Cardiovascular computed tomography for diagnosis and risk stratification of coronary artery disease

Werkhoven, J.M. van

Cardiovascular computed tomography for diagnosis of coronary artery disease

Chapter 2

Multi-slice computed tomography coronary angiography: anatomic vs functional assessment in clinical practice

JM van Werkhoven, JD Schuijf, JW Jukema, EE van der Wall, JJ Bax

Abstract

Non-invasive imaging plays an increasingly important role in the diagnosis and risk stratification of coronary artery disease. Several techniques such as stress echocardiography and myocardial perfusion imaging have become available to assess cardiac function and myocardial perfusion. With the arrival of multi-slice computed tomography coronary angiography (CTA), non-invasive imaging of coronary anatomy has also become possible. Studies concerning the diagnostic accuracy have demonstrated a good agreement with conventional coronary angiography resulting in a sensitivity and specificity of approximately 86% and 96% respectively. The high negative predictive value of 97% renders it particularly useful to rule out the presence of coronary artery disease in patients with an intermediate pre-test likelihood. Moreover comparative studies have demonstrated that anatomic imaging with CTA may provide information complementary to the traditionally used techniques for functional assessment. From these studies can be derived that only approximately 50% of significant stenoses on CTA are functionally relevant; a large proportion of significant (>50%) lesions on CTA does not result in perfusion abnormalities. Alternatively, many patients with a normal perfusion CTA show considerable atherosclerosis on CTA. Therefore the combined use of these techniques may enhance the assessment of the presence and extent of coronary artery disease. In the future diagnostic algorithms combining non-invasive anatomic and functional imaging need to be evaluated in large patient populations to establish their efficacy, safety, and cost effectiveness. Importantly, these investigations should result in the development of comprehensive guidelines on the use of CTA in clinical practice as well.

Introduction

Coronary artery disease (CAD) is one of the leading causes of death in the western world. In the diagnosis and risk stratification of this condition, imaging plays an increasingly important role. The golden standard for detecting CAD is conventional coronary angiography which enables visualization of the coronary lumen. This is a highly accurate and robust diagnostic technique, but because of its invasive nature it is less suitable as a first line diagnostic test. In the past decades non-invasive imaging has been developed for this purpose and functions as a gatekeeper for conventional coronary angiography. Several techniques such as stress echocardiography and myocardial perfusion imaging have become available to assess cardiac function and myocardial perfusion. Myocardial perfusion imaging with single photon emission computed tomography (SPECT) in particular is widely available and frequently used. With the arrival of multi-slice computed tomography coronary angiography (CTA), non-invasive coronary angiography has become possible. The technique has matured rapidly and its introduction has resulted in a shift from pure functional imaging to non-invasive assessment of coronary anatomy as well. In the present review we will provide an overview of the current status of CTA, and its clinical implications.

CTA technique

Background

Accurate imaging of coronary anatomy with CTA is governed by several basic principles. To ensure detailed evaluation of the coronary arteries as well as coronary stenosis, a high spatial resolution is necessary. This is determined by the minimal slice thickness. Other factors are a high temporal resolution, ECG gating, and sufficient coverage, which are all needed to minimize artefacts due to cardiac and respiratory motion. Temporal resolution (shutter speed) is determined by the rotation time, number of X-ray beams, and the reconstruction protocol used. It needs to be high because of the constant motion of the heart and coronary arteries. ECG gating is used to essentially 'freeze' the heart during an optimal phase of the cardiac cycle with the least cardiac motion. Sufficient images of each cardiac phase are obtained by using an overlapping scan protocol. Finally, respiratory motion is counteracted by performing data acquisition during an inspiratory breath hold. Sufficient coverage (i.e. number of slices) ensures a short scan time during a single breath hold.

Technological advances

CTA technology evolved rapidly starting with the first 4-slice spiral CT scanner in 2000.[1, 2] At first, the development of new scanners focused on the number of slices. This increased the coverage and thereby reduced scan time. These advancements enabled a shorter breath hold which reduced the prevalence of uninterpretable scans caused by breathing artefacts, and arrhythmias. Currently 64-slice scanners are the industry standard.

Recent development of new scan technology has moved into different directions. To increase temporal resolution a dual source computed tomography (DSCT) system has been developed, which integrates two X-ray tubes into one scan system, thereby increasing the temporal resolution to 83 ms.[3, 4] This improvement results in superior image quality as well as less dependency on heart rate control.[5, 6] Another improvement has been a reduction of the radiation dose by the development of prospective ECG gating. With this "step-and-shoot" protocol images are made during a fixed part of the RR interval, typically end diastolic. Since data are acquired only during this interval the radiation dose can be substantially lowered to approximately 1.1-3.0 mSv.[7] Finally, entire cardiac coverage in one heart beat can be obtained by the recently introduced 320-slice CT system.[8, 9] Because of the wide detector array a complete volume of the heart can be scanned without the need for overlapping scans. This significantly lowers the scan time, which counters problems with arrythmias, decreases the radiation dose, and reduces the amount of contrast needed.

