

**Diagnostic value of coronary CT angiography with prospective ECG-gating in the diagnosis of coronary artery disease: A systematic review and meta-analysis**

Zhonghua Sun PhD<sup>1</sup>, Kwan-Hoong Ng PhD<sup>2</sup>

1. Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, GPO Box U1987 Perth, Western Australia 6845, Australia
2. Department of Biomedical Imaging, University of Malaya, Kuala Lumpur, 50603, Malaysia

**Corresponding author:**

Associate Professor Zhonghua Sun, Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University of Technology, GPO Box, U1987, Perth, Western Australia 6845, Australia

Tel: +61-8-9266 7509

Fax: +61-8-9266 2377

Email: [z.sun@curtin.edu.au](mailto:z.sun@curtin.edu.au)

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## **Abstract**

**Purpose:** To perform a systematic review and meta-analysis of the diagnostic value of prospective ECG-gating coronary CT angiography in the diagnosis of coronary artery disease.

**Materials and Methods:** A search of biomedical databases for English literature was performed to identify studies investigating the diagnostic value of 64- or more slice CT angiography with use of prospective ECG-gating in the diagnosis of coronary artery disease. Sensitivity, specificity, positive and negative predictive value estimates pooled across studies were tested using a fixed effects model.

**Results:** Fourteen studies met selection criteria for inclusion in the analysis. Pooled estimates and 95% confidence interval (CI) of sensitivity, specificity, positive and negative predictive value of prospective ECG-gating coronary CT angiography for diagnosis of significant coronary stenosis were 99% (95% CI: 98%, 100%), 91% (95% CI: 88%, 94%), 94% (95% CI: 91%, 96%) and 99% (95% CI: 97%, 100%), according to the patient-based assessment. The mean value of sensitivity, specificity, positive and negative predictive value of prospective ECG-gating coronary CT angiography were 95% (95% CI: 93%, 96%), 95% (95% CI: 93%, 95%), 88% (95% CI: 86%, 90%), and 98% (95% CI: 97%, 98%), according to vessel-based assessment; 92% (95% CI: 90%, 93%), 97% (95% CI: 97%, 98%), 84% (95% CI: 82%, 86%), 99% (95% CI: 99%, 99%), according to segment-based assessment, respectively. The mean effective dose was 3.3 mSv (95% CI: 2.3, 4.1 mSv) for the prospective ECG-gating coronary CT angiography.

**Conclusion:** This analysis shows that for a predominantly male population with a high disease prevalence the use of coronary CT angiography with prospective ECG gating allows for a reduced radiation exposure without a sacrifice in diagnostic efficacy.

**Keywords:** Coronary artery disease, image quality, coronary CT angiography, prospective gating, radiation dose

## **Introduction**

Since the introduction of 64- or more-slice CT technology, coronary CT angiography has been increasingly used in the diagnosis of coronary artery disease (CAD) due to its improved spatial and temporal resolution [1-4]. The non-invasiveness and high diagnostic accuracy of coronary CT angiography for coronary artery disease have led to rapidly increasing numbers of cardiac CT examinations performed worldwide. However, the risk of radiation exposure still remains a challenge compared with invasive coronary angiography, given the fact that CT is a high-dose imaging modality [5]. This has raised serious concerns in the medical field due to the possibility for radiation-induced malignancy [6-9].

In response to these concerns, tremendous progress has been made to lower radiation dose for coronary CT angiography, and various strategies have been proposed to address this issue. These include automatic exposure control, ECG-triggered current modulation, lower kVp settings, adjustments of pitch value and scan range and prospective ECG-gating [10]. Of these dose-saving strategies, prospective ECG-gated scanning represents the most effective approach with a significant reduction of radiation dose when compared to conventional retrospective ECG-gating [10, 11].

Early studies demonstrated the feasibility of prospective ECG-gating and later reports confirmed that diagnostic images could be acquired with this new technique while achieving reduction of the effective dose by up to 90% [10, 11]. It has been reported that effective dose of prospective ECG-gating coronary CT angiography in CAD is comparable to or even lower than that of invasive coronary angiography [12, 13]. Most of the studies reported in the literature focus on the assessment of image quality and

radiation dose of prospective ECG-gating with 64- or more slice CT in comparison to retrospective ECG-gating, while the information about diagnostic value of prospective ECG-gating in CAD is limited [12-14]. Since prospective ECG-gating coronary CT angiography shows promising results in the diagnosis of CAD with resultant very low effective dose, it is expected that more and more studies will be performed with this technique in cardiac imaging. Thus, achieving high diagnostic accuracy with prospective ECG-gating is essential to ensure that it can be reliably used as an alternative to high-dose retrospective ECG-gating or invasive coronary angiography in the diagnosis of CAD. The purpose of this study was to perform a systematic review and meta-analysis of diagnostic value of coronary CT angiography with use of prospective ECG-gating in the diagnosis of CAD compared to invasive coronary angiography, based on the currently available literature.

## **Materials and Methods**

### *Search methods*

We searched MEDLINE/PUBMED and COCHRANE databases from January 2008 to December 2011 for articles studying the diagnostic value of prospective ECG-gating using 64-or more slice CT angiography in patients with suspected or confirmed CAD. The literature search ranged from 2008 to present as prospective ECG-gating with multislice CT was first reported in the literature in 2008 [15]. In addition, the reference lists of identified articles were checked to obtain additional relevant articles.

