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Coronary CT Angiography in Coronary Artery Disease: from Diagnosis to Prevention

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ABSTRACT

Coronary CT angiography has emerged as reliable imaging tool for the diagnosis of coronary artery disease. Coronary CT angiography has the ability to demonstrate excellent visualization of anatomical changes in coronary artery with high diagnostic value in the detection of lumen stenosis or occlusion, and characterization of coronary plaque composition. Furthermore, coronary CT angiography offers prognostic value in the prediction of adverse cardiac events. Although coronary CT angiography is limited to the assessment of coronary anatomy and lumen changes, coronary CT angiography-derived computer modeling and hemodynamic analysis has the potential to evaluate functional significance of coronary artery disease. This review article aims to provide an overview of both diagnostic and prognostic value of coronary CT angiography in coronary artery disease. Limitations of coronary CT angiography are briefly discussed, while functional assessment of coronary artery disease with use of coronary CT angiography-generated coronary artery models is highlighted.

KEYWORDS: Coronary artery disease, Coronary computed tomography angiography, Diagnosis, Plaque, Prognosis.

INTRODUCTION

There is a growing body of evidence supporting the fact that Coronary CT Angiography (CCTA) is a well-established imaging modality in the diagnosis of Coronary Artery Disease (CAD) due to its less invasiveness, high diagnostic value, and widespread accessibility.[1-7] Diagnostic accuracy of CCTA has been significantly improved with technological advancements in multislice CT scanning techniques, which are represented by the development from early generation of 4-slice CT to 64-slice, dual-source CT and recently available 320-slice CT.[1-11] It has been reported that CCTA has a very high negative predictive value, thus enabling it as a reliable screening tool in patients with low or intermediate risk of CAD.[7-11] This is clinically important as unnecessary invasive coronary angiography or other examinations can be avoided in patients with a normal CCTA. Furthermore, CCTA has the potential to visualize coronary artery wall and plaque morphology, characterize atherosclerotic plaques and identify non-stenotic plaques that may be undetected by invasive coronary angiography. Findings of CCTA are closely related to the clinical outcomes with very low rate of adverse cardiac events occurring in patients with normal CCTA, but with significantly high rates of these events in patients with obstructive CAD.[12-14,15,16]

Despite these promising reports, one limitation of CCTA lies in the high radiation dose which has been well addressed by recently introduced dose-reduction strategies.[8,9,17-20]

Although CCTA has superior spatial resolution which allows excellent visualization of coronary artery tree and reliable detection of coronary wall changes, another limitation of this technique is that it is still limited to the assessment of morphological changes, but fails to provide functional significance of coronary stenosis. Although recent studies suggest that cardiac CT myocardial perfusion is feasible and provides functional significance of CAD, the diagnostic accuracy suffers from high false positive findings.[21-23] This has been overcome with the use of hemodynamic analysis of blood flow to coronary artery based on numerical simulation using computational fluid dynamic techniques.[24-28] The purpose of this review is to provide an overview of CCTA in CAD, with a focus on the diagnostic and prognostic value. Limitations of CCTA in CAD are discussed while the current research developments with use of CCTA-derived coronary models for simulation of hemodynamic changes are highlighted.

DIAGNOSTIC VALUE OF CCTA IN CAD

The diagnostic value of CCTA in CAD has been significantly augmented with the development of multislice CT scanners and Electrocardiography-Gated (ECG) scanning technique over the last decades. According to several systematic reviews and meta-analyses of 64-slice CCTA studies in the diagnosis of CAD, the sensitivities were more than 97% and specificities were more than 87% in most of the studies.[3,5-7,29,30] These analyses indicate that CCTA has high diagnostic value in the detection and characterization of CAD due to presence of plaques (Figure 1).
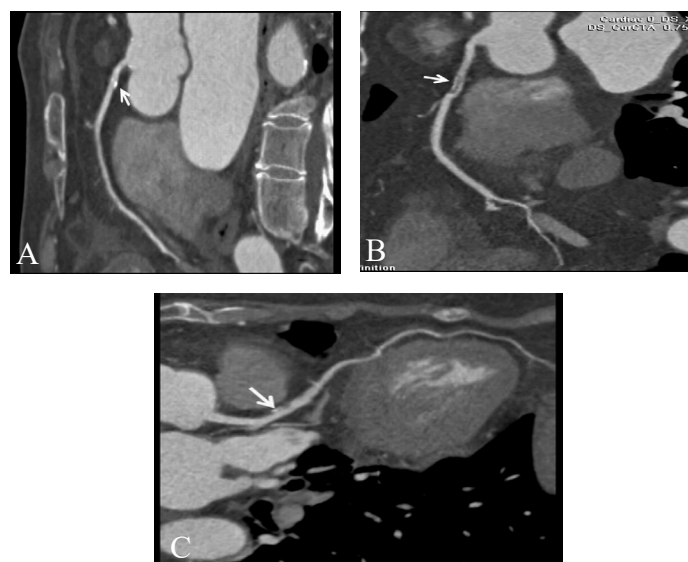

Figure 1: Coronary CT angiography characterization of plaque composition. A. A calcified plaque (arrow) is seen in the proximal segment of right coronary artery in a 65-year-old woman with suspected coronary artery disease. B. A non-calcified plaque (arrow) is detected in the proximal segment of right coronary artery in a 67-year-old woman with known coronary artery disease. C. A mixed plaque (arrow) is observed in the proximal segment of left anterior descending coronary artery in a 55-year-old female with suspected coronary artery disease.