Scan protocol

Patient preparation is an important component of non-invasive coronary angiography. Before each scan, patients should be informed about the procedure, and heart rate is monitored. Most centers administer beta-blockers to patients with heart rates above 65 beats per minute, typically with oral beta-blockers (metoprolol 50 -100 mg), but intravenous beta blockers are also used. Importantly, only patients with sinus rhythm should be studied while imaging should not be performed in patients with arrhythmias. Finally, some centers also administer sublingual nitrates which dilate the coronary arteries thereby enhancing image quality. Importantly, only patients with sinus rhythm should be studied while imaging should not be performed in patients with arrhythmias.

After patient preparation, several exploratory scans are performed to determine accurate start and end positions. Finally, the ECG gated contrast enhanced scan is performed during administration of approximately 80-140 ml of iodinated contrast agent, followed by 40-50 ml saline for optimal arterial enhancement.

After the data have been acquired, the cardiac phase with the least motion is identified and used to reconstruct a dataset of the entire heart. Reconstructions are transferred to an offline workstation for further analysis. The presence of coronary artery stenosis is typically evaluated by assessing the axial images in combination with processed images included 3D volume rendered and curved multiplanar reconstructions or maximum intensity projections. (Figure 1)

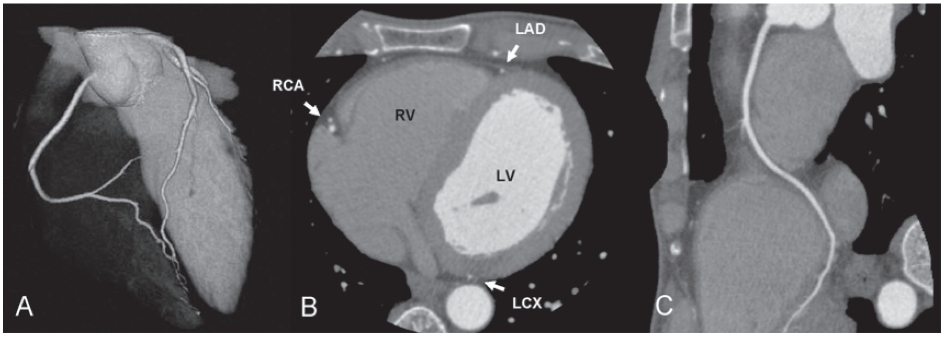

Figure 1. Examples of different reconstruction techniques used for the offline evaluation of CTA exams. Panel A shows a three dimensional volume rendered reconstruction of the right and left coronary arteries. In panel B an axial cross section is depicted in which the left anterior descending coronary artery (LAD), right coronary artery (RCA), and left circumflex artery (LCX) are clearly visible. A multi-planar reconstruction of the right coronary artery is shown in panel C.

Diagnostic accuracy of CTA

Interpretability

The diagnostic accuracy of CTA for the detection of significant CAD (>50% lumen diameter), has been assessed in many comparative studies.[2, 6, 10-26] With each generation of scanners better image quality, a lower number of uninterpretable scans, and an increased diagnostic accuracy has been obtained. Indeed, although 4-slice CTA showed promising diagnostic accuracy, up to 30% of segments were uninterpretable and had to be excluded from analysis.[2, 10, 17] The number of uninterpretable scans decreased substantially with 16-slice CTA,[15, 16, 19] and with the current 64-slice scanners the rate of uninterpretable segments is approximately 4%.[27]

64-slice CTA

A recent meta-analysis by Abulla et al. has evaluated the diagnostic accuracy of 64-slice CTA compared to conventional coronary angiography.[27] The authors included 19 studies that evaluated the native coronary arteries in a total of 1,740 patients. On a patient level the following diagnostic accuracy was observed: sensitivity 86%; specificity 96%, positive predictive value 83%, and negative predictive value 97%. Recently, results from a multi-center trial have been reported by Miller et al.[26] The authors included 316 patients with a calcium score ≤600, of which 291 patients underwent conventional coronary angiography. On a patient level a sensitivity and specificity of respectively 83%, and 91% were observed. Accordingly, these multi-center data confirm the observations from previous single center studies.[11-13, 18, 20-22, 24, 25] An example of the excellent concordance between 64-slice CTA and conventional coronary angiography is illustrated in Figure 2.