### *Selection criteria*

Prospective and retrospective studies were included if they met all of the following criteria: (a) studies included at least 10 patients with suspected or known CAD and must be performed using 64- or more slice CT prospective ECG-gating protocols as a diagnostic tool for evaluation of coronary artery disease, with >50% lumen stenosis defined as the cut-off criterion for significant stenosis; (b) assessment of diagnostic value of prospective ECG-gating 64-or more slice CT angiography in CAD must be addressed at either patient-based, or vessel-based or segment-based analysis when compared to invasive coronary angiography in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV); (c) the absolute number of true positive, true negative, false positive and false negative results of prospective ECG-gating coronary CT angiography were available or could be derived from the available data; (d) effective dose of prospective ECG-gating protocols was reported in each study. Exclusion criteria were: patients after treatment of coronary stenting or coronary artery bypass grafts or percutaneous coronary intervention. When multiple reports from a single centre were published, all reported were reviewed to obtain the most complete information, but studies with potential duplicate or overlapping data were excluded from the analysis.

#### *Data extraction and quality assessment*

Data were independently extracted by two reviewers based on study design and procedure techniques. Each reviewer independently assessed the retrieved articles for possible inclusion according to the selection criteria. The reviewers looked for the following characteristics in each study: year of publication; number of participants; mean age; mean heart rate, heart rate variability and body mass index (BMI); percentage of

male patients and number of patients receiving beta-blockers; type of imaging unit used for coronary CT angiography; effective dose estimated in each group; number of coronary vessels and segments analysed, and diagnostic accuracy of coronary CT angiography in CAD when compared to invasive coronary angiography.

One author independently performed the quality assessment of included studies using an updated quality assessment tool “QUADAS-2” (Quality Assessment of Diagnostic Accuracy Studies) guidelines [16]. This revised tool is a considerable improvement over the original tool as it allows for more transparent rating of bias and applicability of primary diagnostic accuracy studies.

#### *Statistical analysis*

All of the data was entered into Meta Disc (V 1.4, Meta Analysis for Diagnostic and Screening Trials) for analysis. Sensitivity, specificity, PPV and NPV estimates for each study were independently combined across studies using a fixed effects model. Between-study heterogeneity of 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). Statistical hypotheses (2-tailed) were tested at the 5% level of significance.

## **Results**

#### *General information-selection of eligible studies*

Nineteen studies met the selection criteria and 14 studies were finally eligible for analysis [17-35]. Two studies were excluded as the actual number of true positive, true negative, false positive and false negative results was not available in these studies [34, 35].

Although two studies were reported from the same research group, patient data were collected differently, thus both of them were included in the analysis [19, 20]. Six studies were reported from the same research group over different study periods with data being cumulatively accrued [17, 18, 26, 28, 31, 32], but only four of them were used in the analysis [17, 18, 26, 28]. Of these four studies that were eligible for analysis, one study looked at the effect of calcium scores on the diagnostic value of prospective ECG-gating [17], another study consisted of the largest number of data collection [18], one study was conducted with use of the second generation of dual-source CT scanner which is different from the other two studies performed with single-source CT [26], while the remaining study focused on the diagnostic value of prospective ECG-gating at low heart rates [28]. Another study was also excluded, despite its meeting the selection criterion [33], since the study included 33% of patients treated with coronary stents, which interfered with the diagnostic value of coronary CT angiography in CAD. Therefore, a total of 5 studies were excluded from the analysis. Figure 1 is the flow chart showing the search strategy to obtain these references.

### *Study characteristics*

Overall, 3531 coronary arteries and 12056 coronary segments were examined in 910 patients included in the 14 studies. Table 1 lists patient's characteristics and study details related to prospective ECG-gating coronary CT angiography. Seven out of 14 studies were performed with single-source 64-slice CT, four studies were performed with dual-source 64-slice CT, one with second generation of dual-source CT (128-slice), and the remaining two studies with 320-slice CT. Fourteen studies provided data at the patient



level, eleven at the vessel and segment level, respectively. On average, 3% of the coronary segments were reported to be non-diagnostic image quality.

### *Quality assessment*

Quality assessment of all included studies based on the updated QUADAS-2 is shown in Table 2. Overall, the study quality was satisfactory. For all 14 studies, the investigators clearly explained that readers interpreted coronary CT angiography results without any knowledge of the catheter angiography results and vice versa. In addition, operators and readers of coronary CT angiography were unaware of patient history and symptoms in all studies.

### *Patient characteristics*

The mean prevalence of CAD for study patients was 59.5%, and mean BMI was 26.2 kg/m<sup>2</sup>, and the mean age was 63.1 years. The mean heart rate was less than 65 beats per minute (bmp) in 13 studies, while in the remaining study the mean heart rate was 67.7 bmp [29].

Patients were referred for coronary CT angiography and invasive coronary angiography examinations mainly due to the symptom of typical or atypical chest pain in all of the studies. Invasive coronary angiography confirmed that the prevalence of significant CAD (>50% lumen stenosis) was found in more than 50% of patients among 12 studies.

Calcium scores were measured in eight studies with nine comparisons, as one study included two groups of patients with different calcium scores [17]. The mean calcium scores were 299.2, indicating the high prevalence of coronary artery disease in these

studies. Diagnostic accuracy of coronary CT angiography with use of prospective ECG-gating was not affected by the presence of heavy calcifications, as reported in one study [17].