Currently, 320-slice CT represents the recently technological developments in imaging coronary artery disease with good results achieved. Expansion of multislice CT systems from a 64-slice to 320-slice system has allowed for the accurate assessment of stenosis severity and atherosclerotic plaque composi-

tion, or even the acquisition of whole-heart coverage in one gantry rotation. Two recently reported systematic reviews and meta-analyses further confirmed the high diagnostic accuracy of 320-slice CCTA.[31,32] The diagnostic sensitivity was similar to that reported in the 64-slice CCTA, but the specificity was higher in 320-slice CCTA than in 64-slice CCTA studies, indicating the high value of 320-slice CCTA for excluding coronary artery stenosis. However, it has to be recognized that diagnostic performance of 320-slice CCTA is similar to that of 64- and 128-slice for the determination of ≥50% coronary artery stenosis due to its limited temporal resolution, despite improved extended z-axis coverage.[33]

Prospectively ECG-triggered CCTA scan (also called step-and-shoot mode) is triggered by the ECG signal and x-ray tube is only turned on at the selected cardiac phase (diastolic), and turned off during the rest of the cardiac cycle. A significant dose reduction with high image quality has been reported in studies performed with prospectively ECG-triggered CCTA (Figure 2).[34-36,37]
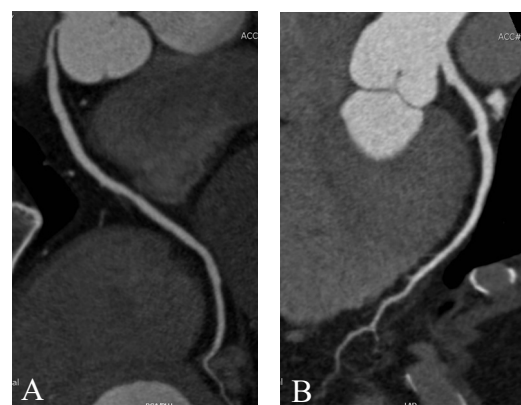
Figure 2: Prospectively ECG-triggered coronary CT angiography in a 54-year-old male with suspected coronary artery disease shows normal right (A) and left coronary arteries (B) with excellent demonstration of anatomical details.

Four systematic reviews and meta-analyses of studies on the use of prospectively ECG-triggered 64-or more slice CCTA reported that the mean patient-based sensitivities and specificities ranged from 99% to 100%, and 89% to 92%, respectively, which is similar to those reported with use of retrospectively ECG-gated CCTA, but with resultant much lower radiation dose.[18,19,38,39] Table 1 summarizes the diagnostic value of these systematic reviews and meta-analyses of studies performed with CCTA in CAD.
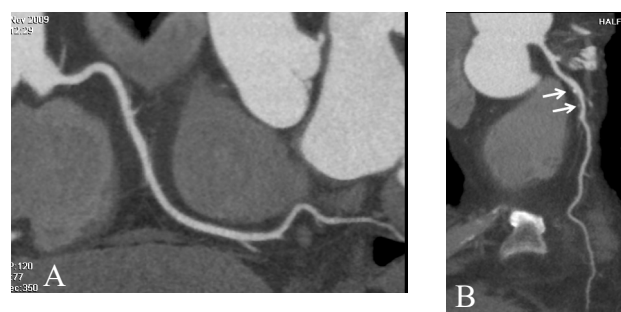
PROGNOSTIC VALUE OF CCTA IN CAD

CCTA can detect non-obstructive and non-calcified plaques as well as plaques with positive remodeling, both of which play an important role in the pathophysiology of acute myocardial infarction and may be indicative of vulnerable plaques, which are closely related to the development of major adverse cardiac events.[40,41]

Type of CT scan	First author	No. of articles in the analysis	Patient-based sensitivity (95% CI)	Patient-based specificity (95% CI)
64-slice coronary CT angiography	Abdulla et al, 2007 (5)	27 studies	97.5% (96-99)	91% (87.5-94)
	Stein et al, 2008 (6)	23 studies	98% (96-98)	88% (85-89)
	Mowatt et al, 2008 (7)	28 studies	99% (97-99)	89% (83-94)
	Sun et al, 2008 (3)	15 studies	97% (94-99)	88% (79-97)
	Guo et al, 2011 (29)	24 studies	98% (99-99)	87% (83-90)
	Salavati et al, 2012 (30)	25 studies	99% (97-99)	89% (84-92)
320-slice coronary CT angiography	Gaudio et al, 2013 (31)	7 studies	95.4% (88.8-98.2)	94.7% (89.1-97.5)
	Li et al, 2013 (32)	10 studies	93% (91-95)	86% (82-89)
Prospectively ECG-triggered coronary CT angiography	Von Ballmoos et al, 2011 (38)	16 studies	100% (98-100)	89% (82-89)
	Sun et al, 2012 (39)	14 studies	99% (98-100)	91% (88-94)
	Sun et al, 2012 (18)	22 studies	97.7% (93.7-100)	92.1% (87.2-97)
	Sabarudin et al, 2013 (19)	23 studies	98.3% (96-100)	90.5% (85.7-96)

Table 1: Diagnostic value of coronary CT angiography in coronary artery disease according to systematic reviews and meta-analyses

