CORONARY CT ANGIOGRAPHY: CURRENT & EVOLVING APPLICATIONS

*MUSHABBAR A. SYED**

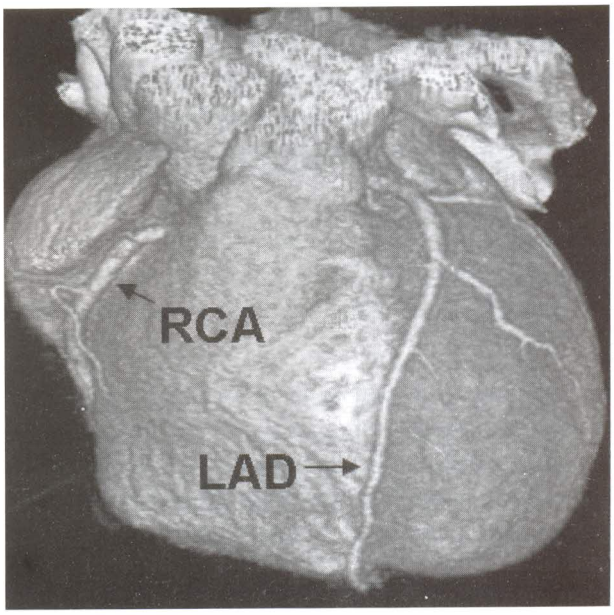
INTRODUCTION

Developments in computed tomography (CT) technology since the early 1980s have led to the emergence of non-invasive coronary CT angiography (CCTA). The introduction of electron beam CT (EBCT) permitted the detection of coronary calcification, opening up the door for CT-based cardiovascular imaging. The EBCT scanner, introduced in 1983, was able to capture a high-resolution image despite the motion of a beating heart; however, EBCT lacked adequate spatial resolution to adequately visualize small structures like coronary arteries. Multidetector CT (MDCT) scanners were introduced in the 1990s and provide higher spatial resolution and the capability to perform a diagnostic-quality CCTA using iodinated contrast agents for coronary lumen opacification. Since then, MDCT technology has exploded and now 16 to 64 slice scanners coupled with advanced software packages for image acquisition and reconstruction are widely available. Tremendous advances have also occurred in workstation technology with capabilities for three-dimensional (3D) data manipulation and image interpretation (Figure 1). These developments have enabled physicians around the world to perform and interpret CCTA on a routine basis. Clinical applications for CCTA have evolved over last few years with research reports of high diagnostic and prognostic value. This review provides a brief overview of current and evolving clinical applications of CCTA, focusing on appropriate patient selection for use of this technology as highlighted in the recent guidelines published by the American College of Cardiology[3].

* Gill Heart Institute, University of Kentucky, Lexington, KY. USA.

Address for correspondence:
Mushabbar A. Syed, MD, FACC
Associate Professor of Medicine & Radiology
Director, Cardiovascular CT & MR Imaging
Division of Cardiovascular Medicine
University of Kentucky
324A Charles T. Wethington Bldg.
900 South Limestone
Lexington, KY 40536-0200
Email: masyed2@uky.edu

Figure 1: CCTA with 3D volume rendered reconstruction showing normal course of left anterior descending artery (LAD) and right coronary artery (RCA)



Why do we need non-invasive coronary angiography?

Invasive coronary angiography (ICA) is widely considered a reference standard for the diagnosis of coronary artery disease (CAD) despite the limitations of a "luminogram." This procedure is routinely performed in cardiac catheterization laboratories and is generally safe. However, due to the invasive nature of coronary angiography, there is a small 1-2% risk of complications, including vascular access problems, myocardial infarction, and death[1]. The proportion of patients with a normal or near normal coronary angiogram is 20–27% with a higher incidence in women than men[2]. Additionally, 30–40% of patients who are found to have CAD on ICA do not require an interventional procedure. Therefore, a substantial number of patients can potentially avoid an invasive and costly ICA procedure by improving non-invasive

diagnostic testing beyond the currently available stress test technology. However, several technical challenges are associated with non-invasive coronary imaging. Coronary arteries are small vessels in the order of 1.5 to 5 mm in diameter and they are embedded in epicardial fat. They are also constantly moving due to beating of the heart and breathing. Non-invasive coronary imaging, therefore, requires high spatial resolution to evaluate small structures, high temporal resolution to freeze cardiac motion, contrast opacification to differentiate coronary arteries from surrounding tissues, and acquisition during breath-holding to avoid respiratory motion artifacts.

