr>
</tbody>
</table>

CABG: coronary artery bypass graft; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery; PPV: positive predictive value; NPV: negative predictive value; No: number

The results in table 1 show that 64-slice CT angiography was highly sensitive for patient-based detection of significant CAD, while the NPV was very high. In segment-level analysis compared with patient-based detection, sensitivity was lower and specificity higher, while the median NPV was similar. Although segmental analysis is useful to validate the accuracy of the test, patient-level data are more useful in determining management. The 64-slice CT performance for identifying in-stent restenosis was reasonably good, but it may vary according to the type, diameter, and location of the stent. The performance of 64-slice CT angiography was very good in assessing graft patency. Overall, 64-slice CT is almost as good as invasive CA in terms of detecting true positives. However, it is poorer in its rate of false positives.

The evidence from the few studies (one full text and four abstracts) reporting prognostic usefulness of 64-slice CT angiography suggests that it can affect the way in which people presenting with acute coronary syndrome are managed and reduced the need for some hospital admissions and invasive CA. However, the patients were of low-risk and had a follow-up of only 30 days.

The authors concluded that the main value of 64-slice CT might be a useful tool to rule out significant CAD. It seems likely that diagnostic strategies involving 64-slice CT will still require invasive CA for CT test positives, to identify false positives and provide other information that CT currently does not. It is unlikely that 64-slice CT could replace CA in assessment for revascularization of patients, particularly as angiography and angioplasty are often done on the same occasion.
Meijer et al. (2008)\textsuperscript{14} assessed the diagnostic performance of 40- and 64-slice multi-detector CT angiography compared with invasive CA for the detection of significant ($\geq 50\%$) stenosis. Twenty-two studies on 40- and 64-slice CT angiography were included in meta-analysis.

Table 2 summarizes the pooled estimates of the diagnostic accuracy of 40- and 64-slice CT angiography for detection of CAD with respect to different levels of analysis. There was no evidence of substantial statistical heterogeneity in terms of sensitivity or specificity in patient-level analysis. There was evidence of substantial statistical heterogeneity across the studies in terms of sensitivity or specificity for segment-level analysis.

<table>
<thead>
<tr>
<th>Levels of analysis</th>
<th>No of included studies</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>SROC (AUC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>20</td>
<td>97.7 (96.2 to 98.7)</td>
<td>91.0 (88.5 to 93.1)</td>
<td>0.984</td>
</tr>
<tr>
<td>All segments</td>
<td>12</td>
<td>90.8 (89.0 to 92.4)</td>
<td>95.7 (95.2 to 96.1)</td>
<td>0.986</td>
</tr>
<tr>
<td>Proximal segments</td>
<td>12</td>
<td>94.2 (92.3 to 95.7)</td>
<td>94.1 (93.4 to 94.8)</td>
<td>0.986</td>
</tr>
<tr>
<td>Distal segments</td>
<td>12</td>
<td>84.8 (81.1 to 88.0)</td>
<td>96.9 (96.4 to 97.4)</td>
<td>0.982</td>
</tr>
</tbody>
</table>

CI: confidence interval; SROC: summary receiver operating characteristic; AUC: area under curve; No: number

The results in Table 2 show that sensitivities and specificities were good-to-excellent for evaluation on a per-patient as well as on a per-segment basis. Sensitivity was better for proximal than for distal coronary artery segments. The areas under curve (AUC) of the summary receiver operating characteristic (SROC) curves [plotting sensitivity (i.e., true positive) against 1-specificity (i.e., false positive)] were closer to 1 in all levels of analysis, indicating that the accuracy of the test was close to perfect.

The authors concluded that the current generation of 40- and 64-slice multi-detector CT angiography scanners had high diagnostic accuracy in detecting or ruling out significant coronary artery stenosis, with better results for proximal than for distal coronary artery segments.

Di Tanna et al. (2008)\textsuperscript{15} assessed the diagnostic accuracy of multi-slice CT angiography ($\geq 16$-slice). The reference standard was the invasive CA. Data on diagnostic accuracy were from 56 studies, accounting for 3764 patients. Of the 56 studies, 35 studies (2499 patients) were of 16-slice CT angiography and 21 studies (1265 patients) were of $>16$-slice CT angiography. The overall prevalence or pre-test probability of CAD was 56.7\% (95\% CI: 55.1\% to 58.3\%). There was evidence of substantial statistical heterogeneity across the studies in terms of sensitivity or specificity from pooling of all studies and studies of 16-slice. There was no evidence of substantial statistical heterogeneity in terms of sensitivity or specificity from pooling of studies of $>16$-slice. Table 3 summarizes the pooled estimates of the diagnostic accuracy of multi-slice ($\geq 16$-slice) CT angiography for detection of CAD.
Table 3: Pooled estimates of the diagnostic accuracy of multi-slice (≥16-slice) CT angiography