*Prospective ECG-gating coronary CT angiography: analysis of study heterogeneity*

We explored sources of clinical and statistical heterogeneity by performing additional analysis of the results. On a segment-based level, a 15-17 segment classification model was used in all of these studies. It is expected that all of the four coronary vessels within any patient should be included in the analysis. Therefore, calculations of sensitivity and specificity involve mixtures (a range of values arising from segments combined with a range of values arising from several vessels, but with variations in contributions, by presence/absence rather than by magnitude, to numerators and denominators). No statistical heterogeneity was found for these analyses ( $p=0.63-1.0$ ) according to patient-based assessment among these studies, so the pooled estimates across studies were used to demonstrate the diagnostic performance. However, severe heterogeneity/inconsistency was noticed at the vessel-based and segment-based assessment levels ( $p<0.05$ ), so pooling was avoided, and only the mean values across these studies were described.

*Diagnostic value of prospective ECG-gating coronary CT angiography*

The mean assessable segments for prospective ECG-gating coronary CT angiography were 98% (95% CI: 97%, 99%). Pooled estimates and 95% confidence interval (CI) of sensitivity, specificity, PPV and NPV of prospective ECG-gating coronary CT angiography for diagnosis of CAD on a patient-based assessment were 99% (95% CI: 98%, 100%), 91% (95% CI: 88%, 94%), 94% (95% CI: 91%, 96%) and 99% (95% CI:

97%, 100%) (Figs 2, 3). The mean values of sensitivity, specificity, PPV and NPV were 95% (95% CI: 93%, 96%), 95% (95% CI: 93%, 95%), 88% (95% CI: 86%, 90%), and 98% (95% CI: 97%, 98%), according to vessel-based assessment; 92% (95% CI: 90%, 93%), 97% (95% CI: 97%, 98%), 84% (95% CI: 82%, 86%), 99% (95% CI: 99%, 99%), according to segment-based assessment, respectively. Figures 4 and 5 are the Forest plots showing that the pooled sensitivities and specificities based on patients, vessels and segments in all studies were 94% (95% CI: 93%, 95%) and 97% (95% CI: 96%, 97%).

Diagnostic value of prospective ECG-gating with inclusion of non-diagnostic segments was reported in two studies [19, 27], however, the analysis of these results was not conducted as inclusion of non-diagnostic segments could make the diagnostic value invalid. In addition to the criterion of 50% coronary stenosis, more than 70% stenosis was also analysed in another study [24]. The limited data of only one study does not allow a statistical analysis.

#### *Effective dose associated with prospective ECG-gating coronary CT angiography*

Effective dose was estimated by multiplying the dose length product with a conversion factor of 0.014 and 0.017 used in three and seven studies, respectively. The calculation of the effective dose in these studies is based on a method proposed by the European Working Group for Guidelines on Quality Criteria in CT [36], deriving radiation dose estimates from the product of the DLP and an organ weighting factor for the chest as the investigated anatomic region ( $k = 0.014$  or  $0.107 \text{ mSv} \cdot \text{mGy}^{-1} \cdot \text{cm}^{-1}$  averaged between male and female models from Monte Carlo simulations [37]). The mean effective dose was 3.3 mSv (95% CI: 2.3, 4.1 mSv) for the prospective ECG-gating coronary CT angiography.

A kVp of 100 and 120 was both applied and compared in two studies with use of prospective ECG-gating, and a reduction of effective dose by up to 46% was found in the studies scanned with 100 kVp (mean dose 1.65 mSv) when compared to those with 120 kVp (mean dose 3.05 mSv), indicating a further dose reduction of radiation dose with use of lower kVp values in patients with BMI less than 25 kg/m<sup>2</sup>.

## **Discussion**

In this analysis, we focused on the diagnostic performance of prospective ECG-gating coronary CT angiography for the detection of obstructive coronary artery disease. Firstly, the mean assessable segments of prospective ECG-gating are very high (98%), and this indicates a very high value of prospective ECG-gating for evaluation of coronary arteries. Secondly, the analysis shows that prospective ECG-gating coronary CT angiography has a high diagnostic value (>90% for both sensitivity and specificity) in the diagnosis of obstructive coronary artery disease in patients with a low heart rate. This indicates that it could be used as a reliable alternative to retrospective ECG-gating and invasive coronary angiography in selected patients. Thirdly, the effective dose associated with prospective ECG-gating is less than 4.0 mSv, which is comparable to or even lower than that of invasive coronary angiography.

Coronary angiography has been increasingly used in cardiac imaging since 64- and more slice CT shows improved and promising results in the diagnosis of CAD [1-4]. Several meta-analyses of studies on the use of retrospectively ECG-gated 64-slice CT reported mean sensitivities and specificities ranging from 85% to 99%, and 86% to 96%, respectively [38-41]. The mean diagnostic performance reported in this analysis is

consistent with those recent reports. The very high positive and negative predictive value of prospective ECG-gating allows this technique to be used reliably as an alternative modality for the diagnosis of CAD. Based on this analysis, it can be concluded that for the group of patients examined to date with coronary CT angiography, use of a prospectively gated exam has not been shown to change patient-based, vessel-based and segment-based sensitivity or specificity when compared to the existing data for retrospectively gated exams.