CCTA imaging protocol: practical points

CCTA requires an advanced MDCT scanner; ideally with 64 (or higher) slice capability and a cardiac software package for data acquisition. An increased number of slices allows for increasing acquisition coverage and therefore decreases the image acquisition time, breath-hold duration, and contrast volume. Number of slices, however, is not the sole determinant of image quality. The major determinants of image quality are temporal and spatial resolution of the scanner and are based on gantry rotation speed, slice collimation, and tube output.

Besides image quality, diagnostic accuracy depends on appropriate patient preparation. A target heart rate of 60–65 beats per minute needs to be achieved, coronary arteries need to be maximally dilated, and appropriate contrast needs to be administered. β-blocker medication is usually given orally or intravenously to slow the heart rate. A slow heart rate not only decreases the incidence of image motion artifacts but also, by prolonging the diastolic phase of cardiac cycle, allows use of low-radiation-dose image acquisition techniques. One such technique is electrocardiogram (ECG)-dependent dose modulation or "ECG-pulsing," which reduces the tube current by 80% during systole and provides a radiation dose reduction of 35–40%[4]. Prospective ECG-gating (also called the step and shoot method) is a technique that only acquires images during the quiescent phase of diastole rather than throughout the cardiac cycle leading to radiation dose reduction of up to 72%[5]. Another way to reduce radiation dose is to decrease tube voltage to 100 kV from the standard 120 kV. This technique has been used in non-obese patients (BMI <25–30kg/m2) and significantly reduces radiation dose by 50–60% without impairing diagnostic image quality[6-7].

We recommend routine use of sublingual nitroglycerine before image acquisition to maximally dilate coronary arteries for better contrast opacification and visualization. We use a high iodine content contrast agent (350–370 mg/ml) and flow rate of 5 cc/sec increased to 6 cc/sec for obese patients. The total contrast dose for CCTA is based on scan duration and contrast flow rate (e.g., scan duration of 15 seconds times contrast flow rate of 5 cc/sec = 75 cc total contrast needed for the study; the minimum dose is 60 cc). With the current 64 slice scanners, the average breath-hold is 8–12 seconds, which is easy to perform.

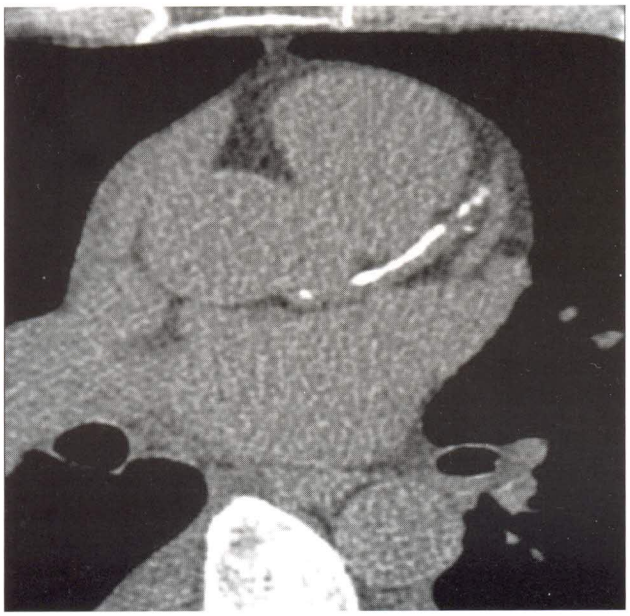
Clinical applications

The American College of Cardiology in collaboration with appropriate societies has published appropriateness criteria for the clinical use of CCTA. These criteria are based upon expert consensus opinion on scientific evidence available at the time of publication but may not include more recently published data. Requirements for cardiovascular CT training have been published with defined targets for time and experience to achieve competency in performance and interpretation of CCTA studies[8].

