Multislice CT angiography in cardiac imaging. Part II: clinical applications in coronary artery disease

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ABSTRACT
Multislice computed tomography (CT) angiography represents a technological evolution in cardiac imaging due to improved spatial and temporal resolution. Rapid improvements in multislice CT scanners over the last decade have allowed this technique to become a viable and effective alternative to invasive coronary angiography in selected patients. Multislice CT angiography has demonstrated high sensitivity and specificity, and in particular, a very high negative predictive value, which makes it a valuable imaging modality for screening patients suspected of coronary artery disease. In addition, multislice CT angiography demonstrates accuracy in the detection and characterisation of coronary plaques, and it has been reported to play an important role in predicting disease progression and cardiac events. The aim of this review was to present an overview of the clinical applications of multislice CT angiography in coronary artery disease, with regard to its diagnostic accuracy and predictive value in coronary artery disease. Emerging areas of multislice CT, including dual-energy CT and CT myocardial perfusion, are also discussed. Limitations of multislice CT angiography and future directions of cardiac multislice CT are highlighted.

Keywords: cardiac imaging, coronary artery disease, coronary plaques, diagnostic accuracy, multislice CT

Singapore Med J 2010;51(4):282-289

INTRODUCTION
Coronary artery disease (CAD) is the leading cause of death in Western countries. Invasive coronary angiography is the gold standard technique for diagnostic and therapeutic purposes in CAD, owing to its superior spatial and temporal resolution. Recently, invasive coronary angiography has been challenged by the emergence and fast-growing technique of multislice computed tomography (MSCT) angiography, which is less invasive.[1-3] The diagnostic accuracy of MSCT angiography in CAD has been significantly improved with the increased performance of MSCT from the early generation of 4-slice CT scanners to later models such as 16-, 64-, dual-source, 256- and 320-slice CT scanners.[2-8] In particular, MSCT angiography has been reported to demonstrate a very high negative predictive value (more than 95%), indicating that it can be used as a reliable technique for excluding patients suspected of CAD, thereby reducing the need for invasive coronary angiography. MSCT angiography is also able to provide independent prognostic information for predicting disease progression and cardiac events.[9] This is of clinical significance because a normal cardiac CT angiography suggests that patients have normal coronary arteries and can be safely reassured without further testing or invasive examinations such as coronary angiography.

Another advantage of MSCT angiography over coronary angiography lies in the fact that MSCT allows for the characterisation of atherosclerotic plaques and the identification of plaque components.[10-13] Coronary angiography is restricted to visualising the luminal stenosis, but fails to provide information about the type of plaques or identify vulnerable plaques that could lead to thrombosis or myocardial infarction.[14] Therefore, MSCT angiography, a less invasive imaging modality, has been increasingly used for the detection of coronary stenosis, the evaluation of coronary plaques and the prediction of disease progression. In this review, we introduce the technological developments of MSCT in cardiac imaging, with a focus on the diagnostic and prognostic value of MSCT angiography in CAD. Emerging areas of MSCT, including dual-energy CT and CT myocardial perfusion, are also discussed, and future directions, including justification of the use of CT in cardiac imaging, are highlighted.

MSCT ANGIOGRAPHY IN CAD: CURRENT STATUS
MSCT angiography has been widely used in cardiac imaging, and its applications are mainly demonstrated in the following areas: calcium detection and scoring,

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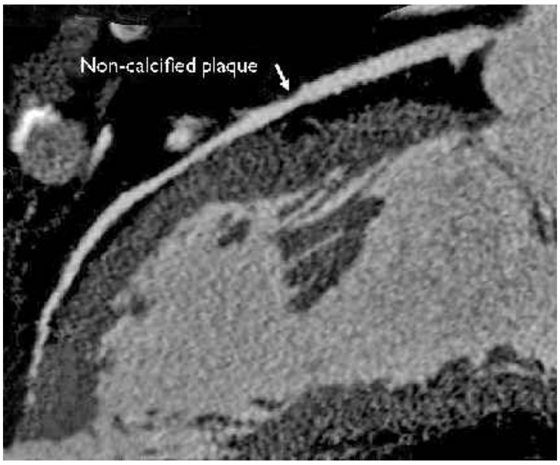

Fig. 1 Curved planar reformatted image acquired with a 64-slice CT angiography shows a non-calcified plaque at the mid-segment of the right coronary artery in a 57-year-old man suspected of coronary artery disease.