Despite promising results having been achieved with coronary angiography, CT has the disadvantage of high radiation dose, which leads to the concern of radiation-associated risks [6-8]. Of various approaches that have been recommended to reduce the radiation dose of coronary CT angiography, prospective ECG-gating has been reported to result in a significant reduction of effective dose when compared to retrospective ECG-gating [42, 43]. This analysis is consistent with these reports with regard to the low effective dose resulting from prospective ECG-gating. With use of prospective ECG-gating, it is possible to produce diagnostic images with effective dose even lower than that of invasive coronary angiography.

Appropriate use of lower kVp values (80 or 100 kVp) for coronary CT angiography examinations can further reduce radiation dose without compromising the image quality. Recent studies utilising dual-source CT compared a 100 kVp protocol to the routine 120 kVp for cardiac CT angiography, and demonstrated a dose reduction of 25-54%, with an estimated effective dose as low as 4.4 mSv [44, 45]. With use of a lower kVp in prospective ECG-gating, a further dose reduction by 46% was achieved with acquisition of diagnostic images with a mean dose of less than 2.0 mSv, as indicated in this analysis.

Thus, a combination of prospective ECG-gating with a low kVp protocol should be recommended in patients with BMI less than 25 kg/m<sup>2</sup>, since changing tube voltage needs to be correlated with the patient's BMI.

Some limitations in this analysis should be addressed. Firstly, the publication bias exists and may affect the results as non-English publications were excluded. However, it is reported that language-restriction meta-analyses overestimated the treatment effect by only 2% on average compared with language-inclusive meta-analyses [46]. Secondly, coronary CT angiography was performed in patients referred for invasive coronary angiography, creating a selection bias of patients with a relatively high prevalence of significant CAD. Significant CAD was confirmed in approximately 60% of the patients by coronary angiography in this analysis, indicating the high prevalence of CAD among the patients. Thus, the present diagnostic performance was achieved in an intermediate-to-high prevalence patient population. As a result, the current data (in terms of very high sensitivity and specificity values) may not be directly applicable to patients with a low-to-intermediate prevalence of CAD. Thirdly, effective dose based on a conversion factor of 0.014 or 0.017 is only an estimate. Because the mathematical modelling done to compute organ doses is based on a standard adult (70kg), effective dose estimation can underestimate the risk for children and thin patients and overestimate the risk for obese patients. Therefore, one should remember that the uncertainty associated with the effective dose estimations could vary as much as 40% in some cases. One has to adopt a correction factor when making comparisons with different studies. Although the use of effective dose estimates for assessing the exposure of patients has severe limitations, the effective dose is still widely used as a dose parameter to reflect the radiation risk and

compare doses from different diagnostic and therapeutic imaging procedures in different hospitals and countries as well as of different technologies for the same medical examinations.

In conclusion, this systematic review and meta-analysis shows that prospective ECG-gating coronary CT angiography has high diagnostic value with a low radiation dose in the diagnosis of obstructive coronary artery disease. The very high specificity and negative predictive value allows it to be used as a reliable alternative to retrospective ECG-gating in patients with a regular and low heart rate.

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## References

1. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA (2005) Diagnostic accuracy of non-invasive coronary angiography using 64-slice spiral computed tomography. *J Am Coll Cardiol* 46:552-557.
2. Feng Q, Yin Y, Hua X, Zhu R, Hua J, Xu J (2010) Prospective ECG triggering versus low-dose retrospective ECG-gated 128-channel CT coronary angiography: comparison of image quality and radiation dose. *Clin Radiol* 65: 809-814.
3. Kitagawa K, Lardo AC, Lima JAC, George RT (2009) Prospective ECG-gated 320 row detector computed tomography: implications for CT angiography and perfusion imaging. *Int J Cardiovasc Imaging* 25: 201-208.
4. Ribicki FJ, Otero HJ, Steigner ML, et al (2008) Initial evaluation of coronary images from 320-detector row computed tomography. *Int J Cardiovasc Imaging* 24: 535-546.
5. Fazel R, Krumholz HM, Wang YF, et al (2009) Exposure to low-dose ionizing radiation from medical imaging procedures. *N Engl J Med* 361: 849-857
6. Paul JF, Abada HT (2007) Strategies for reduction of radiation dose in cardiac multislice CT. *Eur Radiol* 17:2028-2037.
7. Brenner DJ, Hall EJ (2007) Computed tomography—an increasing source of radiation exposure. *N Engl J Med* 357(22):2277–2284.
8. Hausleiter J, Meyer T, Hermann F et al (2009) Estimated radiation dose associated with cardiac CT angiography. *JAMA* 301(5):500–507.
9. Raff GL, Chinnaiyan KM, Share DA, et al (2009) Radiation dose from cardiac computed tomography before and after implementation of radiation dose-reduction techniques. *JAMA* 301:2340-2348.