CCTA in asymptomatic patients

Screening for CAD in asymptomatic patients has been studied with the use of resting ECG, exercise treadmill test, and EBCT coronary artery calcium (CAC) score. A detailed discussion of CAD screening in asymptomatic patients with or without risk factors is beyond the scope of this review. Coronary artery calcium score (Figure 2) by EBCT or MDCT is an estimate of coronary atherosclerosis burden and is predictive of clinical events beyond standard risk factors[9]. According to the ACC/AHA 2007 expert consensus document on coronary calcium scoring[10], it may be reasonable to consider use of CAC measurement in patients at intermediate risk, defined by a Framingham risk score of 10-20%

Figure 2: Coronary calcium score scan in axial orientation showing areas of calcification (calcified plaque) in the left main and LAD



for estimated 10-year risk of coronary events. This recommendation is based on the possibility that such patients might be reclassified to a higher risk status based on high CAC score, and subsequent patient management may be modified. CAC score for screening of patients at low risk (<10% 10-year risk) or high risk (>20% 10-year risk or established coronary disease) is not recommended as CAC information will seldom change patient management in these subgroups. Currently, data on the role of CCTA for CAD screening is very limited and unproven. Additionally, due to concerns about radiation exposure and iodinated contrast use in asymptomatic patients, none of the guidelines recommend use of CCTA for screening asymptomatic patients.

CCTA in symptomatic patients with no prior history of CAD

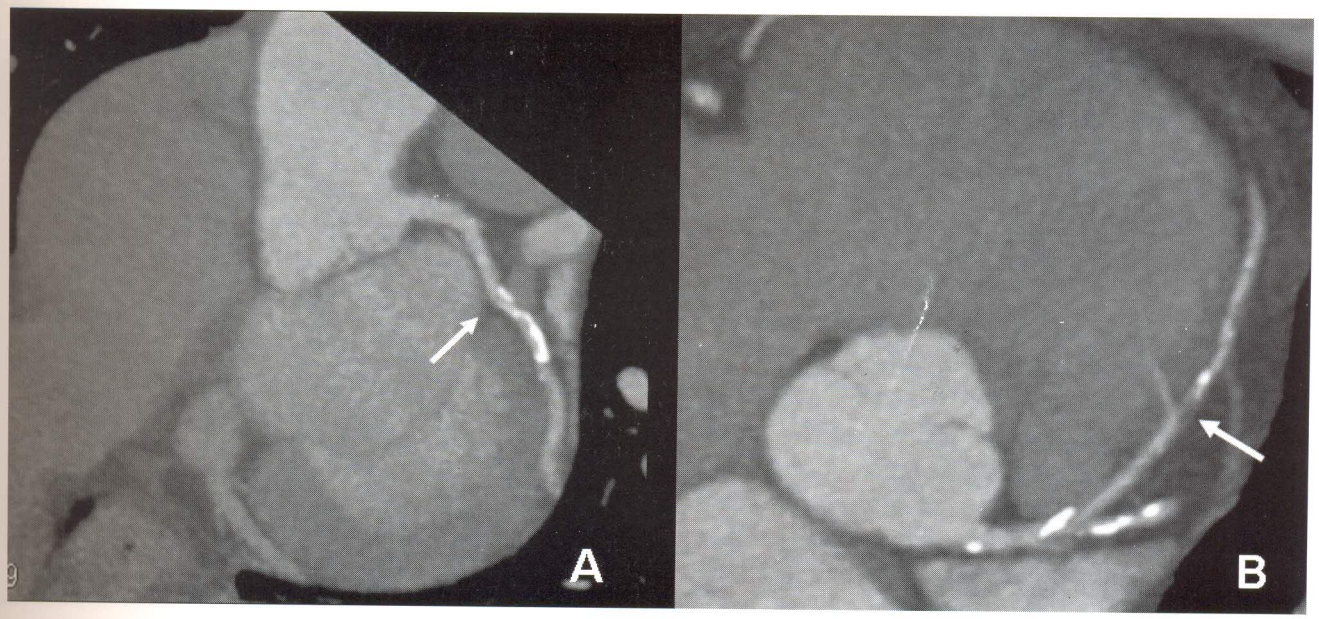
CT technology has rapidly evolved from 16 slice to 64 slice to the recently introduced, more advanced, 320 slice and dual source scanners. Image quality and diagnostic accuracy have significantly improved with each advancement. Several clinical studies have demonstrated the high diagnostic value of CCTA for the diagnosis of significant CAD[11]. These studies compared CCTA with ICA for the detection of significant CAD defined as ≥50% stenosis. On average these studies show a sensitivity of 83–99% and specificity of 93–98%. In addition, a negative predictive value (NPV) of 95–100% suggests that CCTA is a useful tool in ruling out the presence of significant CAD with a high degree of certainty[12]. Most of these studies are from single centers and are comprised of a small number of patients with variable prevalence of CAD. So far two multicenter clinical trials of CCTA accuracy in patients with no prior history of CAD have been reported.