Studies from single center experience based on short and mid-term follow-up showed that there is a direct correlation between CCTA findings and the occurrence of future cardiac events, as normal CCTA is associated with a very low rate of adverse cardiac events (<1%), while in patients with obstructive CAD as observed on CCTA, the event rate is significantly higher, ranging from 3-59% (Figure 3).[15,16,42-45] Long-term follow-up between 4 and 5 years reported similar results with progressive increase in cardiac event rates in patients with non-obstructive and obstructive CAD as defined by CCTA, while almost 0% event rates in normal coronary arteries.[46-49] Dougoud et al. assessed the prognostic value of CCTA in 218 patients with suspected CAD over a mean period of 6.9 years which represented the longest follow-up with use of 64-slice CCTA.[50] Their results are in line with these reports highlighting the excellent long-term prognosis in normal CCTA with a very low likelihood for cardiac events. Two systematic reviews/meta-analyses on the prognostic value of CCTA also confirmed these findings with low cumulative major adverse cardiac events in patients with normal CCTA findings, but much higher event rates in patients with abnormal CCTA showing obstructive CAD.[51,52]

Goldstein et al. in their multicenter study consisting of 700 patients with acute chest pain symptoms further verified the relationship between CCTA findings and prognostic value of cardiac events.[53] Min et al. in their CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) trial evaluated a consecutive cohort of 24,775 patients with suspected CAD who were enrolled at 12 international centers[54] Their results along with others showed that a significant increased risk in adverse cardiac events was observed in patients with CCTA-identified obstructive CAD but with much lower event rates in patients with normal CCTA findings.[54-55,56,57] These results indicate that CCTA could serve as an independent predictor of major adverse cardiac events in patients with suspected CAD, although more studies based on large cohort with long-term follow-up are needed.

LIMITATIONS OF CCTA

Despite rapid technological improvements in CT scanning techniques, CCTA has limitations in the following areas. Firstly, it is a technique with associated high radiation dose which raises concerns in the medical field as there is potential risk of radiation-induced malignancy. With increasing applications of CCTA in the diagnosis of CAD, the research focus has shifted from the previous emphasis on diagnostic value of CCTA to the current focus on reduction of radiation dose with acceptable diagnostic image quality. Using many of the technologies and dose-reduction strategies, it is possible to lower the dose to less than 5mSv, where doses of less than 1mSv is already achievable with the current CT models, which is lower than that of invasive coronary angiography.[8,9,17-20,58-60,61,62] Thus, significant progress has been made over the last decade to lower radiation dose resulting from CCTA.

Secondly, although CCTA allows a comprehensive evaluation of coronary plaques in terms of coronary lumen changes and characterization of plaques (calcified *vs* non-cal

Figure 3.A.Coronary CT angiography shows normal findings in a 66-year-old male with chest discomfort afterexercise. Normal right coronary artery is clearly demonstrated in curved planar reformatted image. B. Coronary CT angiography shows significant stenosis in the left anterior descending (LAD) in the same patient due to presence of mixed plaques as visualized on curved planar reformatted image (arrows).

cified), it is unable to determine which plaques are 'vulnerable' or unstable *versus* those which are stable.[63,64] Therefore, differentiation of lipid-rich content from fibrous content with CCTA remains challenging due to considerable overlap in the attenuation values of lipid and fibrous tissue. Intravascular ultrasound is the gold standard for the assessment of coronary plaque composition and progression in clinical studies.[65,66] Furthermore, extensive coronary artery calcification (coronary calcium score >400) still limits the diagnostic accuracy of CCTA, in particular lowering the sensitivity to some extent due to false positive results, and this is being addressed with improvements in CT imaging.[67,68]

Thirdly, CCTA has superior spatial resolution which allows it to demonstrate excellent visualization of coronary lumen change, however, it has limited value in the diagnostic evaluation of myocardial ischemia. The presence of anatomic lesions does not necessarily correlate with functional significance of CAD, which refers to decreased myocardial perfusion.[69] Studies comparing coronary lesions detected on CCTA with ischemia as documented on myocardial perfusion imaging have shown that CCTA has limited diagnostic value (about 50%) for assessment of abnormal myocardial perfusion in patients with more than 50% coronary stenosis when compared to cardiac ischemia which was confirmed by Single Photon Emission Computed Tomography (SPECT).[70,71] Therefore, SPECT is regarded as the first line diagnostic test for the diagnosis and prognosis of patients with stable CAD as current research evidence is limited with regard to using CCTA as the first line test.[72,73] Table 2 is a summary of characteristics between cardiac SPECT and CCTA in the diagnostic evaluation of CAD.

Characteristics	CCTA	Cardiac SPECT
Diagnostic accuracy	Yes	Yes
Prognostic value	Yes	Yes
Impact on patient management	Uncertain	Yes
Assessment of response to therapy	Uncertain	Yes
Contribution to better outcomes	Uncertain	Yes
Widespread availability	Yes	Yes
Applicable in a wide spectrum of patients	No	Yes
Low radiation dose to patients	Yes	Yes
Cost-effectiveness	Yes	Yes

Table 2: Characteristics of cardiac SPECT and CCTA (modified from reference 72)