10. Sun Z, Ng KH (2010) Multislice CT angiography in cardiac imaging. Part III: radiation risk and dose reduction. *Singapore Med J* 51: 374-380.
11. Sun Z, Ng KH (2011) Prospective versus retrospective ECG-gated multislice CT coronary angiography: A systematic review of radiation dose and image quality. *Eur J Radiol* (Epub ahead of print) doi:10.1016/j.ejrad.2011.01.070.
12. Achenbach S, Marwan M, Ropers D, et al (2010) Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J* 31:340-6.
13. Lell MM, Marwan M, Schepis T, et al (2009) Prospectively ECG-triggered high-pitch spiral acquisition for coronary CT angiography using dual source CT: technique and initial experience. *Eur Radiol* 19:2576-2583.
14. von Ballmoos MY, Haring B, Juillert P, Alkadhi H (2011). Meta-analysis: diagnostic performance of low-radiation-dose coronary computed tomography angiography. *Ann Intern Med* 154: 413-420.
15. Hsieh J, Londt J, Vass M, Li J, Tang X, Okerlund D (2006) Step-and-shoot data acquisition and reconstruction for cardiac x-ray computed tomography. *Med Phys* 33:4236-48.
16. Whiting P, Rutjes AWS, Westwood ME, et al (2011) QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 155: 529-536.
17. Stolzmann P, Scheffel H, Leschka S, et al (2008) Influence of calcification on diagnostic accuracy of coronary CT angiography using prospective ECG triggering. *Am J Roentgenol* 191: 1684-1689.

18. Scheffel H, Alkadhi H, Leschka S, et al (2008) Low-dose CT coronary angiography in the step-and-shoot mode: diagnostic performance. *Heart* 94: 1132-1137.
19. Herzog BA, Husmann L, Burkhard N, et al (2008) Accuracy of low-dose computed tomography coronary angiography using prospective electrocardiogram-triggering: first clinical experience. *Eur Heart J* 29: 3037-3042.
20. Herzog BA, Wyss CA, Husmann L, et al (2009) First head-to-head comparison of effective radiation dose from low-dose 64-slice CT with prospective ECG-triggering versus invasive coronary angiography. *Heart* 95: 1656-1661.
21. Pontone G, Andreini D, Bartorelli A, et al (2009) Diagnostic accuracy of coronary computed tomography angiography: A comparison between prospective and retrospective electrocardiogram triggering. *J Am Coll Cardiol* 54: 346-355.
22. Maruyama T, Takada M, Hasuike T, Yoshikawa A, Namimatsu E, Yoshizumi T (2008) Radiation dose reduction and coronary assessability of prospective electrocardiogram-gated computed tomography coronary angiography: Comparison with retrospective electrocardiogram-gated helical scan. *J Am Coll Cardiol* 52:1450-1455.
23. La Bounty TM, Leipsic J, Mancini J, et al (2010) Effect of a standardized radiation dose reduction protocol on diagnostic accuracy of coronary computed tomographic angiography. *Am J Cardiol* 106: 287-292.
24. Dewey M, Zimmermann E, Deissenrieder F, et al (2009) Noninvasive coronary angiography by 320-row computed tomography with lower radiation exposure and maintained diagnostic accuracy: comparison of results with cardiac catheterization in a head-to-head pilot investigation. *Circulation* 120: 867-875.

25. Carrascoca P, Capunay C, Deviggiano A, et al (2010) Accuracy of low-dose prospectively gated axial coronary CT angiography for the assessment of coronary artery stenosis in patients with stable heart rate. *J Cardiovasc Comput Tomogr* 4: 197-205.
26. Alkadhi H, Stolzmann P, Desbiolles L, et al (2010) Low-dose, 128-slice, dual-source CT coronary angiography: accuracy and radiation dose of the high-pitch and the step-and-shoot mode. *Heart* 96: 933-938.
27. de Graaf FR, Schuijf JD, van Velzen JE, et al (2010) Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of significant coronary artery disease. *Eur Heart J* 31: 1908-1915.
28. Husmann L, Herzog BA, Burger IA, et al (2010) Usefulness of additional coronary calcium scoring in the low-dose CT coronary angiography with prospective ECG-triggering. *Acad Radiol* 17: 201-206.
29. Lu B, Lu JG, Sun ML, et al (2011) Comparison of diagnostic accuracy and radiation dose between prospective triggering and retrospective gated coronary angiography by dual-source computed tomography. *Am J Cardiol* 107: 1278-1284.
30. Stolzmann P, Goetti R, Baumueller S, et al (2011) Prospective and retrospective ECG-gating for CT coronary angiography perform similarly accurate at low heart rates. *Eur J Radiol* 79: 85-91.
31. Scheffel H, Stolzmann P, Alkadhi H, et al (2010) Low-dose CT and cardiac MR for the diagnosis of coronary artery disease: accuracy of single and combined approaches. *Int J Cardiovasc Imaging* 26: 579-590.

32. Donati OF, Stolzmann P, Desbiolles L, et al (2011) Coronary artery disease: which degree of coronary artery stenosis is indicative of ischemia? *Eur J Radiol* (Epub ahead of print) doi:10.1016/j.ejrad.2010.07.010.
33. Chao SP, Law WY, Kuo CJ, et al (2010) The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. *Eur Heart J* 31: 1916-1923.
34. Hong YJ, Kim SJ, Lee SM, et al (2011) Low-dose coronary computed tomography angiography using prospective ECG-triggering compared to invasive coronary angiography. *Int J Cardiovasc Imaging* 27: 425-431.
35. Korosoglou G, Mueller D, Lehrke S, et al (2010) Quantitative assessment of stenosis severity and atherosclerotic plaque composition using 256-slice computed tomography. *Eur Radiol* 20: 1841-1850.
36. Bongartz G, Golding SJ, Jurik AJ, et al (2004) European guidelines for multislice computed tomography: report EUR 16262 EN. Luxembourg: European Commission, 2004.
37. Morin RL (1988) Monte Carlo simulation in the radiological sciences. Boca Raton, FL: CRC Press.
38. Sun Z, Lin CH, Davidson R, Dong C, Liao Y (2008) Diagnostic value of 64-slice CT angiography in coronary artery disease: A systematic review. *Eur J Radiol* 67: 78-84.
39. Abdulla J, Abildstrom Z, Gotzsche O, et al (2007) 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. *Eur Heart J* 28: 3042-3050.