The CORE 64 trial (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) enrolled 291 patients with CAC score ≤600 and compared CCTA with conventional ICA for the presence or absence of ≥50% stenosis[13]. A total of 56% of patients had significant CAD, CCTA was found to have a sensitivity of 85%, specificity of 90%, positive predictive value (PPV) of 91%, and NPV of 83%.

The ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) multicenter trial enrolled 230 patients with intermediate prevalence of CAD. No subjects were excluded for baseline CAC score or body mass index and all patients underwent CCTA and conventional ICA. The sensitivity for detecting ≥50% stenosis was 95%, specificity was 83%, PPV was 64%, and NPV was 99%. For the detection of ≥70% stenosis, sensitivity was 94%, specificity was 83%, PPV was 48%, and NPV was 99%. A CAC score of >400 reduced specificity significantly to 53% compared to 86% with CAC score of <400. These data are consistent with the high sensitivity in detecting CAD, and more importantly, high NPV in ruling out obstructive coronary artery disease in patients with no prior history of CAD (Figure 3 A & B).

The goals of non-invasive imaging include diagnosing or excluding CAD as well as predicting the outcome of future events. The data on CCTA prognostic value has been limited until recently as long-term patient follow-up is required. Ostrom et al. studied 2,538 consecutive patients without known CAD who underwent CCTA and followed them for 78 ± 12 months[15]. Risk-adjusted hazard ratios for CCTA-diagnosed CAD were: 1.7 for 3-vessel nonobstructive, 1.8 for 1-vessel obstructive, 2.3 for 2-vessel

Figure 3: CCTA with significant stenosis of proximal circumflex artery (A) and mid-LAD (B)



obstructive, and 2.6 for 3-vessel obstructive CAD. The diagnosis of CAD and number of coronary vessel involvement by CCTA was an independent predictor of mortality in an adjusted multivariate model. Similar results were reported by Min et al. from their single-center cohort of 1,127 patients[16]. Over a mean follow-up of 15.3 ± 3.9 months, plaque burden and distribution was predictive of all-cause death.

CCTA in symptomatic patients with established CAD

Data are limited on use of CCTA in patients with chest pain and known CAD. CCTA stenosis grading has significant variation and correlation with quantitative coronary angiography has been limited. Generally, CCTA tends to overestimate the degree of stenosis due to lower spatial resolution (0.4 mm) than conventional ICA (0.2 mm). The following stenosis grading scheme is used in our laboratory[17]:

Grade	Percent Stenosis
0	no stenosis
1	1-24%
2	25-49%
3	50-69%
4	70-89%
5	90-100%