CCTA-DERIVED HEMODYNAMIC ANALYSIS

Despite the potential limitations of CCTA in the assessment of hemodynamic significance of anatomic coronary lesions, functional assessment of CAD is an area of active research. In recent years, Computational Fluid Dynamics (CFD) has been increasingly used in the diagnostic evaluation of CAD, with the aim of elucidating the role of hemodynamics in coronary artery disease development and progression, and detecting ischemia-causing coronary lesions.[25-28,74] Promising results have been achieved with use of CFD in patient-specific models for diagnosis of coronary artery disease (Figure 4),[25-28,75-77] although further technical developments of CFD methods and image processing techniques are required to verify these findings.
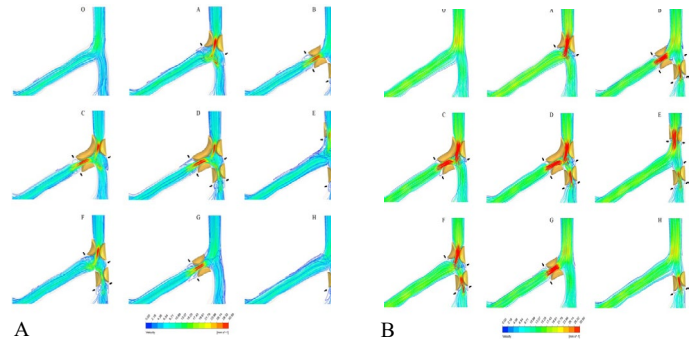

Figure 4: Computational fluid dynamic analysis of the effects of coronary plaques on left coronary blood flow. The velocity patterns inside left coronary artery bifurcation are demonstrated due to presence of plaque locations with eight types of bifurcation plaques and normal condition during the systolic phase (0.2 s) (A) and diastolic phase (0.7 s) (B). Type O-normal coronary artery tree with no plaque present, plaques involving only the left main stem (type A), involving both left anterior descending (LAD) and left circumflex (LCx) (type B), involving left main stem and LAD (type C), involving left main stem, LAD and LCx (type D), involving proximal left main stem and LCx (type E), involving distal left main stem and LCx (type F), involving LAD only (type G) and LCx only (type H). Reprint with permission from ref (28).

Recently, there has been an increasing interest in the investigation of diagnostic performance of non-invasive Fractional Flow Reserve (FFR) derived from CCTA (FFRCT). Computation of FFRCT is performed by CFD modelling after segmentation of coronary arteries and left ventricular myocardium. 3D blood flow simulations of the coronary arteries are performed with blood modelled as a Newtonian fluid using incompressible Navier-Stokes equations, with implementation of appropriate initial and boundary conditions to the models using a finite element method on a supercomputer.[25-28] The FFRCT ratio is obtained by dividing the mean pressure distal to the coronary stenosis by the mean aortic pressure, which can be measured during CFD simulations. An FFR of ≤0.80 is currently used as a cut off value to determine coronary stenoses responsible for ischemia (Figures 5 and 6).[78,79]
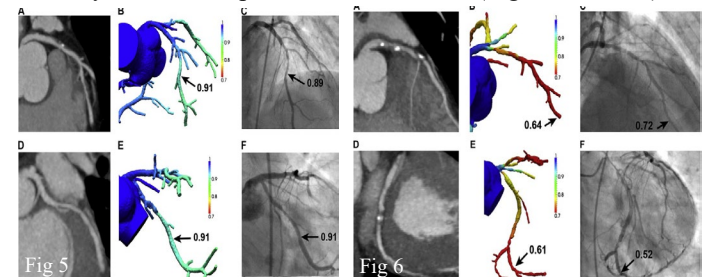

Figure 5: Fractional flow reserve (FFR) derived from CT angiography (FFRCT) results for 66-year-old man with multivessel coronary artery disease but no lesion-specific ischemia. (A) Coronary computed tomography angiography (CCTA) demonstrating stenosis in the left anterior descending coronary artery (LAD). (B) FFRCT demonstrates no ischemia in the LAD, with a computed value of 0.91. (C) Invasive coronary angiography (ICA) with FFR also demonstrates no ischemia in the LAD, with a measured value of 0.89. (D) CCTA demonstrating stenosis in the left circumflex coronary (LCx) artery. (E) FFRCT demonstrates no ischemia in the LCx, with a computed value of 0.91. (F) ICA with FFR also demonstrates no ischemia in the LCx, with a measured value of 0.91. Reprint with permission from ref (78).

Figure 6: FFRCT results for 66-year-old man with multivessel CAD and lesion-specific ischemia. (A) coronary CT angiography (CCTA) demonstrating stenosis in the left anterior descending coronary artery (LAD). (B) FFRCT demonstrates ischemia in the LAD, with a computed value of 0.64. (C) Invasive coronary angiography (ICA) with FFR also demonstrates ischemia in the LAD, with a measured value of 0.72. (D) CCTA demonstrating stenosis in the left circumflex (LCx). (E) FFRCT demonstrates ischemia in the LCx, with a computed value of 0.61. (F) ICA with FFR also demonstrates ischemia in the LCx, with a measured value of 0.52. Reprint with permission from ref (78).

Clinical validation of FFRCT is based on a direct comparison to measured FFR during invasive coronary angiography. Currently, there are three multicenter trials, namely DISCOVER-FLOW (Diagnosis of Ischemia-Causing Coronary Stenoses by Noninvasive FFR Computed from Coronary Computed Tomographic Angiograms), DeFACTO (Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography) and NXT (NeXtsTeps) investigating the diagnostic value of FFRCT in CAD.[80-82] On a per-patient analysis, diagnostic sensitivity and specificity of FFRCT ranged from 86-90% and 54-79%, while on a per-vessel analysis, diagnostic sensitivity and specificity of FFRCT were 84% and 86-88%, respectively. Despite the promising results of FFRCT in the detection of flow-limiting coronary stenosis, more multicenter trials need to be performed to compare the clinical impact of FFRCT guided *versus* standard diagnostic evaluation on clinical outcomes, costs and quality of life in patients with suspected coronary artery disease.

