Diagnostic value of 64-slice CT angiography in coronary artery disease: A systematic review

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Abstract

Purpose: To perform a systematic review of the diagnostic value of 64-multislice CT (MSCT) angiography in the detection of coronary artery disease (CAD) when compared to conventional coronary angiography.

Materials and methods: A search of PUBMED and MEDLINE databases for English literature was performed. Only studies with at least 10 patients comparing 64-slice MSCT angiography with conventional coronary angiography in the detection of CAD were included. Diagnostic value of MSCT angiography compared to coronary angiography was compared and analysed at segment-, vessel- and patient-based assessment.

Results: Fifteen studies met selection criteria and were included for analysis. Pooled sensitivity, specificity, positive predictive value and negative predictive value as well as 95% confidence interval (CI) were 97% (94 and 99%), 88% (79 and 97%), 94% (91 and 97%), and 95% (90 and 99%) for patient-based assessment; 92% (85 and 99%), 92% (85 and 99%), 78% (66 and 91%) and 98% (96 and 99%) for vessel-based assessment; 90% (85 and 94%), 96% (95 and 97%), 75% (68 and 82%) and 98% (98 and 99%) for segment-based assessment, respectively. No significant difference was found in the diagnostic accuracy of 64-slice CT in the detection of CAD when comparison was performed either among four main coronary arteries, or between proximal and middle or distal segments ($p > 0.05$).

Conclusion: Our results showed that 64-slice CT angiography has a high-diagnostic value in the detection of CAD. Severe coronary artery calcification seems to be the major factor affecting the visualisation and assessment.

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Keywords: Multislice CT; Coronary artery disease; Diagnostic value; Systematic review
1. Introduction

Coronary artery disease (CAD) is the leading cause of death in Western countries [1]. The standard of reference for diagnosis of CAD is still conventional coronary angiography, with the advantage of high-spatial resolution and temporal resolution. However, its diagnostic value has been challenged due to its invasiveness and high expenditure by the introduction of multislice CT imaging (MSCT). Previous reports showed that MSCT angiography is a promising technique with the increase of detector rows from 4-slice to 16-slice and 64-slice scanners [2–10]. With the increase of number of detectors, more coronary segments were evaluable, and the sensitivity for a significant coronary stenosis in evaluable segment was reported to increase [8–10]. However, diagnostic value of MSCT angiography with 4-slice and 16-slice was still limited and has not reached the accuracy as that of conventional coronary angiography. Preliminary data showed that 64-slice CT is more sensitive and specific than earlier 4-slice and 16-slice CT in the diagnosis of coronary artery disease [11]. Currently there exists a lack of data for a systematic analysis of the diagnostic value of 64-slice CT in coronary artery disease. Therefore, the aim of this study was to perform a systematic review of 64-slice CT angiography in the detection of CAD with regard to the diagnostic value in comparison to conventional coronary angiography, based on the available studies.

2. Materials and methods

2.1. Criteria for data selection and literature screening

A search of PUBMED and MEDLINE databases for English literature was performed by three reviewers (CD, YL, and ZS) for articles describing the diagnostic value of 64-slice CT angiography in CAD when compared to conventional coronary angiography. The articles must be peer-reviewed and published in English language. The key words used in describing 64-slice CT angiography in coronary artery disease were: 64-slice CT and coronary artery stenosis or disease; MSCT and coronary arteries and MSCT and coronary angiography. The search was limited to reports on human subjects and excluded case reports, conference abstracts, review articles, in vitro studies and articles investigating the coronary stent or bypass graft treatment. Exclusions were also included investigations limited to reports of 64-slice CT techniques or methods, electron beam CT. The search of literature ranged from 1998 to 2007 (March 2007), as MSCT was first introduced into clinical practice in 1998 [12]. In addition, the reference lists of identified articles were checked to obtain additional relevant articles. Prospective and retrospective studies were included if they met all of the following criteria: (a) patients undergoing both 64-slice CT angiography and coronary angiography examinations; (b) studies included at least 10 patients; (c) assessment or comparison of 64-slice CT angiography with coronary angiography was focused on the visualization of coronary arteries and detection or exclusion of coronary artery stenosis; (d) diagnostic value of 64-slice CT angiography was addressed when compared to coronary angiography in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), either segment-based, vessel-based or patient-based assessment.