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
<th>Posttest positive probability* % (95% CI)</th>
<th>Posttest negative probability** % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies</td>
<td>93 (91 to 95)</td>
<td>83 (79 to 87)</td>
<td>5.4 (4.4 to 6.7)</td>
<td>0.09 (0.07 to 0.12)</td>
<td>87.7 (84.3 to 90.3)</td>
<td>10.7 (7.9 to 14.4)</td>
</tr>
<tr>
<td>Studies of 16-slice</td>
<td>91 (89 to 94)</td>
<td>79 (73 to 84)</td>
<td>4.3 (3.4 to 5.3)</td>
<td>0.13 (0.09 to 0.17)</td>
<td>84.8 (80.7 to 88.1)</td>
<td>14.2 (10.3 to 19.2)</td>
</tr>
<tr>
<td>Studies of &gt;16-slice</td>
<td>97 (95 to 99)</td>
<td>91 (88 to 95)</td>
<td>8.6 (6.1 to 12.2)</td>
<td>0.06 (0.04 to 0.08)</td>
<td>91.9 (88.2 to 94.5)</td>
<td>6.7 (4.4 to 10.1)</td>
</tr>
</tbody>
</table>

CI: confidence interval; LR+: likelihood ratio of a positive test; LR-: likelihood ratio of a negative test.
*Posttest positive probability or posttest probability of disease given a positive test is equivalent to positive predictive value.
**Posttest negative probability or posttest probability of disease given a negative test is equal to 1 minus negative predictive value.

The results from pooling all studies (Table 3) show that a positive multi-slice CT finding [pooled likelihood ratio (LR)+: 5.4 (4.4 to 6.7)] increased the probability of CAD from 56.7% (55.1% to 58.3%) to 87.7% (84.3% to 90.3%), whereas a negative multi-slice CT finding (pooled LR-: 0.09 (0.07 to 0.12) decreased the probability of CAD from 56.7% (55.1% to 58.3%) to 10.7% (7.9% to 14.4%). Corresponding figures for 16-slice and >16-slice studies showed a moderate increase (+8.4%) in posttest positive probability (84.8% for 16-slice versus 91.9% for >16-slice) and a substantial decrease (-52.9%) in posttest negative probability (14.2% for 16-slice versus 6.7% for >16-slice).

The authors concluded that multi-slice CT angiography is a promising technology for the assessment of coronary artery stenosis.

Stein et al. (2008) assessed the accuracy of 64-slice CT coronary angiography for the diagnosis of coronary artery disease. Results of 64-slice CT coronary angiography were compared with invasive CA or intravascular ultrasound. Significant stenosis was defined as ≥50% stenosis; high grade stenosis was defined as ≥70% stenosis. Forty-five studies were included for analysis.

The pooled sensitivity of 64-slice CT for significant (≥50%) stenosis was ≥90% in patient-based analysis, named vessels, segments, and coronary bypass grafts. The sensitivity in other types of analysis was 80% to 88%. The pooled specificity was 88% in patient-based analysis, and ≥90% at individual sites. Positive predictive values ranged from 91% to 93% for patient-based analysis, left main coronary artery, and coronary artery bypass grafts, but ranged from 69% to 84% elsewhere. Negative predictive values were 96% to 100%. Positive likelihood ratios were 8.0 in patient-based analysis and ≥9.7 at specific sites. Negative likelihood ratios were <0.1 in most levels of analysis.

The authors concluded that the negative results of 64-slice CT angiography reliably excluded significant coronary disease. However, positive results with CT angiography still require confirmation.

Sun et al. (2008) assessed the diagnostic value of 64-slice CT angiography in the detection of coronary artery disease when compared to conventional coronary angiography (CA). Significant stenosis was defined as >50% stenosis of the coronary artery lumen. Only studies with at least
10 patients comparing 64-slice CT angiography with conventional CA in the detection of CAD were included. Fifteen studies were included for analysis.

Table 4 summarizes the pooled estimates of the diagnostic accuracy of 64-slice CT angiography for detection of CAD with respect to different levels of analysis.

Table 4: Pooled estimates of the diagnostic accuracy of 64-slice CT angiography

<table>
<thead>
<tr>
<th>Level of analysis</th>
<th>No of studies</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-based</td>
<td>12</td>
<td>97 (94 to 99)</td>
<td>88 (79 to 97)</td>
<td>94 (91 to 97)</td>
<td>95 (90 to 99)</td>
</tr>
<tr>
<td>Vessel-based</td>
<td>6</td>
<td>92 (85 to 99)</td>
<td>92 (85 to 99)</td>
<td>78 (66 to 91)</td>
<td>98 (96 to 99)</td>
</tr>
<tr>
<td>Segment-based</td>
<td>12</td>
<td>90 (85 to 94)</td>
<td>96 (95 to 97)</td>
<td>75 (68 to 829)</td>
<td>98 (98 to 99)</td>
</tr>
<tr>
<td>LM artery</td>
<td>6</td>
<td>100</td>
<td>99 (97 to 100)</td>
<td>90 (69 to 100)</td>
<td>100</td>
</tr>
<tr>
<td>LAD artery</td>
<td>6</td>
<td>93 (84 to 99)</td>
<td>93 (89 to 97)</td>
<td>80 (65 to 94)</td>
<td>98 (96 to 99)</td>
</tr>
<tr>
<td>RCA</td>
<td>6</td>
<td>93 (89 to 98)</td>
<td>92 (82 to 99)</td>
<td>82 (75 to 89)</td>
<td>97 (95 to 99)</td>
</tr>
<tr>
<td>LCX artery</td>
<td>6</td>
<td>83 (82 to 99)</td>
<td>91 (815 to 99)</td>
<td>79 (71 to 869)</td>
<td>97 (95 to 100)</td>
</tr>
</tbody>
</table>