SUMMARY AND CONCLUDING REMARKS

Coronary CT angiography has developed as reliable less-invasive imaging modality in the diagnosis of coronary artery disease. Tremendous progress has been made over the last decades in the technological improvements in cardiac CT imaging, thus enabling coronary CT angiography to become a potential alternative to invasive coronary angiography in selected patients. With current CT scanning techniques, coronary CT angiography demonstrates high diagnostic value in coronary artery disease in terms of anatomic lumen assessment. Functional evaluation of significance of coronary stenosis is improving with latest CT models, such as dual-source or dual-energy CT, although the diagnostic accuracy is still inferior to the myocardial perfusion imaging by SPECT. Coronary CT angiography-derived hemodynamic studies and FFRCT show promising clinical outcomes in the diagnostic evaluation of patient-specific lesions. This represents a new research direction in the analysis of cardiovascular hemodynamics and prediction of coronary disease progression. With more research being conducted using advanced cardiac CT imaging techniques and fast computer processing algorithms, it is expected that research findings will provide potential value for improving our understanding of coronary artery disease with regard to pathogenesis and associated complications, thus achieving the goal of early detection of coronary artery disease and prevention of development of major adverse cardiac events.

REFERENCES

1. Sun Z, Cao Y, Li HF. Multislice computed tomography angiography in the diagnosis of coronary artery disease. *J Geriatr Cardiol*. 2011; 8: 104-113. doi: 10.3724/SP.J.1263.2011.00104

2. Sun Z, Jiang W. Diagnostic value of multislice CT angiography in coronary artery disease: A meta-analysis. *Eur J Radiol*. 2006; 60: 279-286. doi: 10.1016/j.ejrad.2006.06.009

3. Sun Z, Lin CH, Davidson R, Dong C, Liao Y. Diagnostic val-ue of 64-slice CT angiography in coronary artery disease: A systematic review. *Eur J Radiol*. 2008; 67: 78-84. doi: 10.1016/j.ejrad.2007.07.014

4. Vanhoenacker P, Heijenbrok-Kal M, Van Heste R, et al. Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis. *Radiology*. 2007; 244: 419-428. doi: 10.1148/radiol.2442061218

5. 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: 3042-3050.

6. Stein PD, Yaekoub AY, Matta F, Sostman HD. 64-slice CT for diagnosis of coronary artery disease: a systematic review. *Am J Med*. 2008; 121: 715-725. doi: 10.1016/j.amjmed.2008.02.039

7. 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: 1386-1393. doi: 10.1136/hrt.2008.145292

8. Sun Z. Cardiac CT imaging in coronary artery disease: current status and future directions. *Quant Imaging Med Surg*. 2012; 2: 98-105. doi: 10.3978/j.issn.2223-4292.2012.05.02

9. Sun Z, Choo GH, Ng KH. Coronary CT angiography: current status and continuing challenges. *Br J Radiol*. 2012; 85: 495-510. doi: 10.1259/bjr/15296170

10. Johnson T, Nikolaou K, Busch S, et al. Diagnostic accuracy of dual-source computed tomography in the diagnosis of coronary artery disease. *Invest Radiol*. 2007; 42: 484-491. doi: 10.1097/RLI.0b013e31806907d0

11. Pelliccia F, Pasceri V, Evangelista A, et al. Diagnostic accuracy of 320-row computed tomography as compared with invasive coronary angiography in unselected, consecutive patients with suspected coronary artery disease. *Int J Cardiovasc Imaging*. 2013; 29: 443-452. doi: 10.1007/s10554-012-0095-4

12. Schlett CL, Banerji D, Siegel E, et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-year outcomes of the ROMICAT trial. *JACC Cardiovasc Imaging*. 2011; 4: 481-491. doi: 10.1016/j.jcmg.2010.12.008

13. HouZh, Lu B, Gao Y, et al. Prognostic value of coronary CT angiography and calcium score for major adverse cardiac events in outpatients. *JACC Cardiovasc Imaging*. 2012; 5: 990-999. doi: 10.1016/j.jcmg.2012.06.006

14. 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: 362-371. doi: 10.1093/eurheartj/ehn605

15. 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. doi: 10.1016/j.jacc.2009.02.068

16. 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. doi: 10.1016/j.jacc.2006.07.070

17. Sabarudin A, Sun Z, Ng KH. A systematic review of radiation dose associated with different generations of multidetector CT coronary angiography. *J Med Imaging Radiat Oncol*. 2012; 56: 5-17. doi: 10.1111/j.1754-9485.2011.02335.x

18. Sun Z, Ng KH. Prospective versus retrospective ECG-gated-multislice CT coronary angiography: A systematic review of radiation dose and image quality. *Eur J Radiol*. 2012; 81: e94-e100.