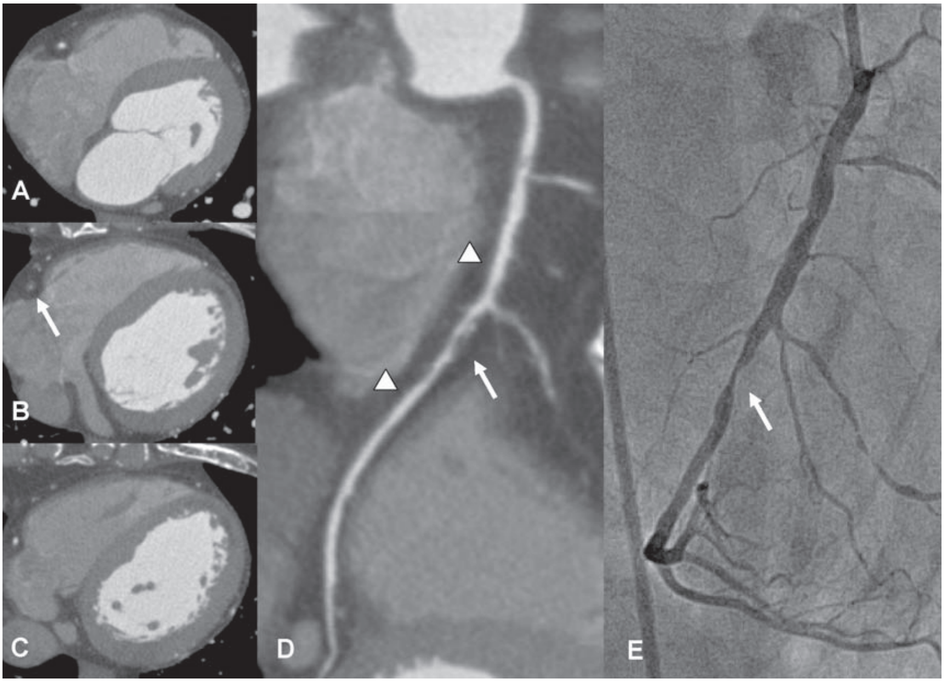

Figure 2. Patient with a significant coronary artery stenosis in the right coronary artery (panels A-D) on CTA. In panels A-C axial slices of the heart are shown at three levels of the right coronary artery corresponding with the markers in panel D: top arrowhead (panel A), middle arrow (panel B), and bottom arrowhead (panel C). While in panels A and C the coronary lumen is clearly visible, substantial reduction of the coronary lumen is visible in panel B. Findings were confirmed by conventional coronary angiography (panel E).

DSCT

The diagnostic accuracy of DSCT has been evaluated in several studies.[6, 14, 23] In a study by Weustink et al. including 100 patients, the DSCT scanner yielded a high diagnostic accuracy with a sensitivity of 99%, specificity 87%, positive predictive value 96%, and negative predictive value 95% on a patient level.[6] Because of the increased temporal resolution (83 ms), a high diagnostic accuracy could be obtained even in patients with a high heart rate. This is further emphasized in the study by Ropers et al. who evaluated the influence of heart rate on the diagnostic accuracy of DSCT.[5] In total, 100 patients were scanned without premedication with beta blockers, allowing comparison of the diagnostic accuracy between 56 patients with a heart rate <65 and 44 patients with a heart ≥65. Although the per-segment evaluability was slightly lower in patients with a high heart rate, no decrease in diagnostic accuracy was observed.

Potential use of CTA in clinical practice

Possible indications

Stable chest pain

The majority of studies on the diagnostic accuracy of CTA have been performed in patients with stable chest pain complaints and referred for coronary angiography due to a high pre-test likelihood for CAD. As a result, most data have been obtained in populations with a high prevalence of CAD. However, non-invasive imaging may be more valuable in patients with a lower likelihood of disease.[28] The relationship between pre-test probability and the usefulness of CTA was recently studied by Meijboom et al. who evaluated the diagnostic accuracy of CTA among patients with a high, intermediate, or low pre-test likelihood. In patients with a high pre-test likelihood for CAD, the additional value of CTA was limited. In contrast, in patients with an intermediate pre-test likelihood, a negative CTA scan allowed reduction of the post test probability of CAD to 0%.[29] Accordingly these data indicate that the main strength of CTA may be to rule out CAD in patients with a low to intermediate pre-test likelihood.

Acute chest pain

CTA may also be proven useful in patients presenting with acute chest pain. In this clinical setting, it is important to obtain a rapid diagnosis to avoid unnecessary hospitalization as well as incorrect discharge of patients.[30, 31] Several studies have evaluated the feasibility of CTA in this population.[32-36] In a large randomized controlled trial by Goldstein et al., 197 low risk chest pain patients were randomized into a CTA group (n=99) and a standard of care group (n=98).[37] In the CTA group, CAD was ruled out in 67 (68%) of 99 patients. In 24 patients with an intermediate or non-diagnostic CT exam a nuclear stress study was performed for further evaluation. In the remaining 8 patients CTA detected severe disease. These patients were directly referred for conventional coronary angiography. An important finding of this study was that the implemented algorithm significantly reduced the diagnostic time compared to the standard of care (3.4 h vs. 15.0 h, $p < 0.001$), while also lowering the costs ($1,586 vs. $1,872, $p < 0.001$). Accordingly, initial data suggests that in patients with an intermediate likelihood without ECG changes and elevated enzymes, in whom diagnosis may be particularly challenging, CTA may be useful.[38] Nevertheless, further evaluation of the accuracy, safety, and cost-effectiveness of CTA in this setting is warranted.