LM: left main; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery; PPV: positive predictive value; NPV: negative predictive value; No: number

The pooled sensitivity, specificity, positive predictive values, and negative predictive values in different levels of analysis ranged from 83% to 100%, 88% to 99%, 75% to 94%, and 95% to 100%, respectively. No significant difference was found in the diagnostic accuracy of the 64-slice CT in the detection of CAD when comparison was performed either among four main coronary arteries, or between proximal, middle, or distal segments (p>0.05). The authors concluded that 64-slice CT has a high diagnostic accuracy in the detection of CAD.

d’Othée et al. (2008)\textsuperscript{18} reviewed the diagnostic accuracy of contrast enhanced coronary CT angiography including the electron beam CT and multi-slice (4- to 8-slice, 16-slice, and 64-slice) CT. Only the results of multi-slice CT are presented here. Twenty eight studies using multi-slice CT (1668 patients) were included for the analysis. Heterogeneity among studies was substantial. Table 5 summarizes the pooled sensitivity and specificity of multi-slice CT angiography for detection of CAD. The conventional CA was the reference standard.

Table 5: Pooled sensitivity and specificity of multi-slice CT angiography

<table>
<thead>
<tr>
<th>Level of analysis</th>
<th>No of studies (No of patients)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-based</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-/8-slice</td>
<td>11 (588)</td>
<td>97</td>
<td>81</td>
</tr>
<tr>
<td>• 16-slice</td>
<td>12 (772)</td>
<td>99</td>
<td>83</td>
</tr>
<tr>
<td>• 64-slice</td>
<td>5 (308)</td>
<td>98</td>
<td>92</td>
</tr>
<tr>
<td>All segments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-/8-slice</td>
<td>11 (588)</td>
<td>89</td>
<td>84</td>
</tr>
<tr>
<td>• 16-slice</td>
<td>12 (772)</td>
<td>86</td>
<td>95</td>
</tr>
<tr>
<td>• 64-slice</td>
<td>5 (308)</td>
<td>98</td>
<td>91</td>
</tr>
<tr>
<td>Assessable segments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-/8-slice</td>
<td>11 (588)</td>
<td>85</td>
<td>96</td>
</tr>
</tbody>
</table>
Diagnostic accuracy (i.e. AUC) results obtained from the SROC curves varied with CT scanner type improving from 4-/8-slice to 64-slice CT. The authors concluded that advances in CT technology have resulted in increases in diagnostic accuracy.

Vanhoenacker et al. (2007)\(^{19}\) assessed the diagnostic performance of multi-slice (≥4-slice) CT angiography in the emergency department setting for detection of non-ST-elevation myocardial infarction and unstable angina pectoris. Significant stenosis was defined as ≥50% stenosis of the coronary artery lumen. Catheter angiography was used as the reference standard. Nine studies (566 patients) were included for analysis. Five studies were on 64-slice CT, one study on 32-slice, 2 studies on 16-slice, and one study on 4-slice.

The pooled diagnostic odd ratio was 132 (95% CI, 51 to 341), sensitivity was 95% (95% CI, 90 to 98), specificity was 90% (95% CI, 87 to 93), positive LR was 8.6 (95% CI, 5.0 to 14.7) and negative LR was 0.12 (95% CI, 0.06 to 0.21).

The authors concluded that multi-slice CT angiography performs good to excellent in the diagnosis of CAD in the acute setting and it can be used for early exclusion of non-ST-elevation myocardial infarction and unstable angina pectoris in patients in the emergency department.

Hamon et al. (2007)\(^{20}\) performed a meta-analysis to compare the diagnostic performance of 16- versus 64-slice CT angiography for diagnosis of CAD. Invasive CA was used a reference standard. Significant stenosis was defined as >50% stenosis of the coronary artery lumen. Thirty seven studies were included for analysis. Twenty-eight studies had data available for a patient-based analysis, of which 16 studies (1292 patients) were of 16-slice CT and 12 studies (695 patients) were of 64-slice CT. Thirty-three studies had data available for a segment-based analysis, of which 20 studies (16,510 segments) were of 16-slice CT and 13 studies (10,388 segments) were of 64-slice CT.

Table 6 summarizes the pooled estimates of the diagnostic accuracy of 16-slice and 64-slice CT angiography for detection of CAD with respect to patient-based and segment-based level of analysis. Heterogeneity was significant (p<0.001) for all diagnostic performance measures.