Several studies have evaluated the role of CCTA for assessment of in-stent restenosis, and their results have been mixed. Stent blooming due to partial volume effect and beam hardening artifact on CCTA limit the evaluation of coronary lumen inside the stents. Therefore, stent imaging should be limited to selected symptomatic patients with large stents (>3.5 mm size) located in proximal vessels. CCTA has also been studied in patients with bypass grafts and has been found to be highly accurate in evaluating graft patency[12, 18]. Imaging of bypass grafts is less challenging than native coronary arteries due to their larger size and less motion. Conversely, the native coronary arteries in bypass patients have advanced atherosclerosis with high prevalence of calcification which makes it challenging to accurately assess the lumen stenosis. CCTA should only be performed in selected bypass patients for this reason. With further technological advances it is anticipated that patients with stents and bypass grafts can be routinely evaluated, however this is an unproven routine indication at this point.

Detection of coronary artery anomalies

The prevalence coronary artery anomalies have been estimated at approximately 1%, and though usually benign, is a recognized cause of 12–19% of deaths in athletes, mostly during exertion[19]. Data on the prevalence of coronary artery anomalies is primarily derived from cardiac catheterization studies in

patients referred for chest pain evaluation and, therefore, the true incidence in the general population is unknown. Prevalence of coronary artery anomalies is expected to be higher in patients with other forms of congenital heart diseases. Angelini and coworkers used strict criteria for assessing coronary normality/abnormality in a study of 1,950 angiograms and found a 5.6% incidence of anomalies,[20] which is higher than previously reported.

CCTA is currently considered the modality of choice for the delineation of anomalous coronary origin and course. CCTA is also routinely used for the evaluation of coronary artery fistula and aneurysms. However, due to concerns about radiation and iodinated contrast agent with CCTA, imaging of coronary artery anomalies and aneurysm in children may be best achieved by magnetic resonance imaging (MRI)[21]. The greatest limitation of coronary MRI is in determining the distal coronary course and this is because MRI has lower spatial resolution than CCTA. In the axial imaging plane in a normal situation the right coronary artery (RCA) originates anteriorly from the right coronary sinus and the left main coronary artery originates around a 4–6 o'clock position from the left coronary sinus and bifurcates into the left anterior descending artery (LAD) coursing in the interventricular groove and the left circumflex artery (LCx) coursing in the left atrioventricular groove (Figures 4 & 5). In clinical practice a right or left coronary artery arising from the opposite coronary sinus (RCA from the left sinus and

Figure 4: CCTA in axial orientation showing normal origin of RCA from aortic root at 12 o'clock position