2.2. Data extraction

Data were extracted repeatedly by three reviewers (CD, YL, and ZS) based on study design and procedure techniques. The reviewers looked for the following characteristics in each study: year of publication; origin of the study performed; number of participants in the study; mean age; mean heart rate; number of patients receiving β-blockers; prevalence of suspected or known CAD; type of imaging unit used for MSCT scanning; scanning protocols; time interval between MSCT and conventional coronary angiography; assessable coronary segments in each study; diagnostic accuracy of 64-slice CT when compared to coronary angiography in terms of the sensitivity, specificity, PPV, NPV and main factors affecting the visualization of coronary artery or lesions. All diagnostic accuracy estimates referred to segment/vessel/patient-based assessment.

2.3. Definition of coronary artery segments and stenosis

Significant stenosis was defined as more than 50% stenosis of the coronary artery lumen which is haemodynamically significant. High-grade stenosis was defined as more than 75% stenosis. In our review, we analysed the diagnostic value of 64-slice MSCT in CAD with more than 50 and 75% stenosis. Coronary artery segments were numbered as defined by the American Heart Association [13]. Assessment of coronary artery was based on variable description as some investigators listed the segments, while others described the portion of the arteries evaluated in terms of numbered segments. The 15/17-segment assessment is commonly used by investigators in these studies comparing 64-slice CT angiography with conventional coronary angiography.
2.4. Statistical analysis

All of the data were entered into SPSS (version 14.0) for analysis. Sensitivity, specificity, PPV, and NPV estimates for each study were combined across studies using one sample test. Comparison was performed by Chi-Square test using $n-1$ degree of freedom to test if there is any significant difference regarding the diagnostic value of MSCT angiography in CAD, between segment-based assessment, vessel-based assessment or patient-based assessment; proximal and middle, distal coronary segment. Statistical hypotheses (2-tailed) were tested at the 5% level of significance.

3. Results

3.1. General information

16 studies met criteria and 15 were included for analysis [10,14–28]. Two studies were reported from the same institution and one of them was excluded because of cumulative addition of previous cases [16,20]. There were two studies involving separate comparisons in different groups, either dealing with the diagnostic value of 64-slice CT in CAD based on degree of calcification [10], on calcium scores [10,21], or based on body mass index [10]. Another two studies were reported with the cumulative addition of previous cases from the same institution [14,25], however, we treated them as separate studies as they dealt with different pathological situations (patients with known/without history of CAD in Ref. [25]; while in Ref. [14], the study was focused on the atherosclerotic lesions). Table 1 shows the general information in each study reviewed. The number of patients enrolled in these studies ranged from 30 to 134. There were only two studies involving more than 100 cases [21,27]. Of 15 studies retrieved, all were performed on 64-slice scanners with spatial resolution of 165–200 ms except in one study, in which scans were performed on a dual source CT scanner with spatial resolution of 83 ms [26]. All MSCT scans were performed with Siemens scanners, except in one study which was done on a Toshiba scanner [22].

Of all studies reviewed, it was found that the male patients were most commonly affected with CAD, with pooled estimate and 95% confidence interval (CI) being 72% (66 and 77%). $\beta$-blocking agent was used in most of the studies (80%) and pooled estimate and 95% CI was 56% (37 and 75%). Diagnostic value of 64-slice CT angiography in the evaluation of assessable segment was reported in 14 studies with pooled estimate and 95% CI being 96% (94 and 98%). Table 2 lists the detailed information regarding classification of coronary segments as well as the segments included for analysis in each study.

In three studies, diagnostic value of 64-slice CT in CAD was investigated for stenosis >50 and 75%, respectively [14,23,25]. However, comparison could not be performed due to limited data and different method of analysis (patient-based or segment-based), although the sensitivity of 64-slice in the evaluation of >75% stenosis showed slightly higher that in >50% stenosis (78% versus 84%).
Table 2
Coronary artery segments included for analysis by 64-slice CT angiography in CAD