### Table 6: Pooled estimates of the diagnostic accuracy of 16-slice and 64-slice CT angiography

<table>
<thead>
<tr>
<th>Analysis and CT scanner type</th>
<th>Sensitivity (%(95% CI))</th>
<th>Specificity (%(95% CI))</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
<th>DOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>95 (93 to 96)</td>
<td>69 (66 to 73)</td>
<td>79 (76 to 82)</td>
<td>92 (88 to 94)</td>
<td>3.5 (2.7 to 5.9)</td>
<td>0.07 (0.04 to 0.13)</td>
<td>72 (31 to 166)</td>
</tr>
<tr>
<td>Segment</td>
<td>77 (75 to 79)</td>
<td>91 (91 to 92)</td>
<td>60 (59 to 62)</td>
<td>96 (96 to 96)</td>
<td>17.4 (9.9 to 30.5)</td>
<td>0.14 (0.06 to 0.21)</td>
<td>122 (52 to 286)</td>
</tr>
</tbody>
</table>

Multi-Slice CT Angiography for CAD
The results showed that pooled diagnostic performance measures improved with 64-slice CT compared with 16-slice CT in a per-segment analysis. In per-patient analysis, there was no significant improvement between 16-slice CT and 64-slice CT in terms of sensitivity and NPV. The high NPV of 16-slice (92%) and 64-slice (96%) made them both excellent tools to rule out CAD. The real improvement in the comparison of 16-slice and 64-slice CT on a per-patient basis was observed with the significant increase in specificity (69% versus 90%, p<0.001) and in PPV (79% versus 93%, p<0.001) with the 64-slice CT. Thus, both 16-slice and 64-slice CT exhibited a high sensitivity and NPV at the clinically relevant patient-based level. However, the improvement in technology in the 64-slice CT led to an increase in specificity and PPV, representing a major advantage of 64-slice CT compared with 16-slice CT.

Vanhoenacker et al. (2007)²¹ assessed the diagnostic performance of multi-slice CT angiography for the detection of CAD. The conventional CA was used as a reference standard. The cut-off for a positive result was >50% stenosis. Fifty-four studies were included in the meta-analysis. Of those 54 studies, 22 were with 4-slice CT, 26 with 16-slice CT, and 6 with 64-slice CT angiography. Table 7 summarizes the pooled estimates of the diagnostic accuracy of 4-slice, 16-slice, and 64-slice CT angiography for detection of CAD with respect to segment-based, vessel-based, and patient-based level of analysis. Heterogeneity was present among the studies on all levels.

Table 7: Pooled sensitivity, specificity, and overall diagnostic performance of multi-slice CT angiography according to type of analysis and CT scanner

<table>
<thead>
<tr>
<th>Analysis and CT scanner type</th>
<th>No of studies</th>
<th>Combined data*</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>Log DOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per-segment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-slice</td>
<td>3</td>
<td>491</td>
<td>87 (78 to 96)</td>
<td>87 (73 to 100)</td>
<td>4.0 (2.1 to 5.9)</td>
</tr>
<tr>
<td>• 16-slice</td>
<td>6</td>
<td>1601</td>
<td>93 (89 to 97)</td>
<td>92 (89 to 96)</td>
<td>4.9 (3.9 to 5.8)</td>
</tr>
<tr>
<td>• 64-slice</td>
<td>2</td>
<td>597</td>
<td>95 (91 to 99)</td>
<td>93 (90 to 95)</td>
<td>5.5 (4.5 to 6.5)</td>
</tr>
<tr>
<td>Per-vessel</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-slice</td>
<td>2</td>
<td>597</td>
<td>95 (91 to 99)</td>
<td>93 (90 to 95)</td>
<td>5.5 (4.5 to 6.5)</td>
</tr>
<tr>
<td>• 16-slice</td>
<td>6</td>
<td>1601</td>
<td>93 (89 to 97)</td>
<td>92 (89 to 96)</td>
<td>4.9 (3.9 to 5.8)</td>
</tr>
<tr>
<td>• 64-slice</td>
<td>2</td>
<td>597</td>
<td>95 (91 to 99)</td>
<td>93 (90 to 95)</td>
<td>5.5 (4.5 to 6.5)</td>
</tr>
<tr>
<td>Per-patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The results showed that with an increasing number of detectors used in the newer generations of CT scanners, sensitivity, specificity, and the log of diagnostic odds ratio increased in all levels of analysis. Thus, the diagnostic performance for the assessment of CAD of the newer generations of multi-detector CT scanners has significantly improved.

Hamon et al. (2006)\textsuperscript{22} assessed the diagnostic performance of multi-slice (≥16-slice) CT angiography for detection of CAD. The reference standard was invasive CA and significant stenosis was defined as >50% stenosis. Of the twenty nine included studies, 18 studies were of 16-slice, one of 32-slice, one of 40-slice, and nine of 64-slice CT.

Table 8 summarizes the pooled estimates of the diagnostic accuracy of multi-slice CT angiography for detection of CAD with respect to segment-based, vessel-based and patient-based level of analysis. Data were pooled from all studies. Statistical heterogeneity was evident for all levels of analysis. The median CAD prevalence was 63.5% (range: 8% to 100%).

Table 8: Pooled estimates of the diagnostic accuracy of multi-slice CT angiography

<table>
<thead>
<tr>
<th>Level of analysis (No of studies)</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
<th>DOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per-segment (27)</td>
<td>81 (72 to 89)</td>
<td>93 (90 to 97)</td>
<td>68 (58 to 78)</td>
<td>97% (95 to 98)</td>
<td>22 (13 to 36)</td>
<td>0.11 (0.06 to 0.21)</td>
<td>189 (94 to 383)</td>
</tr>
<tr>
<td>Per-vessel (8)</td>
<td>82 (80 to 85)</td>
<td>91 (90 to 92)</td>
<td>81 (78 to 83)</td>
<td>92 (91 to 93)</td>
<td>12 (7 to 21)</td>
<td>0.08 (0.02 to 0.32)</td>
<td>147 (32 to 671)</td>
</tr>
<tr>
<td>Per-patient (21)</td>
<td>96 (94 to 98)</td>
<td>74 (65 to 84)</td>
<td>83 (76 to 90)</td>
<td>94 (89 to 99)</td>
<td>5.4 (3.4 to 8.3)</td>
<td>0.05 (0.03 to 0.09)</td>
<td>133 (57 to 309)</td>
</tr>
</tbody>
</table>

CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; LR+: likelihood ratio of a positive test; LR-: likelihood ratio of a negative test; DOR: diagnostic odds ratio; No: number.