Fig. 2 Curved planar reformatted image acquired with a dual-source CT angiography shows calcified plaques at the proximal and distal segments of the left anterior descending artery in a 58-year-old man presenting with symptoms of chest pain.

the detection and characterisation of coronary plaques, the detection and diagnosis of coronary artery stenosis, as well as the prognostic value of CAD progression. In the following sections, applications of MSCT in CAD are discussed corresponding to each particular area.

Coronary calcium scoring

Coronary calcium scoring (CS) using MSCT has been validated as a useful imaging tool for risk stratification and reclassification of the risk of CAD.(15) Coronary atherosclerotic lesions often contain calcified components which used to be accurately measured using electron beam CT, but are currently being replaced with MSCT by the Agatston scoring method.(16,17) Recent guidelines from the American Heart Association reviewed the scientific data for cardiac MSCT imaging of CAD and atherosclerosis in symptomatic and asymptomatic patients, and approved screening using CS as a method to reclassify risk in patients with an intermediate risk based on traditional scores such as the Framingham and Procam algorithms.(18)

CS is usually performed as a screening method with the use of low radiation dose scanning techniques. The purpose of the scan is to detect and calculate the calcium density, volume or mass. The total coronary calcium is used as a way of prognosticating and stratifying the risk of CAD. The rationale behind it is that coronary artery calcification is part of the atherosclerotic degeneration of the arterial vessel wall, and coronary atherosclerosis is the only disease associated with calcium in the coronary arteries. Thus, measurement of the amount of calcium allows for an accurate estimation of the amount of coronary atherosclerosis and therefore, the risk of CAD. The total CS is calculated by adding up the volume of calcium in all coronary arteries by a weighting factor, dependent on the density of each calcified plaque.

CS is regarded as a good predictor of cardiac events and adds incremental prognostic value to risk factors in intermediate risk populations. Patients with a normal or zero CS fall into the lowest risk category, and are thus associated with a low risk of cardiac events, or considered to be clinically absent of any major atherosclerosis. The predictive value of CS is further supported by a recent study with the aim of identifying the incidence and predictors of conversion for a normal to abnormal coronary artery calcium over a period of five years.(19) In a prospective study, Min et al provided insight into the "warranty period" relative to a normal CS scan over time. They concluded that the rate of conversion to an abnormal CS scan was non-linear and occurred at a low frequency before four years of follow-up. Their data suggests that repeat CS should not be performed for a minimum of four years in individuals with a normal CS of zero.(19)

Characterisation of atherosclerotic plaques

Atherosclerotic plaque size and geometry play an important role in the natural progression of the disease and may have important clinical predictive value. It is widely accepted that plaque composition, rather than the degree of luminal narrowing, may be predictive of a patient's risk for cardiac events. Extensively calcified lesions most likely represent atherosclerosis at the later stages of remodelling and may reflect more stable lesions.(20) However, earlier stages of atherosclerosis that do not contain calcium deposits may be more prone to rupture with the subsequent occurrence of acute events.(21) Non-invasive imaging holds promise to not only identify flow-

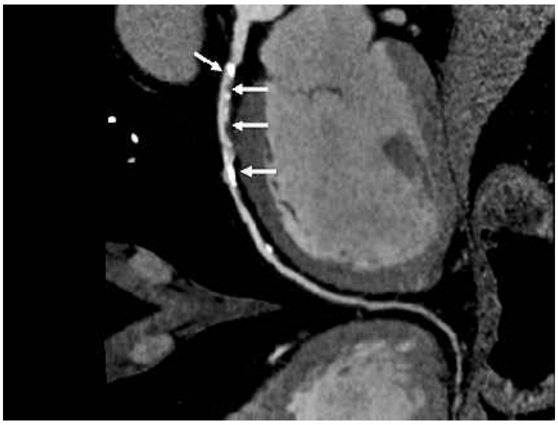

Fig. 3 Curved planar reformatted image acquired with a dual-source CT angiography shows a mixed type of calcified plaque at the mid-segment of the right coronary artery (arrows) in a 73-year-old man with significant coronary stenosis.