Asymptomatic patients

In general use of CTA is considered to be inappropriate in asymptomatic patients because of the associated radiation burden. However several subpopulations have been identified that may benefit from evaluation with CTA, such as patients referred for preoperative cardiac evaluation,[39] or patients with left bundle branch block.[40] Also, in patients with dilated cardiomyopathy CTA may be useful for identification of idiopathic versus ischemic etiology.[41]

Previous revascularization

In patients with previous revascularization (percutaneous coronary intervention or bypass grafting) imaging with CTA is possible but is frequently challenging.[42, 43] The assessability of in-stent restenosis is hampered by the occurrence of metal artefacts caused by the stent struts. As a result, high rates of uninterpretable stents have been reported. The routine use of CTA in patients with previous coronary stenting is therefore not recommended.[28] However in selected patients with larger stent diameter, results with 64-slice CTA have been promising. Cademartiri et al evaluated 182 patients with a total of 192 stents (diameter ≥2.5 mm) and demonstrated a sensitivity and specificity of 95% and 93%. Moreover, a negative predictive value of 99% was obtained indicating that in selected patients, CTA may be used to rule out in-stent restenosis.[28, 44, 45]

CTA imaging of bypass grafts is less affected by motion than the coronary arteries, thereby allowing good visualization of graft patency or stenosis. In general, high accuracies in the range of 90% to 100% have been reported.[46, 47] However, the assessment of grafts can be affected by surgical metal clips which may render the graft uninterpretable. Furthermore, assessment of the native coronary arteries or segments distal to the anastomosis may be difficult due to the frequent presence of extensive coronary calcifications in combination with small vessel size. As a result, higher rates of unevaluable segments as compared to patients without previous coronary artery bypass grafting have been reported.[43] Thus, while coronary artery bypass grafts can be assessed accurately, assessment on a patient level remains challenging. The routine use of CTA is therefore not recommended in patients with previous bypass graft surgery.[28]

Integration into current clinical practice

Anatomy versus function

Traditional non-invasive diagnostic imaging strategies have focused on the assessment of myocardial perfusion and function. Accordingly, the presence of CAD was determined based on the presence of inducible perfusion or wall motion abnormalities, indicating the presence of ischemia. With the arrival of CTA it has become possible to assess cardiac anatomy non-invasively as well. To understand the relative values of these techniques several studies comparing CTA to myocardial perfusion imaging have been performed.[32, 48-50] An overview of the studies comparing 64-slice CTA to myocardial perfusion imaging using SPECT is shown in Table 1. From these studies can be derived that only approximately 50% of significant stenoses on CTA are functionally relevant; a large proportion of significant (>50%) lesions on CTA does not result in perfusion abnormalities. Alternatively, many patients with a normal perfusion scan show considerable atherosclerosis on CTA. Accordingly, these

Table 1. Overview of studies comparing 64-slice CTA to myocardial perfusion imaging (MPI).

		CTA ≤50%		CTA >50%	
	n	MPI -	MPI +	MPI -	MPI +
Schuijf(50)	114	37 (90%)	4 (10%)	40 (55%)	33 (45%)
Hacker(49)	26	12 (86%)	2 (14%)	4 (33%)	8 (67%)
Gaemperli(48)	91	53 (96%)	2 (4%)	18 (50%)	18 (50%)
Galagher(32)	85	66 (90%)	7 (10%)	6 (50%)	6 (50%)

studies illustrate the discrepancy between anatomic and functional testing; CTA detects atherosclerosis, functional testing evaluates the presence of hemodynamically significant lesions. As a result, the techniques may be considered to provide complementary information on the presence and severity of CAD. The combined use of these techniques may therefore potentially enhance the diagnostic workup of patients presenting with chest pain complaints.

Combined anatomic and functional imaging

Two approaches can be used to combine the information from CTA and myocardial perfusion imaging. The first is fusion of the anatomic and functional information, either by hybrid imaging or by retrospective fusion of datasets.[51, 52] The advantage of this approach is that it allows accurate allocation of perfusion defects to the corresponding coronary arteries.[53] A disadvantage however is the associated radiation dose while information on both anatomy and function may not be required in all patients.

An alternative approach to combining anatomic and functional imaging therefore might be sequential imaging. A flow chart advocating such a strategy has been recently published and is provided in Figure 3.[54] Patients presenting with an intermediate pre-test likelihood may benefit the most from CTA. In these patients, CTA can be used as an initial imaging technique to rule out the presence of CAD. Patients with a normal CTA can be safely discharged and do not require further testing. In patients with non-obstructive atherosclerosis (<50%) medical therapy and aggressive risk factor modification may be indicated. Invasive imaging and revascularization may not be needed as the likelihood of ischemia is still low. On the other hand, the likelihood of hemodynamically relevant CAD is high in patients with a severely abnormal CTA, including left main or three vessel disease. These patients may be referred for conventional coronary angiography immediately. Finally, in patients with a borderline stenosis or an equivocal CTA, functional imaging remains required to determine the further management and in general, only patients with ischemia should be referred for conventional coronary angiography in combination with possible revascularization. An example of a patient with a significant stenosis on CTA with a corresponding perfusion defect on SPECT is shown in Figure 4.