40. Vanhoenacker P, Heijenbrok-Kal M, Van Heste R, et al (2007) Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis. *Radiology* 244: 419-428.
41. Mowatt G, Cook JA, Hillis GS, et al (2008) 64-slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. *Heart* 94: 1386–1393.
42. Shuman WP, Branch KR, May JM, et al (2009) Whole-chest 64-MDCT of emergency department patients with nonspecific chest pain: radiation dose and coronary artery image quality with prospective ECG triggering versus retrospective ECG gating. *AJR Am J Roentgenol* 192: 1662-1667.
43. Arnoldi E, Johnson TR, Rist C, et al (2009) Adequate image quality with reduced radiation dose in prospectively triggered coronary CTA compared with retrospective techniques. *Eur Radiol* 19: 2147-2155.
44. Pflederer T, Rudofsky L, Ropers D, et al (2009) Image quality in a low radiation exposure protocol for retrospectively ECG-gated coronary CT angiography. *AJR Am J Roentgenol* 192:1045-1050.
45. Leschka S, Stolzmann P, Schmid F, et al (2008) Low kilovoltage cardiac dual-source CT: attenuation, noise and radiation dose. *Eur Radiol* 18:1809-1817.
46. Lau J, Ioannidis JP, Schmid CH (1998) Summing up evidence: one answer is not always enough. *Lancet* 351: 123-7.

## **Figure legends**

Figure 1. Flow chart shows the search strategy used to identify eligible references.

Figure 2. Plot and table of pooled sensitivity of prospective ECG-gating coronary CT angiography compared to invasive coronary angiography in 14 studies (15 comparisons) based on patient-based assessment. CI-confidence interval. Group A consists of patients with Agatston score less than 316, while Group B consists of patients with Agatston score more than 316.

Figure 3. Plot and table of specificity of prospective ECG-gating 64-slice CT angiography compared to invasive coronary angiography in 14 studies (15 comparisons) based on patient-based assessment. CI-confidence interval. Group A consists of patients with Agatston score less than 316, while Group B consists of patients with Agatston score more than 316.

Figure 4. Forest plot showing the pooled sensitivities based on patients (L1), vessels (L2) and segments (L3) in all studies.

Figure 5. Forest plot showing the pooled specificities based on patients (L1), vessels (L2) and segments (L3) across all studies.