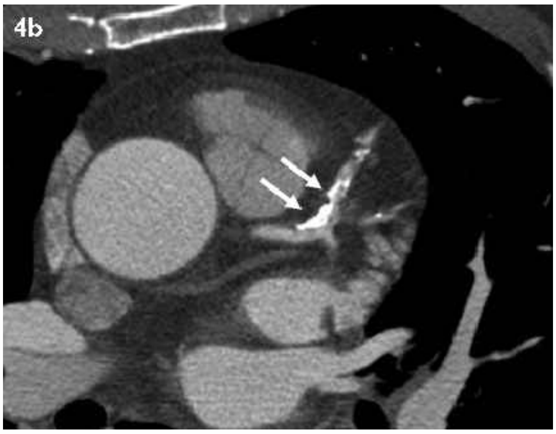

Fig. 4 (a) Focally calcified plaque and (b) extensively calcified plaque are visualised at the right coronary and left anterior descending arteries, respectively, in two patients suspected of coronary artery disease.

limiting coronary stenosis,[22] but also to detect plaque components, measure the atherosclerotic plaque burden and its response to treatment, as well as to differentiate stable plaques from those that are prone to rupture.[14,23] MSCT allows for the non-invasive detection of plaque morphology and composition (calcified vs. non-calcified atherosclerotic plaques) as well as the assessment of the extent of remodelling.[24]

Coronary plaques can be characterised into the following three types based on the CT attenuation:[25] (1) Non-calcified plaques are defined as lesions with a radiodensity greater than the neighbouring soft tissue but lower than the contrast-enhanced coronary lumen (Fig. 1); (2) Calcified plaques indicate lesions with a density higher than the contrast-enhanced coronary lumen (Fig. 2); (3) Mixed plaques are lesions with non-calcified and calcified components (calcium component between 20% and 80%) within a single lesion or within a segment of the coronary artery (Fig. 3). Calcified plaques can also be further classified into focal (Fig. 4a) and extensive types (Fig. 4b), depending on the distribution of plaques along the coronary artery.

Intravascular ultrasonography (IVUS), an invasive catheter-based imaging technique, is regarded as the reference method for studying coronary atherosclerotic plaques because it allows for reliable quantitative and qualitative characterisation of plaque components.[26] Previous studies have shown that MSCT is able to analyse coronary plaques quantitatively and qualitatively, especially by assessing the intra-plaque density.[12,27,28] However, a direct comparison of IVUS and MSCT has revealed general overestimation on MSCT for quantitative measurements of all areas and thickness.[29,30] Chopard et al recently reported that the 64-slice CT failed to analyse plaque morphology and components accurately.[30]

In a recent large, cohort study involving more than 1,000 patients, Motoyama et al evaluated the role of MSCT plaque characterisation in predicting acute coronary events. Their study showed that the composition of plaques on MSCT was closely associated with the risk of developing acute coronary syndrome.[31] Technological improvements in CT scanning, such as the development of 256- and 320-slice CT scanners, further enhance the ability of MSCT in the quantitative analysis of coronary plaques.[6-8] Korosoglou et al concluded that 256-slice CT is able to identify and characterise atherosclerotic plaques with high reproducibility for the assessment of plaque size and subtype categorisation of the observed lesions.[32] Despite these promising results, MSCT is, unfortunately, unable to detect unstable plaques;[33] thus, the differentiation of lipid-rich content from fibrous content with CT remains challenging due to considerable overlap in the attenuation values of lipid and fibrous tissues.[13]

Diagnostic value of MSCT angiography in CAD

Over the last decade, there has been a great deal of interest in the imaging and diagnosis of CAD using MSCT due to its less invasive nature and fast scanning technique with extended z-axis coverage when compared to single-slice CT. Earlier studies with 4-slice and 16-slice CT showed moderate diagnostic accuracy, with the pooled sensitivity and specificity being 78% and 93%, and 82% and 95%, respectively, due to limited spatial and temporal resolution.[34]

