Diagnostic value of 320-slice coronary CT angiography in coronary artery disease: A systematic review and meta-analysis

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Abstract

The aim of this study is to perform a systematic review and meta-analysis of the diagnostic value of 320-slice coronary computed tomography (CT) angiography in the diagnosis of coronary artery disease when compared to invasive coronary angiography. A search of different databases was conducted to identify studies investigating the diagnostic value of 320-slice coronary CT angiography. Sensitivity, specificity, positive and negative predictive value estimates pooled across studies were tested using a fixed effects model and analysed at patient-, vessel- and segment-based assessment. Twelve studies comprising 1592 patients (median, 63 patients, range, 37-240 patients) with a total of 2974 vessels and 21623 segments met selection criteria for inclusion in the analysis. Patients with a high prevalence of coronary artery disease were included in more than 70% of these studies. The mean values and 95% confidence interval (CI) of sensitivity, specificity, positive predictive value and negative predictive value of 320-slice coronary CT angiography were 96.3% (95% CI: 92.9%, 99.8%), 86.4% (95% CI: 77.8%, 94.9%), 89.6% (95% CI: 85.6%, 93.6%) and 93.2% (95% CI: 84.1%, 100%), at patient-based analysis; 91.8% (95% CI: 85.8%, 97.8%), 95.4% (95% CI: 93.6%, 97.1%), 85.9% (95% CI: 79.7%, 92%) and 97.4% (95% CI: 95.9%, 99.1%), at vessel-based analysis; 86.2% (95% CI: 81.8%, 90.6%), 96.5% (95% CI: 95.2%, 98%), 79.9% (95% CI: 75.3%, 84.6%) and 97.8% (95% CI: 96.7%, 99%), at segment-based analysis, respectively. The mean effective dose of 320-slice coronary CT angiography was 10.5 mSv (95% CI: 6.1, 14.8 mSv). Diagnostic value of 320-slice coronary CT angiography was not affected by different heart rates and calcium scores ($p>0.05$). This analysis shows that 320-slice coronary CT angiography has high diagnostic value in patients with high coronary artery disease prevalence. Relatively high radiation dose is mainly due to inclusion of patients with high heart rates and without using the advanced dose-reduction techniques, thus, further dose-saving strategies should be implemented to minimise the resultant radiation dose.

Keywords: coronary artery disease, coronary computed tomography angiography, diagnostic value, radiation dose.

Introduction

Recently, a new generation of 320-slice CT has been introduced and it represents a significant advance from 64-slice technologies in the diagnosis of coronary artery disease (CAD) since it enables acquisition of the entire heart within a single heartbeat due to the extended 16-cm coverage in the z-axis [1-3]. Wide volume coronary CT angiography (CCTA), in combination with prospectively ECG-gated image acquisition enables a significant decrease in scan time, reduced radiation dose and contrast medium when compared to retrospectively helical ECG-gated protocols which require multiple heartbeats. In addition, cardiac motion artifacts can be reduced and stair-step artifacts are eliminated with use of 320-slice CT.

Diagnostic accuracy of 320-slice CCTA has been investigated in previous studies based on low, irregular or high heart rates with satisfactory results achieved [4-7]. However, there is a lack of systematic analysis of the diagnostic value of 320-slice CCTA with regard to the overall diagnostic accuracy and effects of heart rates and calcium scores, as well as the associated radiation dose. The purpose of this paper is to conduct a systematic review of the diagnostic value of 320-slice CCTA, according to the published studies in the literature.

Materials and Methods

Literature searching methods

The literature search for relevant references was performed using different databases including Pubmed/Medline, ScienceDirect, Scopus and Embase to identify studies describing the diagnostic value of 320-slice CCTA in CAD between 2008 (320-slice CT was first introduced into clinical practice in 2008) and 2013 (last search was done in December 2013). The terms used for identification of references were ‘320-slice/320-detector row CT and coronary artery disease/stenosis’, ‘320-slice coronary CT angiography’, ‘320-slice CT angiography in CAD’, cardiac 320-slice CT and ‘320-slice CT in CAD’. The search was limited to include all the studies that have been published in the English language and were on human subjects. Case reports, conference abstracts, review articles, in vitro studies and articles investigating the coronary stents or bypass graft treatments were excluded from the analysis. In addition, the reviewers went through reference lists of eligible studies to identify additional relevant articles.