Fig. 1

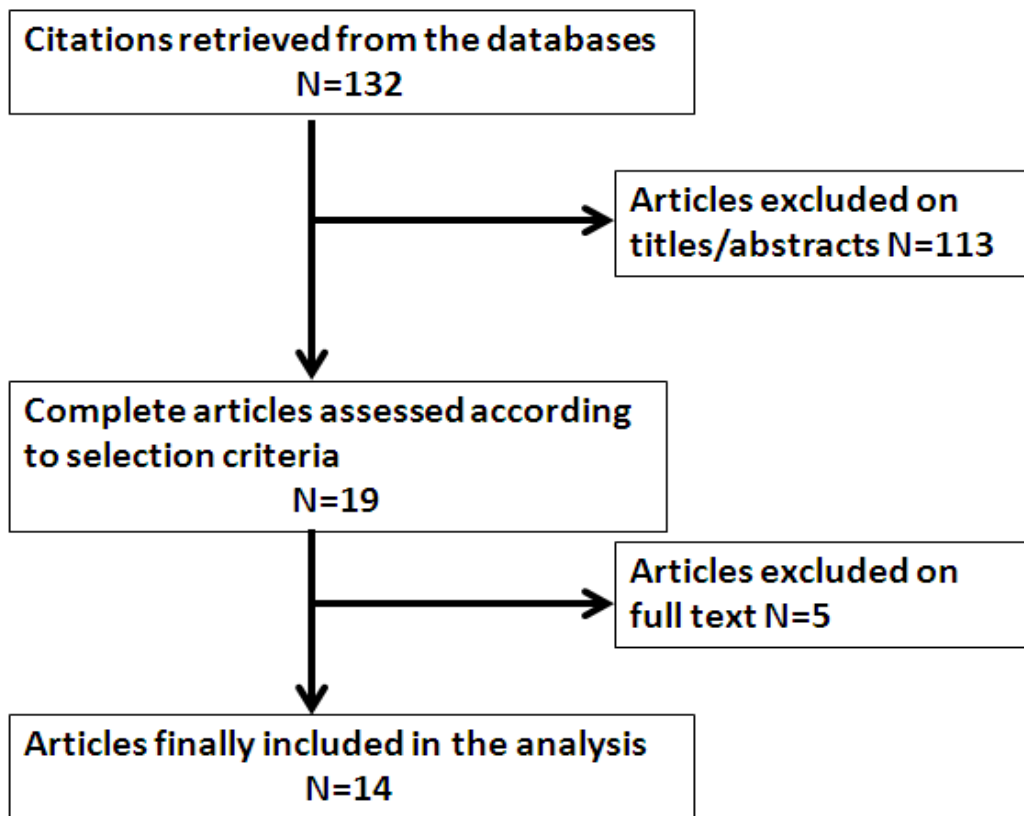




Fig. 2

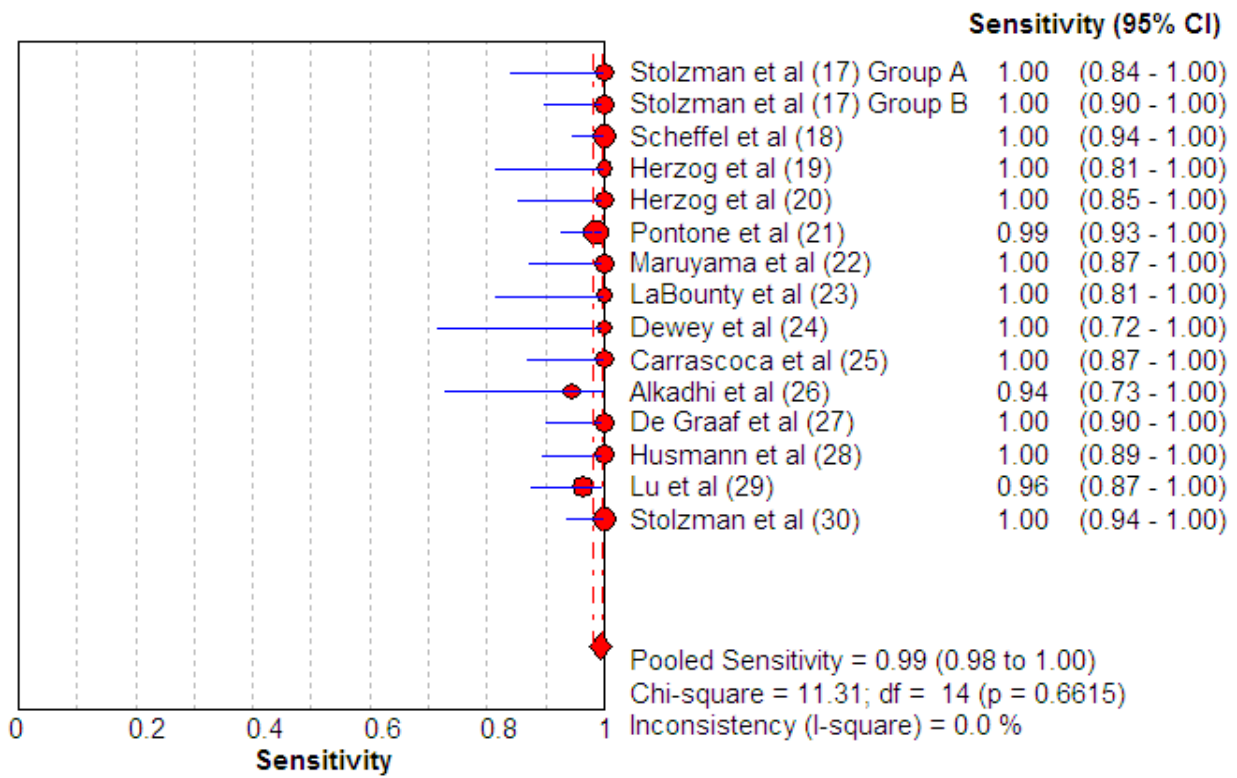