MSCT examination times are shortened and the acquisition of isotropic volume data is made available with further improvements in scanning techniques using 64-slice CT compared with 16-slice and 4-slice CT, owing to improved spatial and temporal resolution. Several meta-analyses of 64-slice CT studies have reported a range of results in sensitivity and specificity: sensitivities of 93% and specificities of 96% in six studies,[35] 97% and 88% in 15 studies,[36] 86% and 96% in 19 studies,[37] as well as 99% and 89% in 28 studies.[38] These studies have indicated that MSCT, especially with 64-slice or more CT, has high diagnostic accuracy for the detection of CAD and could be used as an effective alternative to invasive coronary angiography in selected patients.

The introduction of dual-source CT in 2006 marked another technological improvement to MSCT in cardiac imaging, as the temporal resolution was shortened from 165 ms to 83 ms, and heart rate dependence was eliminated.[39] Studies performed with dual source CT have shown promising results with high diagnostic accuracy for the detection of CAD, and most importantly, the image quality is independent of heart rate.[40-42]

The race for improved technology in multislice CT scanning is continues. The development of wide-area detector CT enables greater coverage per gantry rotation. The expansion of MSCT systems from a prototype 256-slice to a 320-slice system has allowed for the acquisition of whole-heart coverage in one gantry rotation with a slice thickness of 0.5 mm.[6-8] With 320-slice CT, a 16 cm craniocaudal coverage can be obtained in a single heartbeat, with excellent image quality and demonstration of the entire coronary arteries. It has been reported in a recent study that high diagnostic value, in particular, a negative predictive value of 100% (including non-diagnostic images) and a diagnostic accuracy of 95%, were achieved with 320-slice CT angiography for the detection of more than 50% coronary stenosis on a patient-based analysis.[43] This indicates that 320-slice CT angiography is a highly sensitive modality for the detection of significant CAD, although more data is required to confirm its diagnostic accuracy.

Prognostic value of MSCT angiography in CAD

Patient risk stratification and assessment of the prognosis are important to decide on the appropriate management of patients with suspected CAD, to determine whether aggressive therapy is required and to select patients for catheterisation. It has been reported that patients with three-vessel disease on coronary angiography have approximately a two-fold higher 12-year mortality rate than patients with one-vessel disease, and the presence of left main coronary disease is an important negative predictor.[44] Since MSCT is not only able to assess coronary luminal changes, but also has the potential to visualise coronary artery wall morphology, characterise atherosclerotic plaques and identify non-stenotic plaques that may be undetected by conventional coronary angiography, it could be used as a non-invasive technique to provide prognostic information in patients with suspected CAD.

MSCT angiography has been proposed in place of stress-testing for risk stratification in intermediate-risk patients with suspected CAD.[45] Preliminary reports have shown that MSCT angiography is able to provide independent prognostic information for predicting cardiac events and mortality in patients with known or suspected CAD based on short- to mid-term follow-up.[9,46] Findings of MSCT angiography have been closely related to future cardiac events, with 0% or 1% cardiac events being reported in patients with normal cardiac CT or mild CAD, and up to 30% in patients with one or more vessel obstructive CAD.[47,48] The extent of coronary atherosclerotic plaque as well as the presence of proximal atherosclerotic plaque was found to be associated with a significantly higher risk of a major adverse cardiac event.[48]

Functional evaluation of MSCT angiography in CAD

Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are well-accepted and widely established methods for the functional evaluation of CAD because they reveal perfusion defects caused by obstructive coronary stenosis. The most important applications of SPECT and PET are in the diagnosis of CAD, the prediction of disease prognosis, selection for revascularisation and the assessment of acute coronary syndromes. Conventional MSCT imaging only enables the acquisition of anatomic details concerning the degree of coronary stenosis; however, with the emergence of dual-source and dual-energy CT, the acquisition of both anatomic and functional information is possible.[49] With the introduction of the two-tube, two-detector configuration, it is now possible to acquire simultaneous images of high and low radiography energy spectra with a single scan. Previous studies have demonstrated the potential usefulness of cardiac dual-energy CT for the comprehensive diagnosis of CAD and myocardial ischaemia, based on a single, contrast-enhanced electrocardiogram (ECG)-gated CT. [50,51] Dual-energy CT has been reported to have 92% sensitivity and 93% specificity, with 93% accuracy for the detection of any type of myocardial perfusion defect confirmed on SPECT.[50,51]