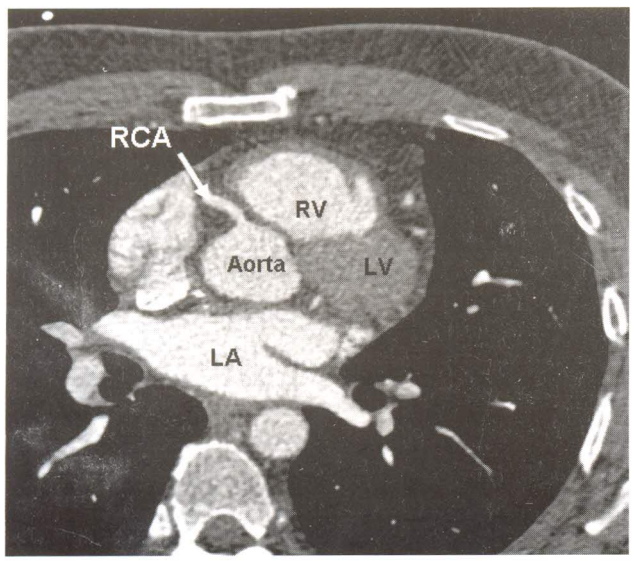
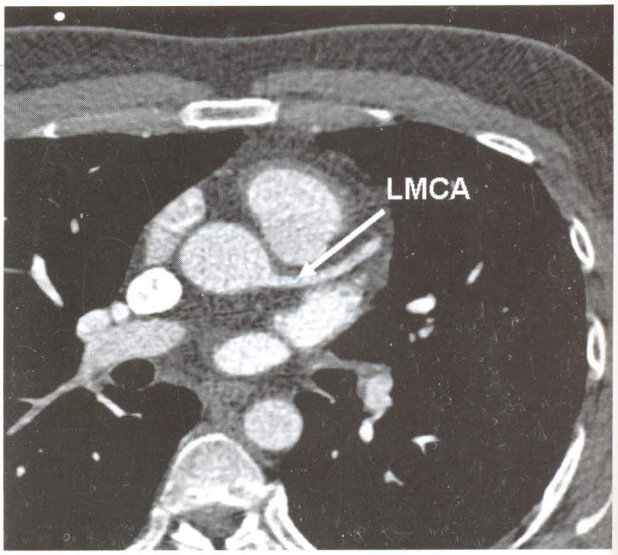
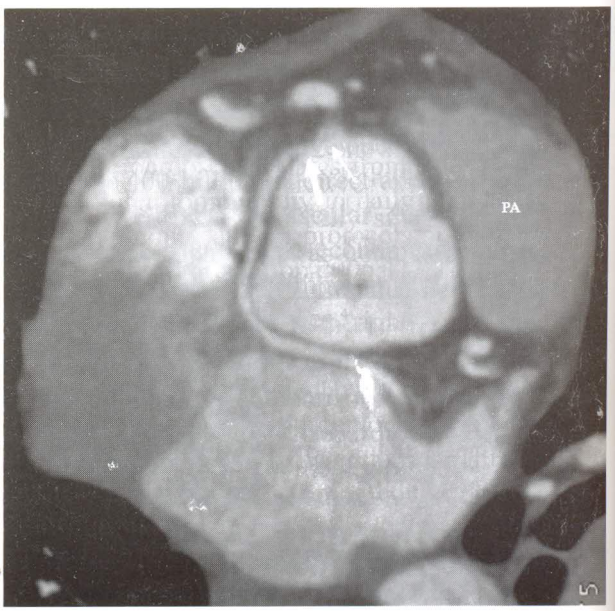


Figure 5: CCTA in axial orientation showing normal origin of left main coronary artery from aortic root between 4 and 6 o'clock position



left main or LAD from the right sinus) poses a diagnostic dilemma. This anomalous origin of coronary arteries may or may not be associated with inter-arterial course (between aorta and pulmonary artery) that may cause symptoms of myocardial ischemia and sudden cardiac death during exertion due to coronary artery compression between the aorta and pulmonary artery (Figure 6). Coronary anomalies may also have consequences other than myocardial

Figure 6: Anomalous origin of circumflex artery (LCx) from right coronary cusp (thick arrow). Note the adjacent origin of RCA (thin arrow). LCx then courses behind aorta (retro-aortic course) to arrive in left AV groove. As LCx does not run between aorta and pulmonary artery (PA), this is considered a benign anomaly



ischemia, including volume overload due to coronary fistulas and complications of coronary artery aneurysms (in situ thrombosis, distal embolization, and rupture). Due to CCTA's 3D imaging capability, accurate evaluation of coronary artery origin, course, distal termination, and morphology can be achieved in the vast majority of patients. However, CCTA imaging of coronary anomalies is usually limited to patients with symptoms or suspicion based on the presence of other forms of congenital heart disease and should not be used for screening of the general population. In our institution most CCTAs for coronary anomalies are performed to further define the anomalous origin and course for treatment or surgical planning after the anomaly has been detected during coronary angiography. Incidental coronary anomalies are also sometimes detected in patients presenting to CCTA for chest pain evaluation, which may lead to further testing in selected patients with severe abnormalities.