Selection criteria

Studies were included if they met all of the following criteria: (a) patients must be adults with suspected or known CAD who underwent both 320-slice CCTA with use of retrospective ECG-gating or prospective ECG-triggering and invasive coronary angiography, with >50% lumen stenosis defined as the cut-off criterion for significant stenosis based on quantitative coronary angiography; (b) diagnostic value of 320-slice CCTA must be assessed at either patient-, or vessel- or segment-based analysis when compared to invasive coronary angiography regarding the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). When multiple studies from the same clinical centre were identified, all reports were examined to obtain the most complete and recent information, however, studies with potential duplicate publication were excluded from the analysis.

Data extraction and quality assessment

Data were extracted independently by two reviewers based on study design and procedure techniques. The reviewer looked for the following characteristics in each study: year of publication; number of patients included in each study; mean age; mean heart rate (beats per minute-bpm); number of male patients; mean body mass index (BMI); number of patients receiving β–blockers; assessable coronary segments in each study; coronary artery calcium scores; radiation dose associated with 320-slice CCTA; diagnostic accuracy of 320-slice CCTA when compared to invasive coronary angiography and main factors affecting the visualization of coronary arteries or diagnostic performance. All diagnostic accuracy estimates referred to patient/vessel/segment-based assessment.

One reviewer independently conducted the quality assessment of eligible studies using an updated quality assessment tool "QUADAS-2" (Quality Assessment of Diagnostic Accuracy Studies) guidelines [8]. This revised tool represents significant improvement over the original QUADAS-1 [9] as it enables more transparent rating of bias and applicability of diagnostic accuracy of primary studies.

Statistical analysis

All of the data were entered into SPSS (version 20.0) for analysis. Sensitivity, specificity, PPV and NPV estimates for each study were independently combined across studies using a fixed effects model. The sensitivity, specificity, PPV and NPV estimates was tested using the Mantel-Haenszel Chi-squared test with n-1 degree of freedom (n is the number of studies) to determine the between-study heterogeneity. A p value of less than 0.05 indicates statistically significant difference.

Results

Figure 1 is the flow chart of studies through the review process of reference searching. After searching through these databases, 181 articles were identified, of which 30 potentially relevant articles were selected for full-text assessment. Twelve studies met the selection criteria, while the remaining 18 studies were excluded due to various reasons: contents duplicates (n=1); results focusing on the image quality and radiation dose, while results of diagnostic accuracy were not presented (n=17).

Study characteristics

The characteristics of the eligible studies [4-7, 10-17] are shown in Table 1. The 12 studies enrolled 1592 patients (median, 63 patients, range, 37-240 patients). This analysis assessed a total of 2974 vessels and 21623 segments. The mean age of the patients ranged from 45 to 68 years (median, 61 years). The prevalence of CAD ranged from 37% to 88.5%.

Of 12 studies, all were performed on 320-slice CT scanners (Toshiba Aquilion One, Toshiba Medical Systems, Japan) with temporal resolution of 175 ms. Coronary CT angiography was performed with prospectively ECG-triggered CCTA in 10 studies, while in the remaining two studies, retrospectively ECG-gated CCTA was used [12, 13]. A combination of prospective triggering and retrospective gating (for left ventricular function assessment) scans was performed in one study [7]. A comparative analysis of the diagnostic performance of prospectively triggered with retrospectively gated CCTA was conducted in another study [11].

The mean value and 95% CI of assessable segments among these 12 studies was 97.6% (95.3%, 99.8%). Coronary artery calcium scores were reported in 4 studies with the mean value being 350 (range, 180-653). The mean heart rate of patients during CCTA scan ranged from 56 to 88.4 bpm (median, 60 bpm). Beta-blocker was used in 5 studies, and no heart rate control was implemented in 2 studies, while in the remaining 5 studies, detailed information about beta-blocker usage was not available.

Radiation dose associated with 320-slice CCTA

Information about radiation dose was available in 9 studies, while in the remaining three studies, this was not reported [12, 13, 16]. The estimated mean effective dose and 95% CI was 10.5 mSv (6.1, 14.9 mSv), and it ranged from 3.1 to 23.2 mSv, depending on the scanning protocols used in each study (prospective triggering or retrospective gating). The mean effective dose in patients with high and low heart rates (> 65 bpm versus < 65 bpm) was 11.7 mSv (3.1, 24.2 mSv) and 4.1 mSv (3.0, 5.3 mSv), respectively, indicating marginal significant difference (p=0.05) between these two groups.