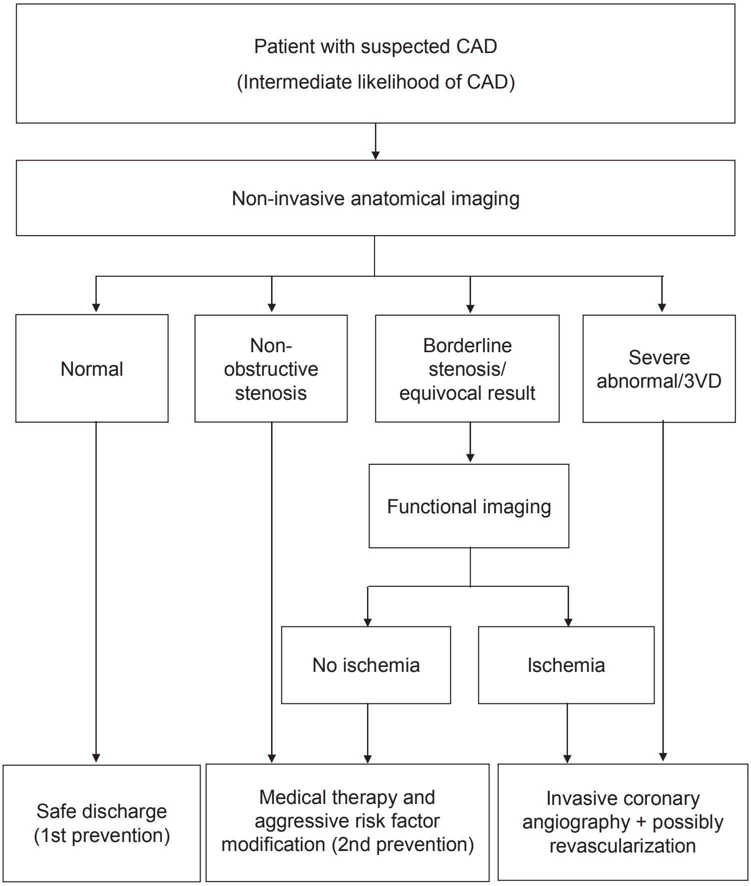

Figure 3. A flow chart describing the combined use of non-invasive anatomical and functional imaging in patients with an intermediate pre-test likelihood of coronary artery disease (CAD). Reprinted with permission from reference 54.

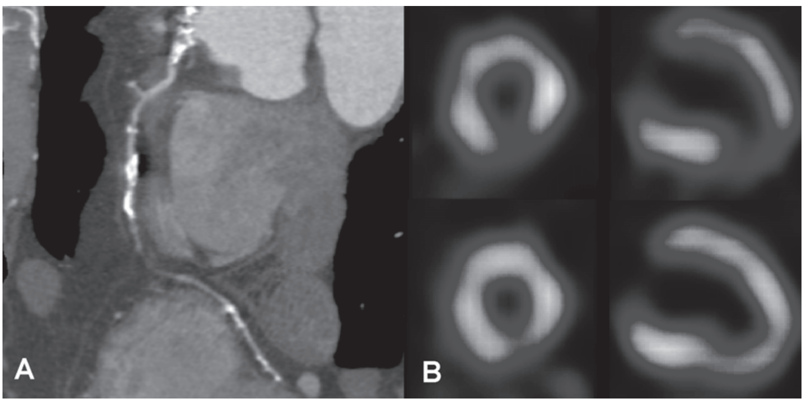

Figure 4. Example of a patient with a significant stenosis in the right coronary artery on CTA (panel A), which resulted in a partially reversible perfusion defect on SPECT (panel B).

Future perspectives

Plaque imaging

Acute coronary syndromes (ACS) are a major cause of morbidity and mortality worldwide.[55] Since CTA allows direct evaluation of the presence and (to some extent) composition of atherosclerosis, the technique may potentially be useful to identify patients with plaque characteristics suggesting a high risk for plaque rupture. Several studies have identified differences in plaque composition between patients presenting with ACS and patients with stable CAD.[56-58] Motoyama et al. studied the characteristics of culprit lesions in 38 patients with ACS and compared them to the lesions observed in 33 patients presenting with stable angina pectoris.[55, 57] The authors observed significantly more positive remodeling, non-calcified plaque, and spotty calcifications in the culprit lesions of ACS patients. Similar findings have been reported in other studies.[56, 58] Although these data suggest that the assessment of plaque characteristics may be of clinical relevance, accurate and reproducible quantification remains challenging. Leber et al. recently reported on the accuracy of 64-slice CTA to classify and quantify plaque volumes in the proximal coronary arteries.[55, 59] CTA was compared with intravascular ultrasound in 19 patients with 36 vessels. CTA detected calcified and mixed plaque with high accuracy (95% and 94%, respectively) but accuracy was lower for non-calcified lesion (83%). When regarding plaque volume, non-calcified plaque and mixed plaque volumes were systematically underestimated whereas calcified plaque volume was overestimated by CTA. Importantly the presence of features associated with plaque vulnerability, including the presence of large lipid cores and spotty calcifications, was also assessed. A lipid pool was correctly identified in 70% of sections and spotty calcification patterns in 90% of sections. The authors concluded that imaging of plaque characteristics related to ACS may be possible with CTA, but that evaluation of plaque burden is only moderately concordant with intravascular ultrasound.