<table>
<thead>
<tr>
<th>Studies</th>
<th>Segment classification used in the study</th>
<th>Number of segments included in the studies</th>
<th>Diameter of segments included for analysis (mm)</th>
<th>Assessable segments (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raff et al. [10]/USA</td>
<td>15</td>
<td>1065</td>
<td>NS</td>
<td>88</td>
</tr>
<tr>
<td>Leber et al. [14]/Germany</td>
<td>15</td>
<td>798</td>
<td>NS</td>
<td>100</td>
</tr>
<tr>
<td>Leschka et al. [15]/Switzerland</td>
<td>15</td>
<td>1005</td>
<td>&gt;1.5</td>
<td>100</td>
</tr>
<tr>
<td>Pugliese et al. [16]/Italy</td>
<td>17</td>
<td>494</td>
<td>All segments</td>
<td>100</td>
</tr>
<tr>
<td>Fine et al. [17]/USA</td>
<td>NS</td>
<td>NS</td>
<td>&gt;1.5</td>
<td>94</td>
</tr>
<tr>
<td>Plass et al. [18]/Switzerland</td>
<td>11</td>
<td>550</td>
<td>&gt;1.5</td>
<td>97</td>
</tr>
<tr>
<td>Ropers et al. [19]/Germany</td>
<td>17</td>
<td>1128</td>
<td>&gt;1.5</td>
<td>96</td>
</tr>
<tr>
<td>Ong et al. [21]/Malaysia</td>
<td>11</td>
<td>748</td>
<td>&gt;1.5</td>
<td>93.6</td>
</tr>
<tr>
<td>Schuif et al. [22]/Netherlands</td>
<td>15</td>
<td>854</td>
<td>NS</td>
<td>99</td>
</tr>
<tr>
<td>Muhlenbruch et al. [23]/Germany</td>
<td>15</td>
<td>765</td>
<td>NS</td>
<td>95</td>
</tr>
<tr>
<td>Ebara et al. [24]/Japan</td>
<td>14</td>
<td>966</td>
<td>All segments</td>
<td>92</td>
</tr>
<tr>
<td>Nilolau et al. [25]/Germany</td>
<td>15</td>
<td>1020</td>
<td>NS</td>
<td>90</td>
</tr>
<tr>
<td>Scheiff et al. [26]/Switzerland</td>
<td>16</td>
<td>420</td>
<td>&gt;1.5</td>
<td>98.6</td>
</tr>
<tr>
<td>Meijboom et al. [27]/Netherlands</td>
<td>17</td>
<td>1525</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Oncel et al. [28]/Turkey</td>
<td>15</td>
<td>1200</td>
<td>All segments</td>
<td>100</td>
</tr>
</tbody>
</table>

NS: not stated.

Conventional coronary angiography was used as the standard of reference in all studies, however, the method of assessment of the degree of coronary artery stenosis or occlusion by coronary angiography was variable among these studies. In six of the studies, quantitative coronary angiography was used which involved quantitative assessment of the coronary artery disease using the QuantCor software to determine the severity stenosis, while in the remaining studies, visual or subjective assessment was utilised in the coronary angiography. The time interval between MSCT angiography and coronary angiography examinations was available in 11 studies and all patients underwent these two procedures within 2 weeks except in one study, in which the average interval between MSCT and conventional angiography was 49 days [22]. Comparisons were performed regarding the diagnostic value of 64-slice CT in CAD between studies utilizing quantitative coronary angiography and those utilizing visual assessment, and our analysis showed that there is no significant difference ($p > 0.05$) in terms of the sensitivity and specificity, whether the analysis was patient-based, vessel-based or segment-based.

3.2. Prevalence of CAD and corresponding diagnostic value of MSCT in CAD

Prevalence of CAD in these studies was variable according to our review, and we categorised it into suspected and known CAD. Patients suspected of CAD indicate that the patients presented with clinical symptoms such as typical or atypical chest pain, elevated ST, and they were recommended for coronary angiography for confirmation of presence of the lesion (stenosis/occlusion). Pooled estimates and 95% CI of suspected CAD was 63% (44 and 82%). In contrast, known CAD refers to these patients which were confirmed to suffer from coronary artery disease (presence of stenosis or occlusion) by coronary angiography. Our analysis showed that high-risk or known CAD ranged from 17 to 88%, with pooled estimates and 95% CI being 53% (40 and 67%). No significant difference was found when compared the prevalence of low-risk CAD or suspected CAD with that of high risk or known CAD ($p > 0.05$).