Multiple heart beats reconstruction was performed in 4 studies, with effective dose reported in 3 studies [7, 10, 14]. The effective dose of 320-slice CCTA was higher in the multiple heartbeat groups (2- to 4-heartbeat acquisition) than that in the single heartbeat acquisition, although statistical analysis could not be performed due to limited data. In another study, the scanning field of view (FOV) was selected according to the patient's heart size [17]. The radiation dose in small-FOV (FOV=200 mm) scanning was found significantly higher than that in medium-FOV (FOV=320 mm) scanning, with no difference in image quality.

Prospective triggering was the most commonly used approach in these studies for dose reduction, while lower tube voltage such as 100 kVp was applied in 9 studies according to patients' BMI. Despite application of lower tube voltage among these studies, a direct comparison of effective dose between the 120 and 100 kVp groups was only performed in one study [15], with a dose reduction of 41% achieved in the lower tube voltage group.

For the calculation of effective dose, different conversion coefficients were used in these studies, with a conversion coefficient of 0.014 and 0.017 mSv x mGy^{-1} x cm^{-1}

applied in 5 and 2 studies, respectively. An updated conversion coefficient of 0.028 and 0.029 mSv x mGy^{-1} x cm^{-1} was used in 2 studies [6, 11]. In the remaining three studies, this information was not provided.

Diagnostic value of 320-slice CCTA-a systematic review

Evaluation of 320-slice CCTA in CAD was available in 10, 8 and 12 studies, respectively, corresponding to the patient-based, vessel-based and segment-based assessment. The mean values and 95% CI of sensitivity, specificity, PPV and NPV of 320-slice CCTA were 96.3% (95% CI: 92.9%, 99.8%), 86.4% (95% CI: 77.8%, 94.9%), 89.6% (95% CI: 85.6%, 93.6%), 93.2% (95% CI: 84.1%, 100%) at patient-based assessment; 91.8% (95% CI: 85.8%, 97.8%), 95.4% (95% CI: 93.6%, 97.1%), 85.9% (95% CI: 79.7%, 92.2%), 97.4% (95% CI: 95.9%, 99.1%) at vessel-based assessment; and 86.2% (95% CI: 81.8%, 90.6%), 96.5% (95% CI: 95.2%, 98%), 79.9% (95% CI: 75.3%, 84.6%), 97.8% (95% CI: 96.7%, 99%) at segment-based assessment, respectively (Table 2).

Diagnostic value of 320-slice CCTA-meta-analysis

We explored whether there is clinical and statistical heterogeneity by performing additional analysis of the results. No statistically significant heterogeneity was found ($p=0.49$-0.9) according to patient-based assessment, so the pooled estimates across studies (meta-analysis) were generated to show the diagnostic value. However, severe heterogeneity/inconsistency was found at the vessel- and segment-based assessment ($p<0.05$) due to inclusion of variable mean assessable vessels (range from 3 to 4 coronary arteries) and segments (range from 11 to 16 coronary segments) among these studies, thus pooled estimates were avoided, and only the mean values across these studies were used as shown in the results presented in the systematic review.

Pooled estimates and 95% CI of sensitivity, specificity, PPV and NPV of 320-slice CCTA for diagnosis of CAD on patient-based assessment were performed in 7 studies which provided all of the assessment details, and these were 99.2% (95% CI: 97.1%, 99.9%), 91.9% (95% CI: 87.7%, 95%), 92.5% (95% CI: 88.6%, 95.3%), 99.1% (95% CI: 96.9%, 99.9%), respectively (Figs 2, 3).

Effect of heart rates and coronary calcium scores

The effect of different heart rates and coronary calcium scores on the diagnostic value of 320-slice CCTA at segment-based analysis was reported in 4 and 3 studies, respectively. Table 2 shows that diagnostic value of 320-slice CCTA is not significantly affected by either high heart rates or high calcium scores (p=0.11-0.48), except for the specificity between different heart rates, which reached significant difference (p=0.012).

Quality assessment

Quality assessment of all eligible studies based on the QUADAS-2 is shown in Table 3. Overall, satisfactory quality was achieved in all studies. Of 12 studies, the investigators clearly explained that readers interpreted CCTA results without any knowledge of the invasive coronary angiography in 9 studies, while in 10 studies, readers interpreted invasive coronary angiography results without any knowledge of the CCTA results.

Discussion

This systematic review and meta-analysis has three findings which are considered useful from a clinical perspective. First, 320-slice CCTA has high diagnostic value in the diagnosis of coronary stenosis. In particular, the very high negative predictive value (>97% in most of the assessments) indicates that 320-slice CCTA can be used as a reliable modality to exclude significant coronary stenosis. Second, diagnostic performance of 320-slice CCTA is independent of heart rates and calcium scores, thus, patients with high or irregular hearts or high calcium scores will benefit from this new technique. Third, radiation dose associated with 320-slice CCTA is relatively high, and the dose value depends on the protocols used in performing CCTA scans.