At per-segment and per-vessel analysis, the relatively high specificity of multi-slice (≥16-slice) CT occurred at the price of a moderate value of sensitivity. The high specificity and NPV would suggest exclusion of CAD in selected subjects considered for conventional CA. However, the specificity with respect to per-patient analysis was relatively low.

The author concluded that multi-slice CT has shortcomings difficult to overcome in daily practice and, at the more clinically relevant per patient analysis, continues to have moderate specificity in patients with high prevalence CAD.
Sun and Jiang (2006) performed a meta-analysis of the diagnostic value of multi-slice CT angiography in the detection of CAD when compared to conventional CA. Only studies with at least 10 patients comparing multi-slice CT with conventional CA were included. Of the 47 included studies, 20 studies were of 4-slice, one was of 8-slice, four were of 12-slice, 15 were of 16-slice, and seven were of 64-slice CT angiography.

Pooled overall sensitivity and specificity for multi-slice (≥4-slice) CT angiography in the detection of CAD were 83% (95% CI 79% to 89%), 93% (95% CI 91% to 96%) for segment-based analysis; 90% (95% CI 87% to 94%), 87% (95% CI 80% to 93%) for vessel-based analysis; and 91% (95% CI 88% to 95%), 86% (95% CI 1% to 92%) for patient-based analysis, respectively. The sensitivity in evaluating assessable segments was significantly improved with the 64-slice scanners (97%, p<0.05) when compared to 4-slice (74%) and 16-slice (92%) scanners.

The authors concluded that multi-slice CT angiography has potential diagnostic accuracy in the detection of CAD, and diagnostic performance of multi-slice CT has been significantly improved with 64-slice scanners.

Schuijf et al. (2006) assessed and compared the diagnostic accuracy of magnetic resonance imaging (MRI) and multi-slice CT coronary angiography in the detection of CAD. The gold standard was conventional angiography. Significant stenosis was defined as ≥50% diameter stenosis of the coronary artery lumen. Fifty-one studies were included for analysis. Diagnostic accuracy of MRI to detect coronary artery stenosis was assessed in 31 studies, of which five studies were of 2D breath hold, five were of 3D breath hold, and 21 were of 3D navigator. Diagnostic accuracy of multi-slice CT to detect coronary artery stenosis was assessed in 24 studies, of which 11 studies were of 4-slice, 2 were of 8-slice, and 11 were of 16-slice. The MRI pooled overall sensitivity and specificity was 72% (95% CI: 69% to 75%) and 87% (95% CI: 86% to 88%), respectively. The multi-slice CT pooled overall sensitivity and specificity was 85% (95% CI: 86% to 88%) and 95% (95% CI: 95%), respectively. The diagnostic odds ratio was significantly higher for multi-slice CT (16.9 fold) as compared with MRI (6.4 fold) (P<0.0001).

The authors concluded that multi-slice CT angiography has currently a significantly higher accuracy than MRI to detect or exclude CAD.

Stein et al. (2006) determined the sensitivity and specificity of multi-slice (4-slice, 8-slice, 16-slice, and 64-slice) CT for the detection of CAD. Significant stenosis was defined as ≥50% diameter stenosis of the coronary artery lumen. Conventional CA was the reference standard. Thirty-three studies were included for analysis. Of these, 15 studies were of 4-slice, two were of 8-slice, 15 were of 16-slice, and one was of 64-slice.

Table 9 summarizes the pooled estimates of the diagnostic accuracy of multi-slice CT angiography for detection of CAD with respect to patient-based and all segments-based level of analysis. The data were stratified according to the CT scanner type.

<table>
<thead>
<tr>
<th>Analysis and CT scanner type</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-based</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 4-slice</td>
<td>95 (86 to 99)</td>
<td>84 (63 to 95)</td>
<td>6.0 (2.4 to 14.6)</td>
<td>0.06 (0.02 to 0.17)</td>
</tr>
<tr>
<td>• 16-slice</td>
<td>95 (91 to 96)</td>
<td>84 (77 to 89)</td>
<td>5.9 (4.1 to 8.5)</td>
<td>0.07 (0.04 to 0.10)</td>
</tr>
<tr>
<td>• 64-slice</td>
<td>100 (92 to 100)</td>
<td>100 (83 to 100)</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>
Pooled data indicated that 4-slice, 16-slice, and 64-slice CT were highly sensitive (95% to 100%) for the patient-based detection of significant CAD. The corresponding specificity was lower (84%) than that of per-segment analysis, except that of the 64-slice (100%). For detection of significant stenosis in any segment, sensitivity and specificity improved with increasing number of detectors. An important difference between results with 4-slice, 16-slice and 64-slice CT was the percentage of segments that could be evaluated. Only 78% of segments could be evaluated with 4-slice CT, 91% could be evaluated with 16-slice CT, and all segments could be evaluated with 64-slice CT.