19. SabarudinA, Sun Z, Ng KH. Coronary CT angiography with-prospective ECG-triggering: A systematic review of image quality and radiation dose. *Singapore Med J*. 2013; 54: 15-23.doi: 10.3978/j.issn.2223-3652.2012.02.04

20. Sabarudin A, Khairuddin Md Yusof A,Tay MF, Ng KH, Sun Z. Dual-source CT coronary angiography: effectiveness of radiationdose reduction with lower tube voltage. *Radiat Prot Dosim*. 2013; 153: 441-447. doi: 10.1093/rpd/ncs127

21. 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(2): 410-419. doi: 10.1093/rpd/ncs127

22. Tashakkor AY, Nicolaou S, Leipsic J, Mancini GBJ. The emerging role of cardiac computed tomography for the assessment of coronary perfusion: a systematic review and meta-analysis. *Can J Cardiol*. 2012; 28: 413-422. doi: 10.1016/j.cjca.2012.02.010

23. Techasith T, Cury RC. Stress myocardial CT perfusion: An update and future perspective. *JACC Cardiovasc Imaging*. 2011; 4: 905-916. doi: 10.1016/j.jcmg.2011.04.017

24. Sun Z. Coronary CT angiography: beyond morphological stenosis analysis. *World J Cardiol*. 2013; 5: 444-452. doi: 10.4330/wjc.v5.i12.444

25. Chaichana T, Sun Z, Jewkes J. Computation of haemodynamics in the left coronary artery with variable angulations. *J Biomech*. 2011; 44: 1869-1878. doi: 10.1016/j.jbiomech.2011.04.033

26. Chaichana T, Sun Z, Jewkes J. Impact of plaques in the left

coronary artery on walls hear stress and pressure gradient in-coronary side branches. *Comput Med Biomech Biomed Eng*. 2014; 17:108-118. doi: 10.1080/10255842.2012.671308

27. Chaichana T, Sun Z, Jewkes J. Hemodynamic impacts of various types of stenosis in the left coronary artery bifurcations: Apatient-specific analysis. *Phys Med*. 2013; 29: 447-452. doi: 10.1016/j.ejmp.2013.02.001

28. Chaichana T, Sun Z, Jewkes. Haemodynamic analysis of the effect of different types of plaque at the left coronary artery. *Comput Med Imaging Graph*. 2013; 37: 197-206. doi: 10.1016/j.compmedimag.2013.02.001

29. Guo SL, Guo YM, Zhai YN, et al. Diagnostic accuracy of first generation dual-source computed tomography in the assessment of coronary artery disease: a meta-analysis from 24 studies. *Int J Cardiovasc Imaging*. 2011; 27: 755-771. doi: 10.1007/s10554-010-9690-4

30. Salavati A, Radmanesh F, Heidari K, et al. Dual-source computed tomography angiography for diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. *J Cardiovasc Comput Tomogr*. 2012; 6: 78-90. doi: 10.1016/j.jcct.2011.10.018

31. Gaudio C, Pellicia F, Evangelista A, et al. 320-row computed tomography angiography vs conventional coronary angiography in patients with suspected coronary artery disease: a systematic review and meta-analysis. *Int J Cardiol*. 2013; 168: 1562-564.

32. Li S, Ni Q, Wu H, et al. Diagnostic accuracy of 320-slice computed tomography angiography for detection of coronary artery stenosis: Meta-analysis. *Int J Cardiol*. 2013; 168: 2699-705. doi: 10.1016/j.ijcard.2013.03.023

33. Sun Z. Comment on: Diagnostic accuracy of 320-slice computed tomography angiography for detection of coronary artery stenosis: meta-analysis (Int J Cardiol, http://dx.doi.org/10.1016/j.ijcard.2013.03.023). *Int J Cardiol*. 2013; 168: 4895-4896. doi: 10.1016/j.ijcard.2013.07.023

34. Sabarudin A, Sun Z, Yusof AK. Coronary CT angiography with single-source and dual-source CT: comparison of image quality and radiation dose between prospective ECG-triggered and retrospective ECG-gated protocols. *Int J Cardiol*. 2013; 168: 746-53. doi: 10.1016/j.ijcard.2012.09.217

35. Earls JP, Berman EL, Urban BA, et al. Prospectively gated transverse coronary CT angiography versus retrospectively gated helical technique: improved image quality and reduced radiation dose. *Radiology*. 2008;246:742-753. doi: 10.1148/radiol.2463070989

36. Shuman W, Branch K, May J, et al. Prospective versus ret

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rospective ECG gating for 64-detector CT of the coronary arteries: comparison of image quality and patient radiation dose. *Radiology*. 2008;248:431-7. doi: 10.1148/radiol.2482072192

37. Xu L, Yang L, Zhang Z, et al. Low-dose adaptive sequential scan for dual-source CT coronary angiography in patients with high heart rate: comparison with retrospective ECG gating. *Eur J Radiol*. 2010; 76: 183-187. doi: 10.1016/j.ejrad.2009.06.003

38. vanBallmoos MW, Haring B, Juillerat P, Alkadhi H. Meta-analysis: diagnostic performance of low-radiation-dose coronary computed tomography angiography. *Ann Intern Med*. 2011; 154: 413-420. doi: 10.7326/0003-4819-154-6-201103150-00007

39. Sun Z, Ng KH. Diagnostic value of coronary CT angiography with prospective ECG-gating in the diagnosis of coronary artery disease: a systematic review and meta-analysis. *Int J Cardiovasc Imaging*. 2012; 28: 2109-2119. doi: 10.1007/s10554-011-0006-0

40. Naghavi M, Libby P, Falk E, et al. From vulnerable plaque to vulnerable patient: A callfor new definitions and risk assessment strategies: Part II. *Circulation*. 2003; 108: 1772-1778. doi: 10.1161/01.CIR.0000087480.94275.97