The extended longitudinal coverage of up to 16 cm makes 320-slice CT possible to image the whole heart in one heartbeat. This eliminates "stair-step" artifacts that are observed during 64-slice cardiac CT scans. Full cardiac coverage with one gantry rotation allows for evaluation of coronary arteries in patients with arrhythmias, such as with atrial fibrillation. It has been reported that high diagnostic value has been achieved with 320-slice CCTA for detection of >50% coronary stenosis [4, 5, 18, 19]. In patients with atrial fibrillation, 320-slice CCTA was reported to visualize 96% of all coronary segments with sufficient image quality to enable a diagnosis [2, 15, 19]. Analysis of this review is consistent with these findings as 320-slice CCTA has high diagnostic value with assessable segments being more than 97%.

Although only 12 studies were available in this systematic review, patients with different heart rates or coronary calcium scores were included for analysis. Two recently published systematic reviews and meta-analyses of 320-slice CCTA have shown that 320-slice CCTA has high diagnostic accuracy in the diagnosis of CAD

[20, 21]. However, these analyses did not address the effect of different heart rates or calcium scores on the diagnostic performance of CCTA. Thus, this systematic review offers additional information to these reports, further confirming the superiority of 320-slice CCTA over previous generations of 64-slice CCTA. Although temporal resolution of 320-slice CCTA (175 ms) is not superior to 64-slice (165 ms) or dual-source CCTA (66 ms) [22], full cardiac coverage within a single gantry rotation allows for a significant reduction of contrast medium and breath-hold time, and elimination of “stair-step” artifacts when compared with 64-slice or dual-source CCTA which requires multiple heartbeats to acquire images covering the entire heart.

Prospective ECG-triggering was used many years ago with electron-beam CT for purpose of calcium scoring; however, it was introduced in recent years for cardiac CT imaging, and this imaging protocol has been increasingly reported in the literature due to its advantage of lowering radiation dose significantly. Prospectively ECG-triggered CCTA reduces radiation dose considerably compared to the conventional retrospectively ECG-gated protocol, with a dose reduction ranging from 76% to 83% [23-26]. The effective radiation dose for prospectively ECG-triggered CCTA in patients with a low and regular heart rate has been reported to range from 2.7 mSv to 6.8 mSv, according to several recent studies and systematic reviews [27-31]. The mean effective dose of 320-slice CCTA in this analysis was 10.5 mSv, and the high dose value is due to inclusion of patients with high or irregular heart rates among these studies. This is similar to that reported in a recent systematic review and meta-analysis of radiation dose of CCTA in atrial fibrillation, with the mean effective dose being 11 mSv in patients with atrial fibrillation, while the radiation dose was 6.5 mSv in patients with sinus rhythm [32]. When comparing the effective dose in patients with low heart rates to those with high heart rates, it was found in this systematic review that the mean effective dose was reduced to 4.1 mSv in the low heart rate group, which is comparable to the dose range reported in the literature. Consequently, dose-saving strategies should be implemented in patients with high heart rates when undergoing 320-slice CCTA.

Various dose-reduction techniques have been introduced to minimise radiation dose since 320-slice CT was introduced. Steigner et al in their early study reported that narrowing the phase window to 10% in prospectively ECG-triggered 320-slice CCTA resulted in low radiation dose of 5.3 mSv while still achieving diagnostic images in more than 95% of patients [33]. For a 10% phase window width, more than 20% dose reduction was achieved with use of the asymmetric approach when compared to the standard symmetric approach (4.05 mSv vs 5.33 mSv) as shown in a recent study conducted by Bedayat et al [34]. Tung et al based on their single centre experience concluded that up to 80% reduction in median radiation dose in CCTA down to 2.18 mSv from the initial installation to the most recent experience of using 320-slice CT using different approaches comprising narrowing phase window width, minimising scan length, application of advanced tube current modulation and advanced image reconstruction algorithms [35]. More recently, the median effective dose of 0.93 mSv with the use of second-generation 320-slice CT was reported in 107 consecutive patients with all images having diagnostic quality and this represents at least a 75% reduction compared with previous reports from the first generation of 320-slice CT [36]. These results suggest that integration of various dose-reduction strategies may be a useful approach to further reduce radiation dose.