The authors concluded that multi-slice CT has the potential to be used as screening test in appropriate patients. The 16-slice CT has reasonable sensitivity and specificity for detection of CAD, but has shortcomings. Preliminary data with 64-slice CT suggested that this type of scanner is more sensitive and specific.

Summary of the diagnostic accuracy of multi-slice CT angiography

Table 10 summarizes the conclusion drawn from the included systematic reviews/meta-analyses on the diagnostic accuracy of multi-slice CT angiography for the detection of CAD.

### Table 10: Multi-slice CT angiography for the detection of CAD

<table>
<thead>
<tr>
<th>Source</th>
<th>Type of scanner (No of included studies)</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mowatt et al. (2008)</td>
<td>64-slice or higher (41)</td>
<td>64-slice CT might be a useful tool to rule out significant CAD. It seems likely that diagnostic strategies involving 64-slice CT will still require invasive CA for CT test positives, to identify false positives, and provide other information that CT currently does not. It is unlikely that 64-slice CT could replace CA in assessment for revascularization of patients.</td>
</tr>
<tr>
<td>Meijer et al. (2008)</td>
<td>40- and 64-slice (22)</td>
<td>The current generation of 40- and 64-slice multi-detector CT angiography scanners had high diagnostic accuracy in detecting or ruling out significant coronary artery stenosis, with better results for proximal than for distal coronary artery segments.</td>
</tr>
<tr>
<td>Di Tanna et al. (2008)</td>
<td>16-slice (35) &gt;16-slice (21)</td>
<td>Corresponding figures for 16- and &gt;16-slice studies showed that &gt;16-slice CT had a higher diagnostic accuracy than 16-slice CT. Multi-slice CT angiography is a promising technology for the assessment of coronary artery stenosis.</td>
</tr>
<tr>
<td>Source</td>
<td>Type of scanner (No of included studies)</td>
<td>Conclusion</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Stein et al. (2008)(^{16})</td>
<td>• 64-slice (45)</td>
<td>The negative results of 64-slice CT angiography reliably excluded significant coronary disease. However, positive results still require confirmation.</td>
</tr>
<tr>
<td>Sun et al. (2008)(^{17})</td>
<td>• 64-slice (15)</td>
<td>The 64-slice CT has a high diagnostic accuracy in the detection of CAD.</td>
</tr>
<tr>
<td>d’Othée et al. (2008)(^{18})</td>
<td>• 4-/8-slice (11) • 16-slice (12) • 64-slice (5)</td>
<td>Advances in CT technology have resulted in increases in diagnostic accuracy.</td>
</tr>
<tr>
<td>Vanhoenacker et al. (2007)(^{19})</td>
<td>• 4-slice (1) • 16-slice (2) • 32-slice (1) • 64-slice (5)</td>
<td>Multi-slice CT angiography performs good to excellent in the diagnosis of CAD in the acute setting and it can be used for early exclusion of non-ST-elevation myocardial infarction and unstable angina pectoris in patients in the emergency department.</td>
</tr>
<tr>
<td>Hamon et al. (2007)(^{20})</td>
<td>• 16-slice (16) • 64-slice (12)</td>
<td>Both 16-slice and 64-slice CT exhibited a high sensitivity and NPV at the clinically relevant patient-based level. However, the improvement in technology in the 64-slice CT led to an increase in specificity and PPV, representing a major advantage of 64-slice CT compared with 16-slice CT.</td>
</tr>
<tr>
<td>Vanhoenacker et al. (2007)(^{21})</td>
<td>• 4-slice (22) • 16-slice (26) • 64-slice (6)</td>
<td>With an increasing number of detectors used in the newer generations of CT scanners, sensitivity, specificity, and the log of diagnostic odds ratio increased in all levels of analysis. Thus, the diagnostic performance for the assessment of CAD of the newer generations of multi-detector CT scanners has significantly improved.</td>
</tr>
<tr>
<td>Hamon et al. (2006)(^{22})</td>
<td>• 16-slice (18) • 32-slice (1) • 40-slice (1) • 64-slice (9)</td>
<td>Multi-slice CT has shortcomings difficult to overcome in daily practice and, at the more clinically relevant per patient analysis, continues to have moderate specificity in patients with high prevalence CAD.</td>
</tr>
<tr>
<td>Sun and Jiang (2006)(^{23})</td>
<td>• 4-slice (20) • 8-slice (1) • 12-slice (4) • 16-slice (15) • 64-slice (7)</td>
<td>Multi-slice CT angiography has potential diagnostic accuracy in the detection of CAD, and diagnostic performance of multi-slice CT has been significantly improved with 64-slice scanners.</td>
</tr>
<tr>
<td>Schuijf et al. (2006)(^{24})</td>
<td>4-slice CT (11), 8-slice (2), 16-slice (11) versus MRI (31)</td>
<td>Multi-slice CT angiography has a significantly higher accuracy than MRI to detect or exclude CAD.</td>
</tr>
<tr>
<td>Stein et al. (2006)(^{25})</td>
<td>• 4-slice (15) • 8-slice (2) • 16-slice (15) • 64-slice (1)</td>
<td>Multi-slice CT has the potential to be used as screening test in appropriate patients. The 16-slice CT has reasonable sensitivity and specificity for detection of CAD, but has shortcomings. Preliminary data with 64-CT suggest that this type of scanner is more sensitive and specific.</td>
</tr>
</tbody>
</table>