Rocha-Filho et al recently reported the incremental value of adenosine-mediated stress CT perfusion imaging to coronary CT angiography for the detection of haemodynamically significant CAD with the aid of dual-source CT. The study demonstrated that a combined dual-source CT protocol for evaluating stress myocardial perfusion and coronary anatomy is feasible with an acceptable contrast medium load and a reasonable radiation dose. Moreover, the study increases our understanding of how stress CT perfusion can play a role in a clinical scenario, particularly in patients with a high pretest probability for CAD.[52] Despite promising results, large patient cohorts are required to confirm the potential application of a single protocol for the anatomic and functional assessment of CAD.

LIMITATIONS OF MSCT ANGIOGRAPHY IN CAD

It has been well established that MSCT angiography in highly calcified coronary arteries is difficult because of artifacts caused by high-density calcification. Accordingly, patients with high Agatston calcium scores were generally excluded from previous studies of MSCT, including 64-slice CT. The majority of the studies indicate that a highly negative predictive value of MSCT angiography can reliably rule out obstructive CAD.[36,53,54] However, the sensitivity, especially the positive predictive value of MSCT angiography in CAD, was reported to be variable according to several meta-analyses.[35-38] Specifically, CS > 400 were found to significantly reduce diagnostic specificity.

In the ACCURACY prospective multicentre study of patients with chest pain without known CAD and intermediate disease prevalence, 64-slice CT angiography had a patient-based sensitivity of 94% and specificity of 83% in detecting coronary stenosis ≥ 70% (patients with high calcium scores were included in the study).[53] In the CORE prospective multicentre study of patients with suspected symptomatic CAD, 64-slice CT angiography had a patient-based sensitivity of 85% and specificity of 90% (patients with a CS of more than 600 were excluded from the study) for detecting coronary stenosis ≥ 50%.[55] However, the negative predictive value of 83% for MSCT angiography in this study is much lower than the 99% value reported in the Budoff's study.[53] These conflicting findings represent the limitations of the current studies due to the use of different study designs in each single centre and the different degree of rigour applied in controlling bias in a small study. It has been shown that significant statistical heterogeneity exists among published studies, with smaller studies reporting a higher diagnostic accuracy of MSCT angiography in CAD.[56] Therefore, results of the diagnostic value of MSCT angiography in CAD reported in the literature must be interpreted with caution.

LIMITATIONS OF MSCT IN CALCIUM SCORING

Although zero CS are associated with a low risk for developing cardiovascular events in the following two to five years,[57] even zero CS may not exclude luminal obstructive disease. Rubinshtein et al concluded that 7% of patients with acute or long-term chest pain who had zero CS were found to have significant CAD.[58] It has been reported that a negative CS cannot be reliably used for ruling out obstructive CAD, especially in patients who are young and presenting with acute coronary syndrome.[59,60] Most of the studies reported that the cumulative incidence of a zero or low CS was associated with a risk of 0.1% and 0.7% of cardiac events with a follow-up period of three to five years.[61] One study showed a higher cumulative incidence of 4.4% cardiac events during more than six years of follow-up.[62] This is due to the use of 6.0-mm slice reconstruction instead of 3.0-mm for CS in that study, which resulted in missing calcified lesions. This was also confirmed by a recent study using 320-slice CT for CS.[63] 21% of patients with coronary calcium who were detected on the 0.5-mm slice reconstruction were missed on the 3.0-mm slice reconstruction. It was concluded in that study that prospective ECG-triggering at 0.5-mm slice reconstruction led to an increased sensitivity for calcium detection compared to 3.0-mm slice reconstruction.