41. Sun Z, Dimpudus FJ, Nugroho J, Adipranoto JD. CT virtual intravascular endoscopy assessment of coronary artery plaques: A preliminary study. *Eur J Radiol*. 2010; 75: e112-e119. doi: 10.1016/j.ejrad.2009.09.007

42. Lou YC, Sun Z, ChanT, et al. Significance of coronary calcification for prediction of coronary artery disease cardiac events based on 64-slice computed tomography coronary angiography. *Biomed Res Int*. 2013; (2013): 472347. doi: http://dx.doi.org/10.1155/2013/472347

43. Chow BJ, Wells GA, Chen L, et al. Prognostic value of 64-slice cardiac computed tomographyseverity of coronary artery disease, coronary atherosclerosis, and leftventricular ejection fraction. *J Am Coll Cardiol*. 2010; 55:1017-1028. doi: 10.1016/j.jacc.2009.10.039

44. Miszalski-Jamka T, Klimeczek P, Banys R, et al. The composition and extent of coronary artery plaque detected by multislice computed tomographic angiography provides incremental prognostic value in patients with suspected coronary artery disease. *Int J Cardiovasc Imaging*. 2012; 28: 621-631. doi: 10.1007/s10554-011-9799-0

45. Yiu KH, de Graaf FR, Schuijf JD, et al. Age- and gender-specific differences in the prognostic value of CT coronary angiography. *Heart*. 2012; 98: 232-237. doi: 10.1136/heartjnl-2011-300038

46. Andreini D, Pontone G, Mushtaq S, et al. A long-term prognostic value of coronaryCT angiography in suspected coronary artery disease. *JACC Cardiovasc Imaging*. 2012; 5: 690-701. doi: 10.1016/j.jcmg.2012.03.009

47. Sozzi FB, Civaia F, Rossi P, et al. Long-term follow-up of patients with first-time chest pain having 64-slice computed tomography. *Am J Cardiol*. 2011; 107: 516-521. doi: 10.1016/j.amjcard.2010.10.006

48. Hadamitzky M, Taubert S, Deseive S, et al. Prognostic value of coronary computed tomography angiography during 5 years of follow-up in patientswith suspected coronary artery disease. *Eur Heart J*. 2013; 34:3 277-3285. doi: 10.1093/eurheartj/eht293

49. Shaw LJ, Min JK, Narula J, et al. Sex differences in mortalityassociated with computed tomographic angiographic measurements of obstructive and nonobstructive coronary artery disease. *Circ Cardiovasc Imaging*. 2010; 3: 473-481. doi: 10.1161/CIRCIMAGING.109.860981

50. Dougoud S, Fuchs TA, Stehli J, et al. Prognostic value of coronary CT angiography on long-term follow-up of 6.9 years. *Int JCardiovasc Imaging*. 2014; 30: 969-976. doi: 10.1007/s10554-014-0420-1

51. Abdulla J, Asferg C, Kofoed KF. Prognostic value of absence or presence of coronary artery disease determined by 64-slice computed tomography coronary angiography: a systematic review and meta-analysis. *Int J Cardiovasc Imaging*. 2011; 27: 413-420. doi: 10.1007/s10554-010-9652-x

52. Hulten EA, Carbonaro S, Petrillo SP, Mitchell JD, VillinesTC. Prognostic value of cardiac computed tomography angiography: A systematic review and meta-analysis. *J Am Coll Cardiol*. 2011; 57: 1237-1247. doi: 10.1016/j.jacc.2010.10.011

53. Goldstein JA, Chinnaiyan KM, Abidov A, et al. The CT-STAT (Coronary computed tomographic angiography for systematic triage of acute chest painpatients to treatment) trial. *J Am Coll Cardiol*. 2011; 58: 1414-1422. doi: 10.1016/j.jacc.2011.03.068

54. Min JK, Dunning A, Lin FY, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiographyfindings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: an International Multicenter Registry) of 23,854patients without known coronary artery disease. *J Am Coll Cardiol*. 2011; 58: 849-860. doi: 10.1016/j.jacc.2011.02.074

55. Min JK, Lin FY, Dunning AM, et al. Incremental prognostic significance of left ventricular dysfunction to coronary artery disease detection by 64-detector row coronary computed tomographic angiography for the prediction of all-cause mortality: results from a two centre study of 5330 patients. *Eur Heart J*. 2010; 31: 1212-1219. doi: 10.1093/eurheartj/ehq020

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56. Min JK, Feignoux J, Treutenaere J, Laperche T, Sablayrolles J. Theprognostic value of multidetector coronary CT angiography for theprediction of major adverse cardiovascular events: a multicenter observationalcohort study. *Int J Cardiovasc Imaging*. 2010; 26: 721-728. doi: 10.1007/s10554-010-9613-4

57. Hadamitzky M, Freissmuth B, Meyer T, et al. Prognostic value ofcoronary computed tomographic angiography for prediction of cardiacevents in patients with suspected coronary artery disease. *JACC Cardiovasc Imaging*. 2009; 2: 404 -411. doi: 10.1016/j.jcmg.2008.11.015

58. Achenbach S, Marwan M, Ropers D, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J*. 2010; 31: 340-346. doi: 10.1093/eurheartj/ehp470

59. Lell M, Marvan M, Schepis T, et al. Prospectively ECG-triggered high-pitch spiral acquisition for coronary CT angiography using dual source CT: technique and initial experience. *Eur Radiol*. 2009; 19: 2576-2583. doi: 10.1007/s00330-009-1558-4

60. Lee TY, Chhem RK. Impact of new technologies on dose reduction in CT. *Eur J Radiol*. 2010; 76: 28-35. doi: 10.1016/j.ejrad.2010.06.036

61. Leipsic J, Heilbron BG, Hague C. Iterative reconstruction for coronary CT angiography: findings its way. *Int J Cardiovasc Imaging*. 2012; 28: 613-620. doi: 10.1007/s10554-011-9832-3

62. Sun Z, Ng KH. Coronary computed tomography angiography in coronary artery disease. *World J Cardiol*. 2011; 3: 303-310.