These preliminary studies demonstrate the ability of CTA to provide information on atherosclerotic plaque patterns. Potentially, this information may be used for risk stratification, although only limited outcome data of CTA are currently available.[60, 61]

CTA perfusion imaging

Another potential feature of CTA is the evaluation of myocardial perfusion, which has generated substantial interest. Based on differences in the attenuation values during contrast administration, differentiation between territories with normal and abnormal perfusion is possible. Indeed, using the same protocol as used for coronary angiography, areas of previous myocardial infarction are identified as hypoenhanced regions.[62-64] Similar to MRI, identification of scar tissue is possible with delayed enhancement imaging. Using this technique myocardial segments with scar tissue appear as hyperenhanced regions.[65, 66] An excellent agreement has been shown between infarct imaging with CTA and other techniques including magnetic resonance imaging and SPECT.[63, 67]

Importantly, preliminary data suggest that CTA can also be used to assess the presence of inducible perfusion abnormalities indicating the presence of ischemia.[68] However, the administration of adenosine may frequently induce tachycardia, which in turn may hamper simultaneous assessment of the coronary arteries. The introduction of new generation scanners such as 256- and 320-slice CT however may substantially facilitate combined evaluation of coronary anatomy and stress perfusion in a single procedure.[69] Further studies should demonstrate whether CTA may indeed have the potential to provide combined assessment of anatomy and function in a single session.

Conclusions

With the current generation scanners CTA has become a robust non-invasive imaging technique. Studies concerning the diagnostic accuracy have demonstrated a good agreement with conventional coronary angiography. The high negative predictive value of CTA renders it particularly useful to rule out the presence of CAD in patients with an intermediate pretest likelihood. Comparative studies have demonstrated that anatomic imaging with CTA may provide information complementary to the traditionally used techniques for functional assessment. Moreover, the combined use of these techniques may enhance the assessment of the presence and extent of CAD. In the future diagnostic algorithms combining non-invasive anatomic and functional imaging need to be evaluated in large patient populations to establish their efficacy, safety, and cost effectiveness. Importantly, these investigations should result in the development of comprehensive guidelines on the use of CTA in clinical practice as well.

References

1. Hu H, He HD, Foley WD, et al. Four multidetector-row helical CT: image quality and volume coverage speed. Radiology 2000;215:55-62.
2. Nieman K, Oudkerk M, Rensing BJ, et al. Coronary angiography with multi-slice computed tomography. Lancet 2001;357:599-603.
3. Achenbach S, Ropers D, Kuettner A, et al. Contrast-enhanced coronary artery visualization by dual-source computed tomography--initial experience. Eur J Radiol 2006;57:331-5.
4. Flohr TG, McCollough CH, Bruder H, et al. First performance evaluation of a dual-source CT (DSCT) system. Eur Radiol 2006;16:256-68.
5. Ropers U, Ropers D, Pflederer T, et al. Influence of heart rate on the diagnostic accuracy of dual-source computed tomography coronary angiography. J Am Coll Cardiol 2007;50:2393-8.
6. Weustink AC, Meijboom WB, Mollet NR, et al. Reliable high-speed coronary computed tomography in symptomatic patients. J Am Coll Cardiol 2007;50:786-94.
7. Husmann L, Valenta I, Gaemperli O, et al. Feasibility of low-dose coronary CT angiography: first experience with prospective ECG-gating. Eur Heart J 2008;29:191-7.
8. Kitagawa K, Arbab-Zadeh A, Hannon KM, et al. Comparison of 256X0.5mm and 64X0.5mm Multidetector Computed Tomography Image Quality and Accuracy in a Custom-Designed, Motion-Simulating Phantom of Coronary Artery Stenosis (abstract 1902). American Heart Association Scientific Sessions 2007.
9. Motoyama S, Sarai M, Anno H, et al. Image Quality of Coronary CT Angiography in 256-slice CT (abstract 2758). American Heart Association Scientific Sessions 2007.
10. 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.
11. Ehara M, Surmely JF, Kawai M, et al. Diagnostic accuracy of 64-slice computed tomography for detecting angiographically significant coronary artery stenosis in an unselected consecutive patient population: comparison with conventional invasive angiography. Circ J 2006;70:564-71.
12. Hausleiter J, Meyer T, Hadamitzky M, et al. Non-invasive coronary computed tomographic angiography for patients with suspected coronary artery disease: the Coronary Angiography by Computed Tomography with the Use of a Submillimeter resolution (CACTUS) trial. Eur Heart J 2007;28:3034-41.
13. Herzog C, Zwerner PL, Doll JR, et al. Significant coronary artery stenosis: comparison on per-patient and per-vessel or per-segment basis at 64-section CT angiography. Radiology 2007;244:112-20.
14. Heuschmid M, Burgstahler C, Reimann A, et al. Usefulness of noninvasive cardiac imaging using dual-source computed tomography in an unselected population with high prevalence of coronary artery disease. Am J Cardiol 2007;100:587-92.
15. Hoffmann U, Moselewski F, Cury RC, et al. Predictive value of 16-slice multidetector spiral computed tomography to detect significant obstructive coronary artery disease in patients at high risk for coronary artery disease: patient-versus segment-based analysis. Circulation 2004;110:2638-43.
16. Kaiser C, Bremerich J, Haller S, et al. Limited diagnostic yield of non-invasive coronary angiography by 16-slice multi-detector spiral computed tomography in routine patients referred for evaluation of coronary artery disease. Eur Heart J 2005;26:1987-92.
17. Kopp AF, Schroeder S, Kuettner A, et al. Non-invasive coronary angiography with high resolution multidetector-row computed tomography. Results in 102 patients. Eur Heart J 2002;23:1714-25.
18. Leschka S, Alkadhi H, Plass A, et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. Eur Heart J 2005;26:1482-7.
19. Mollet NR, Cademartiri F, Nieman K, et al. Multislice spiral computed tomography coronary angiography in patients with stable angina pectoris. J Am Coll Cardiol 2004;43:2265-70.