ACC/SCCT appropriateness criteria for CCTA

CCTA is a relatively expensive technology and has the potential for harm related to uncontrolled utilization, downstream testing, unwarranted coronary revascularization procedures, and exposure to radiation and nephrotoxic contrast agents. It is therefore imperative for us to understand the appropriate indications, contraindications, and limitations of CCTA to successfully incorporate this modality into clinical practice. The ACC and Society of Cardiovascular Computed Tomography (SCCT) in association with other key specialty and subspecialty societies published appropriateness criteria in 2006 for the clinical practice of CCTA[3]. The review committee assessed risk and benefits of CCTA for several indications and clinical scenarios and scored them on a scale of 1 to 9: appropriate (score 7–9), inappropriate (score 1–3), and uncertain (score 4–6). Based on these recommendations the appropriate indications are:

1. Evaluation of chest pain: CCTA is indicated in place of pharmacological stress test in patients with intermediate pre-test probability of disease with non-diagnostic ECG or when unable to perform an exercise stress test. If a patient is able, an exercise-based stress test (treadmill or bicycle) is preferred.
2. Evaluation of suspected coronary anomalies: As discussed above, CCTA is appropriate for delineation of anomalous coronary origin and course and for evaluation of coronary artery fistula and aneurysms in adults (but MRI is preferred for children). CCTA is usually limited to patients with symptoms or suspicion based on the presence of other forms of congenital heart disease and should not be used for screening of the general population.
3. Acute chest pain with no ischemic ECG changes and normal cardiac enzymes. This indication is for evaluation in an emergency room or acute setting for diagnosis and risk stratification after ruling out acute myocardial infarction.
4. Evaluation of chest pain when stress test (exercise, perfusion, or stress echo) results are equivocal or uninterpretable. CCTA is not indicated if there is evidence of moderate or severe ischemia on stress test when a conventional coronary angiography would be most appropriate.
5. Evaluation of coronary arteries in patients with new onset heart failure to assess etiology.
6. Evaluation of cardiac mass in patients with technically limited images from echocardiogram, transesophageal echocardiogram (TEE), or MRI.
7. Evaluation of pericardial conditions (mass, constrictive pericarditis, or complications of cardiac surgery).
8. Evaluation of suspected aortic dissection, thoracic aortic aneurysm, or suspected pulmonary embolism.
9. Some of the other appropriate indications include: congenital heart disease evaluation, pulmonary vein imaging prior to ablation for atrial fibrillation, coronary vein mapping prior to placement of biventricular pacemaker, and coronary arterial mapping particularly for left internal mammary artery (LIMA) location prior to repeat cardiac surgery.

It is important to note that by itself, either low or high probability of CAD is not considered appropriate indications for CCTA. Most low pre-test probability chest pain can be adequately evaluated by clinical history, ECG, and stress test. CCTA may be used in selected low-risk patients who continue to have symptoms despite normal evaluation by stress test. Patients at high pre-test probability of disease or with ST-segment changes on ECG or positive cardiac enzymes usually require coronary angiography with a plan for revascularization. As previously mentioned, CCTA for asymptomatic screening is not an appropriate indication.

LIMITATIONS

CCTA has several technical and clinical limitations. For an accurate assessment of coronary artery disease, it is critical to acquire a high-quality study. This requires appropriate patient selection, use of a β-blocker and nitroglycerine, as well as optimizing contrast timing and scan parameters. Motion artifacts and calcification are the major source of inaccurate results. Motion artifacts are usually related to high heart rate or irregular rhythm including sinus arrhythmia or patient motion. Patients with atrial fibrillation or frequent ectopy have significant motion artifacts that limit coronary evaluation and should be avoided. Presence of dense calcification interferes with accurate assessment of coronary artery lumen with a tendency to overestimate the degree of stenosis. We generally don't use a calcium score cutoff prior to CCTA in our laboratory, however, some studies have suggested limiting CCTA in patients with high calcium scores (>600–1000). Quantitation of lesion severity by CCTA is not as accurate as quantitative coronary angiography due to differences in temporal and spatial resolution. Due to the anatomical nature of this imaging modality, functional significance cannot be assessed; however, there is evolving data on CT perfusion which is at a preliminary stage[22]. Close attention must be paid to radiation dose issues and scan parameters to achieve the lowest dose reasonably possible for a diagnostic-quality study. Patients with contrast allergy and renal dysfunction should only be scanned on a case-by-case basis under close supervision and with adequate preparation.