63. Matter CM, Stuber M, Nahrendorf M. Imaging of the unstable plaque: how far have we got? *Eur Heart J*. 2009; 30: 2566-2574. doi: 10.1093/eurheartj/ehp419

64. 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 angina by multidetector computed tomography. *J Am Coll Cardiol*. 2006; 47: 1655-1662. doi: 10.1016/j.jacc.2006.01.041

65. Nissen SE, Nicholls SJ, Sipahi I, et al. Effect of very high-intensitystatin therapy on regression of coronary atherosclerosis: the ASTEROID trial. *JAMA*. 2006; 295: 1556-1565. doi: 10.1001/jama.295.13.jpc60002

66. Nissen SE, Tuzcu EM, Schoenhagen P, et al. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. *N Engl J Med*. 2005; 352: 29-38. doi: 10.1056/NEJMoa042000

67. Achenbach S, Ropers D, Kuettner A, et al. Contrast-enhanced-coronary artery visualization by dual-source computed tomography-initial experience. *Eur J Radiol*. 2006; 57: 331-335. doi: 10.1016/j.ejrad.2005.12.017

68. 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: 346-355. doi: 10.1148/radiol.2472070906

69. Sato A, Hiroe M, Tamura M, et al. Quantitative measures of coronary stenosis severity by 64-slice CT angiography and relation to physiologic significance of perfusion in nonobese patients: comparison with stress myocardial perfusion imaging. *J Nucl Med*. 2008; 49: 564-572. doi: 10.2967/jnumed.107.042481

70. Hachamovitch R, Di Carli MF. Nuclear cardiology will remain the"gatekeeper" over CT angiography. *J Nucl Cardiol*. 2007; 14: 634-644. doi: 10.1016/j.nuclcard.2007.06.118

71. Tamarappoo BK, Gutstein A, Cheng VY, et al. Assessment of the relationship between stenosis severity and distribution of coronary artery stenoses on multislice computed tomographic angiographyand myocardial ischemia detected by single photon emissioncomputed tomography. *J Nucl Cardiol*. 2010; 17: 791-802. doi: 10.1007/s12350-010-9230-6

72. Trzaska ZJ, Cohen MC. SPECT vs CT: CT is the not the first line test for the diagnosis and prognosis of stable coronary artery disease. *J Nucl Cardiol*. 2013; 20: 473-478. doi: 10.1007/s12350-013-9709-z

73. Alijzeeri A, Cocker MS, Chow BJW. CT vs SPECT: CT is the first-line test for the diagnosis and prognosis of stable coronary artery disease. *J Nucl Cardiol*. 2013; 20: 465-72.

74. Zhang JM, Zhong L, Su B, et al. Perspective on CFD studies of coronary artery disease lesions and hemodynamics: A review. *Int J Numer Metho Biomed Eng*. 2014. doi: 10.1007/s12350-013-9690-6

75. Knight J, Olgac U, Saur SC, et al. Choosing the optimal wall shear parameter for the prediction of plaque location-A patient-specific computational study in human right coronary arteries. *Atherosclerosis*. 2010; 211: 445-450. doi: 10.1016/j.atherosclerosis.2010.03.001

76. Wellnhofer E, Osman J, Kertzscher U, Affeld K, Fleck E, Gou¬bergrits L. Flow simulation studies in coronary arteries--impact of side-branches. *Atherosclerosis*. 2010; 213: 475-448. doi: 10.1016/j.atherosclerosis.2010.09.007

77. Holzapfel GA, Mulvihill JJ, Cunnane EM, Walsh MT. Computational approaches for analyzing the mechanics of atherosclerotic plaques: a review. *J Biomech*. 2014; 47: 859-869. doi: 10.1016/j.jbiomech.2014.01.011

78. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: Scientific basis. *J Am Coll Cardiol*. 2013; 61: 2233-2241. doi: 10.1016/j.

jacc.2012.11.083

79. Zarins CK, Taylor CA, Min JK. Computed fractional flow reserve (FFRCT) derived from coronary CT angiography. *J Cardiovasc Trans Res*. 2013; 6: 708-714. doi: 10.1007/s12265-013-9498-4

80. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter discover-flow (diagnosis of ischemia-causing stenoses obtained via noninvasive fractional flow reserve) study. *J Am Coll Cardiol*. 2011; 58: 1989-1997. doi: 10.1016/j.jacc.2011.06.066

81. Min JK, Berman DS, Budoff MJ, et al. Rationale and design of the DeFACTO (Determination of Fractional Flow Reserve by Anatomic Computed Tomographic AngiOgraphy) study. *J Cardiovasc Comput Tomogr*. 2011; 5: 301-309. doi: 10.1016/j.jcct.2011.08.003

82. Norgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of non-invasive fractional flow reserve derived from coronary CT angiography in suspected coronary artery disease: The NXT trial. *J Am Coll Cardiol*. 2014; 63: 1145-1155. doi: 10.1016/j.jacc.2013.11.043