20. Mollet NR, Cademartiri F, Van Mieghem CA, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005;112:2318-23.
21. Raff GL, Gallagher MJ, O'Neill WW, et al. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. J Am Coll Cardiol 2005;46:552-7.
22. Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64- x 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343-8.
23. Scheffel H, Alkadhi H, Plass A, et al. Accuracy of dual-source CT coronary angiography: First experience in a high pre-test probability population without heart rate control. Eur Radiol 2006;16:2739-47.
24. Schuijf JD, Pundziute G, Jukema JW, et al. Diagnostic accuracy of 64-slice multislice computed tomography in the noninvasive evaluation of significant coronary artery disease. Am J Cardiol 2006;98:145-8.
25. Shabestari AA, Abdi S, Akhlaghpoor S, et al. Diagnostic performance of 64-channel multislice computed tomography in assessment of significant coronary artery disease in symptomatic subjects. Am J Cardiol 2007;99:1656-61.
26. Late-Breaking Clinical Trial Abstracts From the American Heart Assocation's Scientific Sessions 2007. Circulation 2008;116:2627-33.
27. Abdulla J, Abildstrom SZ, 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.
28. Schroeder S, Achenbach S, Bengel F, et al. Cardiac computed tomography: indications, applications, limitations, and training requirements: Report of a Writing Group deployed by the Working Group Nuclear Cardiology and Cardiac CT of the European Society of Cardiology and the European Council of Nuclear Cardiology. Eur Heart J 2007.
29. Meijboom WB, Van Mieghem CA, Mollet NR, et al. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. J Am Coll Cardiol 2007;50:1469-75.
30. Lee TH, Ting HH, Shammash JB, et al. Long-term survival of emergency department patients with acute chest pain. Am J Cardiol 1992;69:145-51.
31. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med 2000;342:1163-70.
32. Gallagher MJ, Ross MA, Raff GL, et al. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low-risk chest pain patients. Ann Emerg Med 2007;49:125-36.
33. Goldstein JA, Gallagher MJ, O'Neill WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863-71.
34. Hoffmann U, Nagurney JT, Moselewski F, et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. Circulation 2006;114:2251-60.
35. Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-Slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007;93:1386-92.
36. Rubinshtein R, Halon DA, Gaspar T, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation 2007;115:1762-68.
37. Goldstein JA, Gallagher MJ, O'Neill WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863-71.
38. Kramer CM, Budoff MJ, Fayad ZA, et al. ACCF/AHA 2007 clinical competence statement on vascular imaging with computed tomography and magnetic resonance: a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians

Task Force on Clinical Competence and Training: developed in collaboration with the Society of Atherosclerosis Imaging and Prevention, the Society for Cardiovascular Angiography and Interventions, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society for Vascular Medicine and Biology. Circulation 2007;116:1318-35.
39. Meijboom WB, Mollet NR, Van Mieghem CA, et al. Pre-operative computed tomography coronary angiography to detect significant coronary artery disease in patients referred for cardiac valve surgery. J Am Coll Cardiol 2006;48:1658-65.
40. Ghostine S, Caussin C, Daoud B, et al. Non-invasive detection of coronary artery disease in patients with left bundle branch block using 64-slice computed tomography. J Am Coll Cardiol 2006;48:1929-34.
41. Andreini D, Pontone G, Pepi M, al. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. J Am Coll Cardiol 2007;49:2044-50.
42. Rixe J, Achenbach S, Ropers D, et al. Assessment of coronary artery stent restenosis by 64-slice multi-detector computed tomography. Eur Heart J 2006;27:2567-72.
43. Ropers D, Pohle FK, Kuettner A, et al. Diagnostic accuracy of noninvasive coronary angiography in patients after bypass surgery using 64-slice spiral computed tomography with 330-ms gantry rotation. Circulation 2006;114:2334-41.
44. Cademartiri F, Schuijf JD, Pugliese F, et al. Usefulness of 64-slice multislice computed tomography coronary angiography to assess in-stent restenosis. J Am Coll Cardiol 2007;49:2204-10.
45. Schuijf JD, Pundziute G, Jukema JW, et al. Evaluation of patients with previous coronary stent implantation with 64-section CT. Radiology 2007;245:416-23.
46. Meyer TS, Martinoff S, Hadamitzky M, et al. Improved noninvasive assessment of coronary artery bypass grafts with 64-slice computed tomographic angiography in an unselected patient population. J Am Coll Cardiol 2007;49:946-50.
47. Malagutti P, Nieman K, Meijboom WB, et al. Use of 64-slice CT in symptomatic patients after coronary bypass surgery: evaluation of grafts and coronary arteries. Eur Heart J 2007;28:1879-85.
48. Gaemperli O, Schepis T, Koepfli P, et al. Accuracy of 64-slice CT angiography for the detection of functionally relevant coronary stenoses as assessed with myocardial perfusion SPECT. Eur J Nucl Med Mol Imaging 2007;34:1162-71.
49. Hacker M, Jakobs T, Hack N, et al. Sixty-four slice spiral CT angiography does not predict the functional relevance of coronary artery stenoses in patients with stable angina. Eur J Nucl Med Mol Imaging 2007;34:4-10.
50. Schuijf JD, Wijns W, Jukema JW, et al. Relationship between noninvasive coronary angiography with multi-slice computed tomography and myocardial perfusion imaging. J Am Coll Cardiol 2006;48:2508-14.
51. Gaemperli O, Schepis T, Valenta I, et al. Cardiac image fusion from stand-alone SPECT and CT: clinical experience. J Nucl Med 2007;48:696-703.
52. Rispler S, Keidar Z, Ghersin E, et al. Integrated single-photon emission computed tomography and computed tomography coronary angiography for the assessment of hemodynamically significant coronary artery lesions. J Am Coll Cardiol 2007;49:1059-67.
53. Gaemperli O, Kaufmann PA. Hybrid cardiac imaging: more than the sum of its parts? J Nucl Cardiol 2008;15:123-6.
54. Schuijf JD, Jukema JW, van der Wall EE, et al. The current status of multislice computed tomography in the diagnosis and prognosis of coronary artery disease. J Nucl Cardiol 2007;14:604-12.
55. Virmani R, Burke AP, Farb A, et al. Pathology of the vulnerable plaque. J Am Coll Cardiol 2006;47:C13-C18.

56. 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.
57. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. J Am Coll Cardiol 2007;50:319-26.
58. 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.
59. Leber AW, Becker A, Knez A, et al. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. J Am Coll Cardiol 2006;47:672-7.
60. Min JK, Shaw LJ, Devereux RB, et al. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007;50:1161-70.
61. 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.
62. Henneman MM, Schuijf JD, Jukema JW, et al. Comprehensive cardiac assessment with multislice computed tomography: evaluation of left ventricular function and perfusion in addition to coronary anatomy in patients with previous myocardial infarction. Heart 2006;92:1779-83.
63. Henneman MM, Schuijf JD, Dibbets-Schneider P, et al. Comparison of multislice computed tomography to gated single-photon emission computed tomography for imaging of healed myocardial infarcts. Am J Cardiol 2008;101:144-8.
64. Ko SM, Seo JB, Hong MK, et al. Myocardial enhancement pattern in patients with acute myocardial infarction on two-phase contrast-enhanced ECG-gated multidetector-row computed tomography. Clin Radiol 2006;61:417-22.
65. Habis M, Capderou A, Ghostine S, et al. Acute myocardial infarction early viability assessment by 64-slice computed tomography immediately after coronary angiography: comparison with low-dose dobutamine echocardiography. J Am Coll Cardiol 2007;49:1178-85.
66. Lardo AC, Cordeiro MA, Silva C, et al. Contrast-enhanced multidetector computed tomography viability imaging after myocardial infarction: characterization of myocyte death, microvascular obstruction, and chronic scar. Circulation 2006;113:394-404.
67. Sanz J, Weeks D, Nikolaou K, et al. Detection of healed myocardial infarction with multidetector-row computed tomography and comparison with cardiac magnetic resonance delayed hyperenhancement. Am J Cardiol 2006;98:149-55.
68. George RT, Silva C, Cordeiro MA, et al. Multidetector computed tomography myocardial perfusion imaging during adenosine stress. J Am Coll Cardiol 2006;48:153-60.
69. George RT, Lardo AC, Kitagawa K, et al. Combined Perfusion and Non-Invasive Coronary Angiography in Patients with Suspected Coronary Disease using 256 Row, 0.5mm Slice Thickness non-Helical Multi-Detector Computed Tomography (abstract 2589). American Heart Association Scientific Sessions 2007.