CA: coronary angiography; CAD: coronary artery disease; CT: computed tomography; NPV: negative predictive value; PPV: positive predictive value; MRI: magnetic resonance imaging
The followings are key recommendations of three guidelines on the use of multi-slice CT for CAD.\textsuperscript{12,26,27}

The American Heart Association (AHA) Scientific Statement (2008)\textsuperscript{26} provides the following recommendations on the use of magnetic resonance angiography (MRA) and multi-slice CT angiography, which may be used for coronary artery evaluation. The Writing Committee conducted a comprehensive review of the literature published between 1990 and 2006. The Committee provided a discussion of technical issues, applications, advantages, and limitations, after which recommendations were offered for current and future uses of the two technologies.

- Neither coronary CT angiography nor MRA should be used to screen for coronary artery disease in patients who have no signs or symptoms suggestive of coronary disease. (Class III, level of evidence C)
- No multivendor trial data are available for coronary multi-slice CT or for present whole heart coronary MRA. Thus, the applicability of these methods beyond reporting research centers is unknown. Ideally, both multivendor and additional multicenter validation of these methods should be performed. (Class I, level of evidence C)
- The potential benefit of noninvasive coronary angiography is likely to be greatest and is reasonable for symptomatic patients who are at intermediate risk for coronary artery disease after initial risk stratification, including patients with equivocal stress-test results. (Class IIa, level of evidence B) Diagnostic accuracy favors coronary CT angiography over MRA for these patients. (Class I, level of evidence B) Concerns regarding radiation dose limit the use of CT angiography in high risk patients who have a very low pre-test likelihood of coronary stenoses; patients with a high pre-test likelihood of coronary stenoses are likely to require intervention and invasive catheter angiography for definitive evaluation; thus, CT angiography is not recommended for those individuals. (Class III, level of evidence C) Pronounced coronary calcification may negatively impact interpretability and accuracy of CT angiography and thus, the usefulness of CT angiography is uncertain in these individuals. (Class IIb, level of evidence B)
- Anomalous coronary artery evaluation can be performed by either CT angiography or MRA; radiation-protection concerns indicate that MRA is preferred when it is available. (Class IIa, level of evidence B)
- Reporting of coronary CT angiography and MRA results should describe any limitations to the technical quality of the examination and the size of the vessels, descriptions of coronary anomalies, coronary stenosis, and significant non-cardiac findings within the fields of view. (Class I, level of evidence A)
- Continue research in cardiac CT and MR imaging is encouraged to determine the potential of these non-catheter-based modalities to detect, characterize, and measure atherosclerosis plaque burden, as well as its change over time or as the result of therapy. (Class I, level of evidence C) (p598)\textsuperscript{26}

The Canadian Cardiovascular Society/the Canadian Association of Radiologists/the Canadian Association of Nuclear Medicine/the Canadian Nuclear Cardiology Society/the Canadian Society of Cardiac Magnetic Resonance (CCS/CAR/CANM/CNCS/CanSCMR) Joint Position Statement (2007)\textsuperscript{27} provides recommendations on the use of advance noninvasive cardiac imaging (positron emission tomography, magnetic resonance imaging and multi-detector computed tomography) in the diagnosis and evaluation of ischemic heart disease. Primary and secondary panels of experts and practitioners conducted a systematic review to 2005 for three imaging modalities. All members of the subgroups reviewed the papers for their specific modality. Based on the data reviewed, preliminary draft recommendations were prepared and
presented to the panels using standard score methods adapted from the previous guidelines from the American College of Cardiology, the American Heart Association, and the American Society of nuclear Cardiology. Consensus was then achieved. Only recommendations for multi-CT are presented here:

- The interpretation of cardiac CT and CT angiography should be carried out only by physicians and institutions with adequate training and experience.

Class I indication
1. Assessment of anomalous coronary arteries (Level C evidence)

Class IIa indications
1. 16- or 64-slice multi-detector CT for patient diagnosis of significant CAD (50% diameter stenosis or more) (Level B evidence)
2. 16- or 64-slice multi-detector CT for identification of coronary artery segments with significant stenosis (50% diameter stenosis or more) in coronary segments 1.5 mm or more in diameter (Level B evidence)
3. 16- or 64-slice multi-detector CT for assessment of graft patency (Level B evidence)

Class IIb indication
1. 64-slice multi-detector CT for the assessment of all coronary segments, including those with vessel diameters less than 1.5 mm (Level B evidence)

Class III (no benefit or harmful)
1. Diagnosis of CAD in patients with
   a. irregular dysrhythmias (atrial fibrillation, frequent extrasystoles)
   b. severe coronary calcification
   c. inability to perform sufficient breath-holds
   d. renal failure or other contraindications to intravenous contrast agents
   e. contraindications to radiation exposure (p112-113)

The Australian HTA (2007) provided recommendations based on the findings and conclusions from its assessment on clinical effectiveness of multi-slice CT angiography in the evaluation and diagnosis of CAD. The MSAC adopted an evidence-based approach to its assessments based on reviews of the scientific literature and other information sources, including clinical expertise.