3.3. Patient-based, vessel-based and segment-based analysis of MSCT in CAD

Of 15 studies, evaluation of 64-slice CT in CAD on patient-based, vessel-based and segment-based assessment was available in 12, 6, and 12 studies, respectively. Pooled estimates and 95% CI of the sensitivity, specificity, PPV and NPV were 97% (94 and 99%), 88% (79 and 97%), 94% (91 and 97%), and 95% (90 and 99%) for patient-based assessment; 92% (85 and 99%), 92% (85 and 99%), 78% (66 and 91%) and 98% (96 and 99%) for vessel-based assessment; 90% (85 and 94%), 96% (95 and 97%), 75% (68 and 82%) and 98% (98 and 99%) for segment-based assessment, respectively.

3.4. Evaluation of four main coronary arteries

Assessment of the diagnostic value of 64-slice CT angiography in the four main coronary arteries including left main (LM), left anterior descending (LAD), right coronary artery (RCA) and left circumflex (LCX) were available in six studies. Pooled estimates and 95% CI of sensitivity, specificity, PPV and NPV were 100 and 99% (97 and 100%), 90% (69 and 100%) and 100% for LM; 93% (84 and 99%), 93% (88 and 97%), 80% (65 and 94%) and 98% (96 and 99%) for LAD; 93% (89 and 98%), 92% (82 and 99%), 82% (75 and 89%) and 97% (95 and 99%) for RCA; 83% (82 and 99%), 91% (81 and 99%), 79% (71 and 86%) and 97% (95 and 100%) for LCX, respectively. A significant difference was only reached in the sensitivity of 64-slice CT in CAD when comparing LM with RCA and LM with LCX ($p < 0.05$), and no significant different was found among other comparisons ($p > 0.05$).
3.5. Evaluation of proximal, middle and distal segments

Evaluation of 64-slice CT angiography in the detection of CAD in proximal, middle and distal coronary artery segments was only available in five studies with six comparisons. Although diagnostic accuracy of MSCT in CAD showed decreased tendency when looking at the middle and distal artery branches compared to proximal branches, no significant difference was reached between comparisons of these segments \((p > 0.05)\), except in the comparison of proximal with distal RCA segment, which demonstrated significant difference in sensitivity \((p < 0.05)\).

3.6. Factors affecting the diagnostic value of MSCT in CAD

Diagnostic accuracy of 64-slice CT in CAD was influenced by the presence of calcification and its relationship to the degree of calcium score was investigated in three studies \([9,21,26]\), and analysis of the effect of coronary calcification on diagnostic accuracy of MSCT could not be performed due to variable criteria applied in these studies (calcium score based on 142 or 400). Diagnostic accuracy of MSCT in CAD was affected in the presence of extensive calcification, even with dual source CT scanning as shown in the study reviewed \([26]\).

Relationship between body mass index (BMI) and the diagnostic accuracy of 64-slice angiography in CAD was investigated in one study and the results showed that sensitivity, specificity, PPV and NPV were the highest at normal BMI \((p > 0.05)\), except in the comparison of proximal with distal RCA segment, which demonstrated significant difference in sensitivity \((p < 0.05)\).

4. Discussion

This systematic review showed that 64-slice CT angiography has high diagnostic accuracy in the detection of CAD. In comparison to earlier scanners such as 4-slice and 16-slice CT, 64-slice CT angiography has demonstrated significant improvement in the assessment of coronary artery branches, including distal segments. Studies performed on the 16-slice CT scanners in the detection of CAD showed that the sensitivity of MSCT angiography decreased when assessing the distal coronary segments due to limited spatial and temporal resolution \([11]\). However, this was not observed in this study since no significant difference was found when comparing proximal with middle or distal segments. In comparison to 16-slice MSCT scanners, the current 64-slice scanner has increased slices per gantry rotation and fast gantry speed \((330 \text{ ms/rotation versus } 375)\), which translate into superior spatial resolution \((0.4 \text{ mm versus } 0.75)\) and temporal resolution \((83 \text{ or } 165 \text{ versus } 188 \text{ ms})\). The reduction in voxel size allows acquisition of isotropic volume data and makes distinction between hypointense soft plaque and contrast enhanced blood more evident. Moreover, more coronary segments can be assessed with 64-slice CT angiography with the percentage of assessable segments being higher than that from 16-slice scanners. Percentage of assessable segments was significantly higher than that of 16- and 4-slice scanners as shown in our results \((96\% \text{ versus } 92\% \text{ and } 74\%)\) \([29]\).