Fig. 3

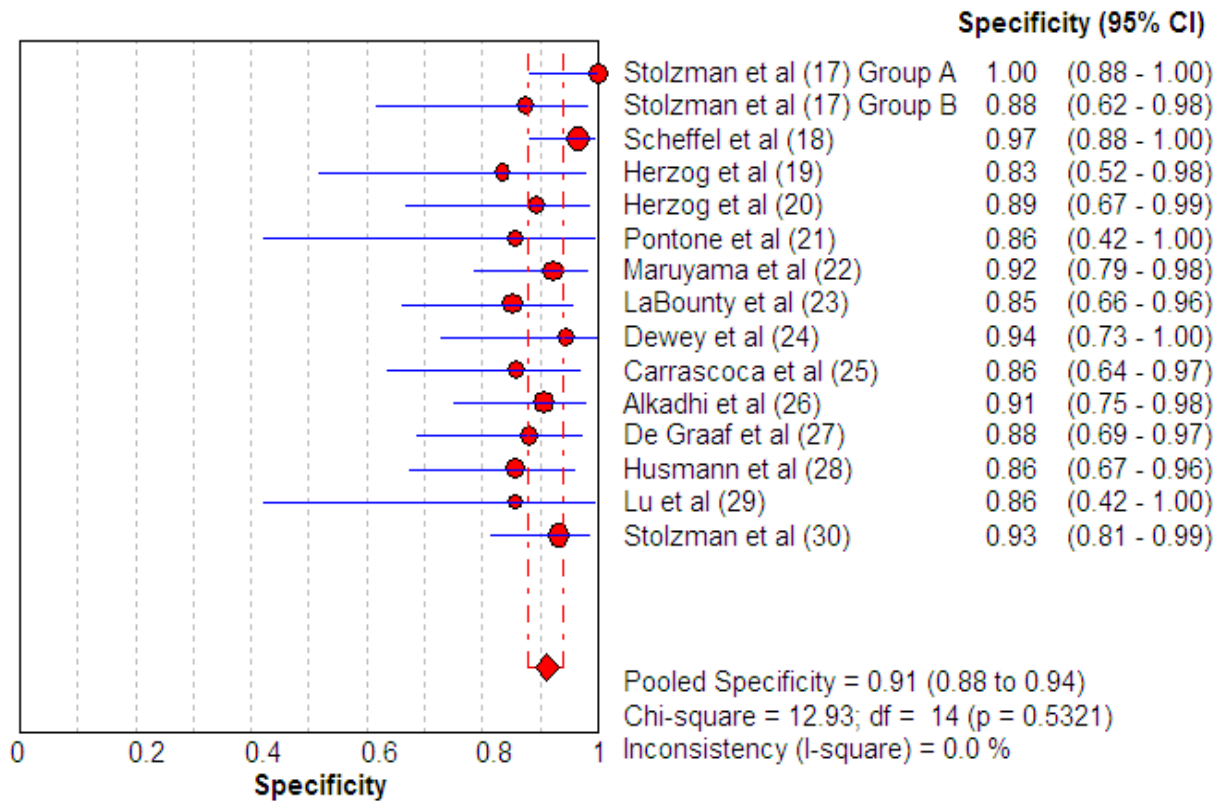


Fig. 4

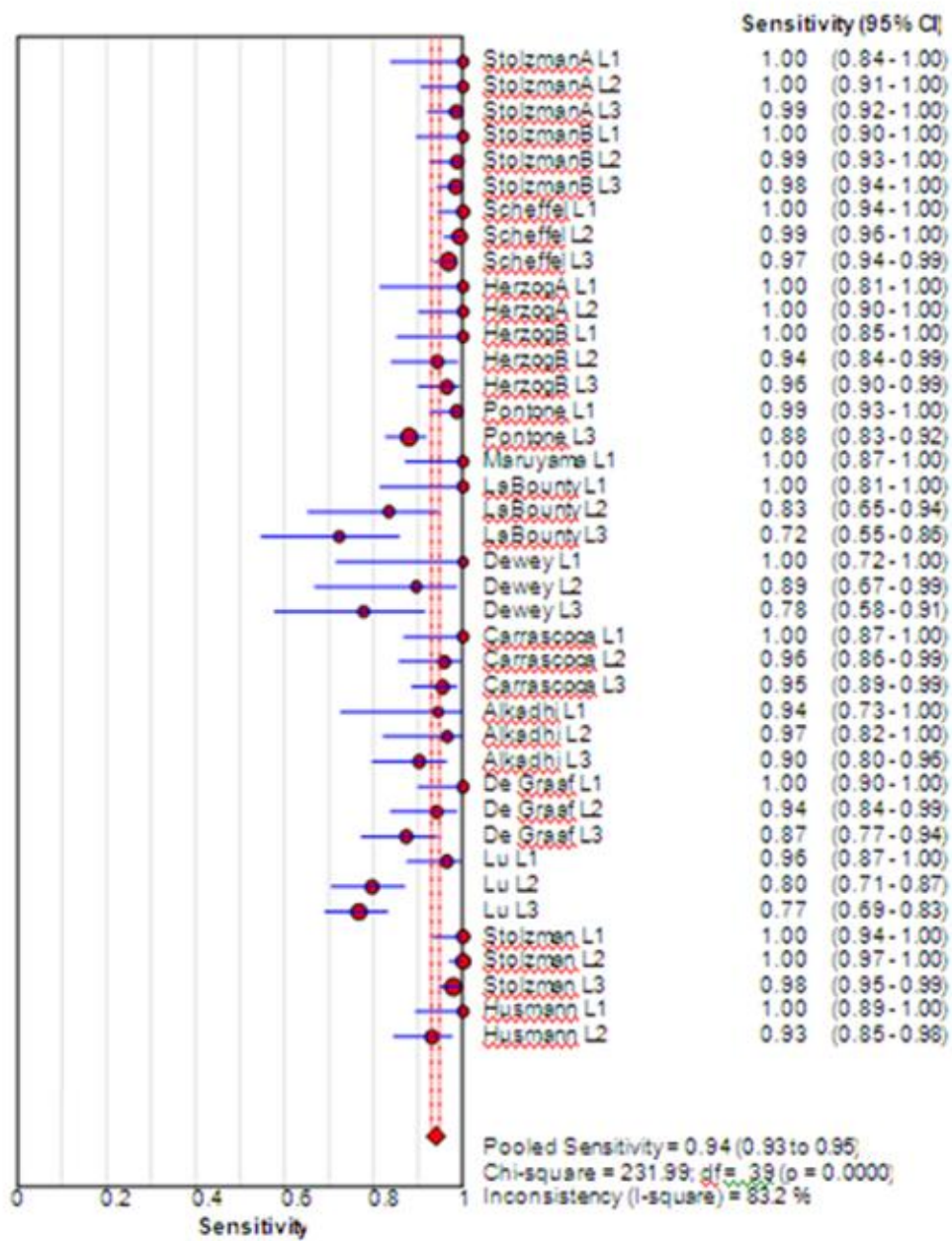


Fig. 5