**Indication 1 – Evaluation of patients with symptoms consistent with coronary ischemia**
- The Advisory Panel recommends the use of multi-slice CT angiography for this indication, based on specialist referral for patients with symptoms consistent with coronary ischemia at low to intermediate risk of CAD who are currently being considered for invasive CA.

**Indication 2 – Exclusion of coronary anomaly and fistula**
- The Advisory Panel recommends the use of multi-slice CT angiography for this indication despite the limited evidence available.

**Indication 3 – Evaluation of coronary arteries in patients with cardiomyopathy**
- The Advisory Panel does not support the use of multi-slice CT angiography for this indication.

**Indication 4 – Evaluation of coronary arteries in patients undergoing non-coronary cardiothoracic surgery**
- The Advisory Panel found that there was insufficient evidence regarding 64-slice CT angiography to support its use for this indication. (p.163)
Limitations

The rapid advancement of the CT technology has resulted in many of the studies and systematic reviews and meta-analyses to become outdated. Results from systematic reviews and meta-analyses of 2006 and before showed a lower diagnostic accuracy of the multi-slice CT angiography than that of the recent reviews. The 2008 systematic reviews concentrated in the diagnostic accuracy of the 64-slice CT angiography and provided more detail with respect to levels of analysis. The methodology and quality of the included systematic reviews appear to be comparable. Limited evidence exists concerning the impact of the multi-slice CT angiography results on patient management and patient outcomes. Although there are significant advances in the CT technology, its full potential awaits further leaps in this technology that may expand its clinical application. Most of the systematic reviews mentioned that the included studies selected patients with known CAD, and therefore the applicability of the technology to the real world setting remains unknown. It is expected that results of more studies will be available in the coming years addressing the questions about the radiation dose, impact on patient outcomes, and appropriate patient selection.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The included studies suggest that multi-slice CT angiography is currently the best method for non-invasive imaging of the coronary arteries, with 64-slice scanners outperforming 16-slice scanners. All included systematic reviews and meta-analyses found that multi-slice CT angiography has relatively high sensitivity and specificity to identify significant stenosis in selected intermediate to high CAD prevalence populations in comparison with conventional CA. The negative results of multi-slice CT angiography reliably excluded significant coronary disease.

The guidelines recommended the use of multi-slice CT in the diagnosis of CAD in patients with intermediate risk for coronary artery disease after initial risk stratification, including patients with equivocal stress-test results. However, multi-slice CT is not recommended as a substitute for conventional CA for the diagnosis of CAD, since positive results still require confirmation. The guidelines did not recommend use of multi-slice CT to screen for stenosis in patients with no signs or symptoms of CAD, nor to evaluate coronary artery in patients with cardiomyopathy or in patients undergoing non-coronary cardiothoracic surgery. It is also not recommended to use multi-slice CT angiography in patients of high CAD risk who will definitely require invasive catheter angiography. The patient management and prognosis of CAD depend on the functional impact of the coronary stenosis, which cannot be assessed by multi-slice CT angiography alone.

Although the included systematic reviews and meta-analyses indicate that multi-slice CT angiography is useful in diagnosis of CAD, there is currently no evidence regarding the impact of multi-slice CT angiography in patients’ quality of life, heart attack prevention or life saving. Questions remain over patient selection, patient outcomes, and radiation dose.

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REFERENCES:


APPENDIX: Definitions of common terms used in the assessment of diagnostic accuracy

- **Sensitivity** is the proportion of patients with disease (D+) who test positive (T+). 
  \[ P(T^+|D^+) = \frac{TP}{TP+FN} \]
  TP: true positive means number of patients with disease who test positive; FN: false negative means number of patients with disease who test negative

- **Specificity** is the proportion of patients without disease (D-) who test negative (T-). 
  \[ P(T^-|D^-) = \frac{TN}{TN+FP} \]
  TN: true negative means number of patients without disease who test negative; FP: false positive means number of patients without disease who test positive

- **Pretest probability** is the estimated likelihood of disease before the test is done. It is equivalent to prior probability or the prevalence of disease in the population. 
  \[ P(D^+) = \frac{TP+FN}{TP+FP+TN+FN} \]

- **Predictive value of a positive test** is the proportion of patients with positive tests who have disease. 
  \[ P(D^+|T^+) = \frac{TP}{TP+FP} \] 
  This is equivalent to posttest probability of disease given a positive test. It measures how well the test rules in disease

- **Predictive value of a negative test** is the proportion of patients with negative tests who do not have disease. 
  \[ P(D^-|T^-) = \frac{TN}{TN+FN} \] 
  It measures how well the test rules out disease. [Notice that this is not the same as posttest probability of disease given a negative test]

- **Likelihood ratio (LR)** is the probability of a given test result among people with a disease divided by the probability of that test result among people without the disease. 
  \[ LR = \frac{P(T|D^+)}{P(T|D^-)} \]
  \[ LR^+ = \frac{TP}{1-FP} \] 
  \[ LR^- = \frac{FP}{TP} \]

- **Accuracy** is measured by the area under the SROC curve. An area of 1 represents a perfect test; an area of 0.5 represents a worthless test.