Recent studies have reported that two major limitations for affecting the MSCT evaluation of coronary artery segments are motion artifacts and severe coronary calcifications. In order to reduce motion artifacts, \(\beta\)-blockers were commonly used prior to CT examination, even if in the 64-slice scanners, as shown in the results. Consistent use of \(\beta\)-blocking agents before the scan to keep patients’ heart rates below 60 bpm could produce better results in some studies. The latest development of dual source CT has been reported to improve temporal resolution when compared to early 64-slice scanners, and coronary arteries were visualised without motion artifacts at any heart rate and beta-blocker utilization could be discarded \([30,31]\). Initial experience on dual source CT showed the advantages of imaging patients with high heart rates and reduction of occurrence of motion artifacts in comparison to earlier 64-slice scanners \([31]\), although further studies need to be performed to establish the diagnostic accuracy of dual source CT in the diagnosis of CAD. Only one study performed on a dual source MSCT was included in our analysis, therefore, a comparison between dual source CT and earlier 64-slice scanners cannot be performed, although dual source demonstrated improved results even if in patients with higher heart rate.

Another common factor that affects evaluation of coronary artery lumen is the presence of extensive calcification. Similar to 4-slice and 16-slice CT, extensive artery calcifications are a frequent source for impairing vessel assessment, even with 64-slice CT, although the degree of artifacts due to partial volume effects seem to be less severe. Severe calcification obscures coronary lumen and can lead to overestimation of the severity of the lesions due to blooming artifacts, making quantification of the degree of coronary artery stenosis difficult. The interference of calcification with assessment of coronary artery lumen was reported in three studies, and results showed that the specificity was decreased with the increase of the calcium score, indicating the relatively high false positive cases in the presence of extensive calcification. Thus, caution should be taken into account in imaging patients with severe calcification.

Body mass index (BMI) seems to be another factor that may affect the diagnostic accuracy of 64-slice CT in the detection of CAD. This was investigated in one study which demonstrated the relationship between BMI and diagnostic value of 64-slice CT \([10]\). Relevant research has been performed to investigate the relationship between body weight/BMI and image noise for reduction of radiation exposure without loss of diagnostic information in CT scanning protocols \([32,33]\). Yoshimura et al recently reported that image noise correlated well with body weight in coronary MSCT angiography \([32]\). Therefore, relationship between radiation dose, image noise and diagnostic accuracy should be investigated to minimise radiation dose while maintaining adequate diagnostic information for clinical investigation of coronary artery disease.

It must be noted that in practice, MSCT angiography is more likely to be applied to patients who have low to intermediate probability of CAD. While the negative predictive value
of MSCT coronary angiography remains relatively high with 16- and 64-slice scanners, the positive predictive value will be low in a population with a lower prevalence of CAD. However this was not found in our current results. We analysed the diagnostic value of 64-slice CT based on the prevalence of CAD in different patient groups, and our results did not show significant difference between patients suspected of CAD and those confirmed with CAD, although the prevalence of suspected CAD was slightly higher than that of confirmed CAD. With the current MSCT scanners, we can conclude that 64-slice CT is able to diagnose patients suspected of CAD with relatively high diagnostic accuracy when compared to conventional coronary angiography.

There are some limitations in the study which will be addressed. First, publication bias may have affected the results as non-English references were excluded. Second, lack of uniform criteria of assessment is another limitation inherent in most of the studies analysed. Inclusion of variable number of coronary segments makes the analysis and comparison of MSCT performance difficult. Not all of the studies provided detailed information about the diagnostic value of 64-slice CT. Assessment of four main coronary branches was only reported in about one third of the studies, while evaluation of distal coronary artery segments was available in only five studies. Finally, radiation dose was only addressed in five studies. The increase in dose estimates with 64-slice CT when compared to 4- and 16-slice scanners is due to the higher spatial and temporal resolution achieved with the current CT scanner technology and therefore, radiation dose related to 64-slice CT in cardiac imaging deserves to be investigated.

In conclusion, this systematic review demonstrated that 64-slice CT has a high diagnostic accuracy in the detection of coronary artery disease. More coronary artery segments including distal branches were assessed by 64-slice CT angiography. Dual source CT could be an alternative method in patients with higher heart rate. For patients with extensive calcifications in the coronary lumen or coronary artery stenoses defined by MSCT angiography are of uncertain significance, myocardial perfusion SPECT should be performed for purposes of risk stratification and guiding patient management.

References