SUMMARY AND CONCLUSION

Multislice CT has been recognised as the most valuable and potentially effective alternative to invasive coronary angiography for the detection and diagnosis of CAD due to its rapid technological development and improved diagnostic accuracy. Multislice CT demonstrates a high level of accuracy for the detection of coronary calcium, the characterisation of atherosclerotic plaques and the prediction of disease progression. Currently, with a moderate to high diagnostic value, multislice CT angiography cannot be recommended as an effective alternative to invasive coronary angiography in patients suspected of CAD. However, with a very high negative predictive value, it is generally agreed that multislice CT angiography can be used as a reliable technique for patient screening, thus reducing the number of unnecessary invasive coronary angiography examinations.

Multislice CT angiography also serves as an independent predictor for predicting disease progress and cardiac events. This is of clinical significance because a normal cardiac CT angiography suggests that patients have normal coronary arteries and can be safely reassured without further testing or invasive examinations such as coronary angiography. Future directions of MSCT should focus on the continued improvement of temporal resolution and the development of advanced image reconstruction algorithms to minimise the effects of severe coronary calcification. Another important aspect to be emphasised is the radiation dose associated with cardiac multislice CT angiography, which will be discussed in Part III of this series.

REFERENCES

1. McCollough CH, Zink FE. Performance evaluation of a multi-slice CT system. Med Phys 1999; 26:2223-30.
2. Nieman K, Oudkerk M, Rensing BJ, et al. Coronary angiography with multi-slice computed tomography. Lancet 2001; 357:599-603.
3. Achenbach S, Giesler T, Ropers D, et al. Detection of coronary artery stenoses by contrast-enhanced, retrospectively electrocardiographically-gated, multislice spiral computed tomography. Circulation 2001; 103:2535-8.
4. Kuettner A, Trabold T, Schroeder S, et al. Noninvasive detection of coronary lesions using 16-detector multislice spiral computed tomography technology: initial clinical results. J Am Coll Cardiol 2004; 44:1230-7.
5. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. J Am Coll Cardiol 2005; 46:552-7.
6. Chao SP, Law WY, Kuo CJ, et al. The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. Eur Heart J 2010. [Epub ahead of print]
7. Rybicki FJ, Otero HJ, Steigner ML, et al. Initial evaluation of coronary images from 320-detector row computed tomography. Int J Cardiovasc Imaging 2008; 24:535-46.
8. Dewey M, Zimmermann E, Deissenrieder F, et al. 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 2009; 120:867-75.
9. Gaemperli O, Valenta I, Schepis T, et al. Coronary 64-slice CT angiography predicts outcome in patients with known or suspected coronary artery disease. Eur Radiol 2008; 18:1162-73.
10. Schroeder S, Kuettner A, Leitritz M, et al. Reliability of differentiating human coronary plaque morphology using contrast-enhanced multislice spiral computed tomography: a comparison with histology. J Comput Assist Tomogr 2004; 28:449-54.
11. Schroeder S, Kopp AF, Baumbach A, et al. Noninvasive detection and evaluation of atherosclerotic coronary plaques with multislice computed tomography. J Am Coll Cardiol 2001; 37:1430-5.
12. Leber AW, Knez A, Becker A, et al. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intracoronary ultrasound. J Am Coll Cardiol 2004; 43:1241-7.
13. Hoffmann U, Moselewski F, Nieman K, et al. Noninvasive assessment of plaque morphology and composition in culprit and stable lesions in acute coronary syndrome and stable lesions in stable angina by multidetector computed tomography. J Am Coll Cardiol 2006; 47:1655-62.
14. Takumi T, Lee S, Hamasaki S, et al. Limitation of angiography to identify the culprit plaque in acute myocardial infarction with coronary total occlusion utility of coronary plaque temperature measurement to identify the culprit plaque. J Am Coll Cardiol 2007; 50:2197-203.
15. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2007; 49:378-402.
16. Oudkerk M, Stillman AE, Halliburton SS, et al. Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging. Eur Radiol 2008; 18:2785- 807.
17. Rumberger JA. Tomographic plaque imaging with CT: technical considerations and capabilities. Prog Cardiovasc Dis 2003; 46:123-34.
18. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006; 114:1761–91.
19. Min JK, Lin FY, Gidseg DS, et al. Determinants of coronary calcium conversion among patients with a normal coronary calcium scan: what is the "warranty period" for remaining normal? J Am Coll Cardiol 2010; 55:1110-7.
20. O'Rourke RA, Brundage BH, Froelicher VF, et al. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. J Am Coll Cardiol 2000; 36:326-40.
21. Schuijf JD, Beck T, Burgstahler C, et al. Differences in plaque composition and distribution in stable coronary artery disease versus acute coronary syndromes; non-invasive evaluation with multi-slice computed tomography. Acute Card Care 2007; 9:48-53.
22. Meijboom WB, Meijs MF, Schuijf JD, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. J Am Coll Cardiol 2008; 52:2135-44.
23. Kitagawa T, Yamamoto H, Horiguchi J, et al. Characterization of noncalcified coronary plaques and identification of culprit lesions in patients with acute coronary syndrome by 64-slice computed tomography. JACC Cardiovasc Imaging 2009; 2:153-60.
24. Sun Z, Dimpudus FJ, Nugroho J, Adipranoto JD. CT virtual