Although high diagnostic value can be achieved with use of 320-slice CT in patients with high or irregular heart rates, heart rate control to less than 65 bpm is still necessary and it comprises an essential step even in 320-slice CCTA to guarantee acquisition of diagnostic images. Of 12 studies included in this systematic review, 5 of them reported the use of beta-blockers in patients with heart rate >65 bpm to slow down the heart rate prior to CT scanning. Multiple heartbeat acquisition was used in patients with high heart rates or atrial fibrillation [7, 14], but at the expense of high radiation exposure. Therefore, further studies are needed to reduce radiation dose in this group of patients while achieving diagnostic images [37].

The diagnostic value of coronary CT angiography is widely known to be affected by the heavy calcification in the coronary artery tree. High-density calcification produces blooming artifacts which lead to overestimation of the degree of coronary stenosis, thus resulting in low specificity and positive predictive value [38]. Meng et al. described that CCTA with use of dual-source CT provided high diagnostic accuracy even in patients with high heart rates and presence of coronary calcification, however, the sensitivity in patients with severe calcification (CAC >400) was significantly affected [39]. On the other hand, using prospectively ECG-triggered CCTA, Stolzmann et al. stated in their study that CCTA had high diagnostic accuracy despite the presence of heavy calcifications with sensitivity and specificity being 99% and 99% in patients with median CAC score <316, and 98% and 99% in patients with median CAC score >316 [40]. This analysis did not show any significant differences in the diagnostic value of 320-slice CCTA between low and high coronary calcium scores. This is because the single gantry rotation of 320-slice CT reduced the blooming artifacts resulting from heavily calcified plaques. Despite high diagnostic value in patients with high calcium scores, the specificity and positive predictive value were decreased to some extent. Therefore, severe calcification still remains a factor that affects the diagnostic performance of 320-slice CCTA.

Some limitations in this analysis should be acknowledged. First, publication bias may have affected the results since we just included articles in English and excluded non-English references. Second, only a very small number of studies were eligible according to the selection criteria, as most of the currently available studies focused on the comparison of image quality and radiation dose without addressing the diagnostic accuracy of 320-slice CCTA. Third, among these eligible studies, not all of them provided detailed information regarding the diagnostic performance of 320-slice CCTA. Fourth, the prevalence of CAD in these studies shows a wide range of prevalence of disease, which ranges from 37% to 88.5%. Furthermore, in half of the studies, patients were recruited with high pretest probability of CAD. Thus, future studies should focus on the diagnostic value of 320-slice CCTA in patients with low pretest probability of CAD. Fifth, it has been reported that as a dose measurement parameter, dose length product (DLP) represents most closely the radiation dose received by an individual patient and is suggested to be used for setting reference values for a given type of CT examination. This helps ensure patient doses at CT are as low as reasonably achievable. However, DLP values were only reported in two studies [10, 15], according to this analysis. It is therefore recommended that DLP should be recorded for each study and serve as the basis of quality assurance [30, 41]. Last, there exists significant heterogeneity/inconsistency at the vessel- and segment-based assessment. Thus, only a systematic review was performed, and meta-analysis of these studies at per-vessel and per-segment assessment could not be conducted.

In conclusion, this systematic review and meta-analysis shows that 320-slice CCTA has high diagnostic value in the diagnosis of coronary artery disease. Diagnostic performance of 320-slice CCTA is less affected by the presence of different heart rates and calcium scores, although this needs to be verified by further studies. The relatively high radiation dose associated with 320-slice CCTA in these studies is due to inclusion of patients with high heart rates without implementing the advanced dose-saving strategies, therefore, future studies with use of dose-saving strategies are needed to minimise the radiation dose while achieving diagnostic images, in particular, in patients with high heart rates.

Conflict of Interest: None.

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Figure legends

Figure 1. Flow chart shows the search strategy to obtain eligible studies on 320-slice coronary CT angiography.

Figure 2. Plot and table of pooled sensitivity of 320-slice coronary CT angiography compared to invasive coronary angiography in 7 studies (8 comparisons) at per patient-based assessment. CI-confidence interval. Zhang et al (prem) refers to the group of patients with ventricular premature heartbeats, while Zhang et al (control) indicates the group of patients with normal and rhythm heartbeats.

Figure 3. Plot and table of pooled specificity of 320-slice coronary CT angiography compared to invasive coronary angiography in 7 studies (8 comparisons) at per patient-based assessment. CI-confidence interval. Zhang et al (prem) refers to the group of patients with ventricular premature heartbeats, while Zhang et al (control) indicates the group of patients with normal and rhythm heartbeats.