intravascular endoscopy assessment of coronary artery plaques: A preliminary study. Eur J Radiol 2009. [Epub ahead of print]
25. Pundziute G, Schuijf JD, Jukema JW, et al. Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007; 49:62-70.
26. von Birgelen C, Klinkhart W, Mintz GS, et al. Plaque distribution and vascular remodeling of ruptured and nonruptured coronary plaques in the same vessel: an intravascular ultrasound study in vivo. J Am Coll Cardiol 2001; 37:1864-70.
27. Moselewski F, Ropers D, Pohle K, et al. Comparison of measurement of cross-sectional coronary atherosclerotic plaque and vessel areas by 16-slice multidetector computed tomography versus intravascular ultrasound. Am J Cardiol 2004; 94:1294-7.
28. Achenbach S, Ropers D, Hoffmann U, et al. Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. J Am Coll Cardiol 2004; 43:842-7.
29. Leber AW, Knez A, von Ziegler F, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. J Am Coll Cardiol 2005; 46:147-54.
30. Chopard R, Boussel L, Motreff P, et al. How reliable are 40 MHz IVUS and 64-slice MDCT in characterizing coronary plaque composition? An ex vivo study with histopathological comparison. Int J Cardiovasc Imaging 2010; 26:373-83.
31. Motoyama S, Sarai M, Harigay H, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. J Am Coll Cardiol 2009; 54:49-57.
32. Korosoglou G, Mueller D, Lehrke S, et al. Quantitative assessment of stenosis severity and atherosclerotic plaque composition using 256-slice computed tomography. Eur Radiol 2010. [Epub ahead of print]
33. Matter CM, Stuber M, Nahrendorf M. Imaging of the unstable plaque: how far have we got? Eur Heart J 2009; 30:2566-74.
34. Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: a meta-analysis. Eur J Radiol 2006; 60:279-86.
35. Vanhoenacker PK, Heijenbrok-Kal MH, Van Heste R, et al. Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis. Radiology 2007; 244:419-28.
36. Sun Z, Lin C, Davidson R, Dong C, Liao Y. Diagnostic value of 64-slice CT angiography in coronary artery disease: a systematic review. Eur J Radiol 2008; 67:78-84.
37. Abdulla J, Abildstrom Z, Gotzsche O, et al. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. Eur Heart J 2007; 28:3042-50.
38. Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. Heart 2008; 94:1386-93.
39. Flohr TG, McCollough CH, Bruder H, et al. First performance evaluation of a dual-source CT (DSCT) system. Eur Radiol 2006; 16:256-68.
40. Leber AW, Johnson T, Becker A, et al. Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. Eur Heart J 2007; 28:2354-60.
41. Brodoefel H, Burgstahler C, Tsiflikas I, et al. Dual-source CT: effect of heart rate, heart rate variability, and calcification on image quality and diagnostic accuracy. Radiology 2008; 247:346-55.
42. Johnson TR, Nikolaou K, Busch S, et al. Diagnostic accuracy of dual-source computed tomography in the diagnosis of coronary artery disease. Invest Radiol 2007; 42:684-91.
43. de Graaf FR, Schuijf JD, van Velzen JE, et al. Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of significant coronary artery disease. Eur Heart J 2010. [Epub ahead of print]
44. Emond M, Mock MB, Davis KB, et al. Long-term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. Circulation 2004; 90:2645-57.
45. Hendel RC, Patel MR, Kramer CM, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J Am Coll Cardiol 2006; 48:1475–97.
46. Gilard M, Le Gal G, Cornily JC, et al. Midterm prognosis of patients with suspected coronary artery disease and normal multislice computed tomographic findings: a prospective management outcome study. Arch Intern Med 2007; 167:1686-9.
47. Aldrovandi A, Maffei E, Palumbo A, et al. Prognostic value of computed tomography coronary angiography in patients with suspected coronary artery disease: a 24-month follow-up study. Eur Radiol 2009; 19:1653-60.
48. Carrigan TP, Nair D, Schoenhagen P, et al. Prognostic utility of 64-slice computed tomography in patients with suspected but no documented coronary artery disease. Eur Heart J 2009; 30:362-71.
49. Schwarz F, Ruzsics B, Schoepf UJ, et al. Dual-energy CT of the heart--principles and protocols. Eur J Radiol 2008; 68:423-33.
50. Ruzsics B, Lee H, Zwerner PL, et al. Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia-initial experience. Eur Radiol 2008; 18:2414-24.
51. Ruzsics B, Schwarz F, Schoepf UJ, et al. Comparison of dual-energy computed tomography of the heart with single photon emission computed tomography for assessment of coronary artery stenosis and of the myocardial blood supply. Am J Cardiol 2009; 104:318-26.
52. Rocha-Filho JA, Blankstein R, Shturman LD, et al. Incremental value of adenosine-induced stress myocardial perfusion imaging with dual-source CT at cardiac CT angiography. Radiology 2010; 254:410-9.
53. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol 2008; 52:1724-32.
54. Mowatt G, Cummins E, Waugh N, et al. Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease. Health Technol Assess 2008;12:iii-iv, ix-143.
55. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. N Engl J Med 2008;

359:2324-36.
56. Hamon M, Biondi-Zoccai GG, Malagutti P, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography: a meta-analysis. J Am Coll Cardiol 2006; 48:1896-910.
57. Cheng VY, Lepor NE, Madyoon H, et al. Presence and severity of noncalcified coronary plaque on 64-slice computed tomographic coronary angiography in patients with zero and low coronary artery calcium. Am J Cardiol 2007; 99:1183-6.
58. Rubinshtein R, Gaspar T, Halon DA, et al. Prevalence and extent of obstructive coronary artery disease in patients with zero or low calcium score undergoing 64-slice cardiac multidetector computed tomography for evaluation of a chest pain syndrome. Am J Cardiol 2007; 99:472-5.
59. Marwan M, Ropers D, Pflederer T, Daniel WG, Achenbach S. Clinical characteristics of patients with obstructive coronary lesions in the absence of coronary calcification: an evaluation by coronary CT angiography. Heart 2009; 95:1056-60.
60. Henneman MM, Schuijf JD, Pundziute G, et al. Noninvasive evaluation with multislice computed tomography in suspected acute coronary syndrome: plaque morphology on multislice computed tomography versus coronary calcium score. J Am Coll Cardiol 2008; 52:216-22.
61. Oudkerk M, Stillman AE, Halliburton SS, et al. Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging. Int J Cardiovasc Imaging 2008; 24:645-71.
62. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004; 291:210-15.
63. van der Bijl N, de Bruin PW, Geleijns J, et al. Assessment of coronary artery calcium by using volumetric 320-row multi-detector computed tomography: comparison of 0.5 mm with 3.0 mm slice reconstructions. Int J Cardiovasc Imaging 2010; 26:473-82.

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