CONCLUSIONS

CCTA has evolved into a clinically useful method for evaluation of coronary artery disease. Several studies have documented a high sensitivity and negative predictive value for ruling out significant coronary artery disease. Similar to other imaging modalities, results depend upon equipment, image quality, imaging protocol, patient selection and reader expertise. Appropriate clinical indications have been published by specialty societies which can be incorporated in clinical practice.

REFERENCES

1. Bashore TM, Bates ER, Berger PB, et al. Cardiac catheterization laboratory standards: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents (ACC/SCA&I Committee to Develop an Expert Consensus Document on Cardiac Catheterization Laboratory Standards). J Am Coll Cardiol 2001;37:2170 –214.

2. Johnson LW, Krone R. Cardiac catheterization 1991: a report of the Registry of the Society for Cardiac Angiography and Interventions (SCA&I). Cathet Cardiovasc Diagn. 1993;28:219-220.

3. Hendel RC, Kramer C, Patel MR, Poon M: ACCF/ACR/SCCT/SCMR/ASNC/NASCI/ SCAI/SIR appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging. J Am Coll Cardiol 2006, 48:1476–1497.

4. Hausleiter J, Meyer T, Hadamitzky M, et al. Radiation dose estimates from cardiac multislice computed tomography in daily practice. Impact of different scanning protocols on effective dose estimates. Circulation 2006;113:1305-1310.

5. Pontone G, Andreini D, Bartorelli AL, et al. Diagnostic accuracy of coronary computed tomography. A comparison between prospective and retrospective electrocardiogram triggering. J Am Coll Cardiol 2009;54:346-55.

6. Bischoff B, Hein F, Meyer T, et al. Impact of a reduced tube voltage on CT angiography and

radiation dose: results from the PROTECTION I study. JACC Cardiovasc Imaging 2009;2:940-6.

7. Feuchtner GM, Jodocy D, Klauser A, et al. Radiation dose reduction by using 100-kV tube voltage in cardiac 64-slice computed tomography: A comparative study. Eur J Radiol 2009 Aug 9 (Epub ahead of print).

8. Budoff MJ, Achenbach S, Berman DS, et al. Task Force 13: Training in advanced cardiovascular imaging (computed tomography). J Am Coll Cardiol 2008;51:409-414.

9. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all cause mortality. Radiology 2003:228:826-833.

10. 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). J Am Coll Cardiol 2007;49:378 – 402.

11. Beach S, Syed M. Current and upcoming roles of CT and MRI in clinical cardiac imagery. Curr Cardiol Reports 2007;9:420-427.

12. Achenbach S. Computed Tomography Coronary Angiography. J Am Coll Cardiol 2006;48:1919-28.

13. 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.

14. 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. J Am Coll Cardiol 2008;52:1724-32.

15. Ostrom MP, Gopal A, Ahmadi N, et al. Mortality incidence and the severity of coronary atherosclerosis assessed by computed tomography angiography. J Am Coll Cardiol 2008;52:1335-43.

16. 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.

17. Cheng V, Gutstein A, Wolak A, et al. Moving beyond binary grading of coronary arterial stenoses on coronary computed tomographic angiography: insights for the imager and referring clinician. JACC Imaging 2008;1:460-71.

18. Ropers D, Pohle FK, Kuettner A, et al. Diagnostic accuracy of noninvasive coronary angiography in patients with bypass surgery using 64-slice spiral computed tomography with 330-ms gantry rotation. Circulation 2006;114:2334-41.

19. Maron BJ, Thompson PD, Pugger JC, et al. Cardiovascular preparticpation screening of competitive athletes: a statement for health professionals from the Sudden Death Committee (Clinical Cardiology) and Congenital Cardiac Defects Committee (Cardiovascular Disease in the Young), American Heart Association. Circulation 1996;94L850-856.

20. Angelini P, Velasco JA, Flamm S. Coronary anomalies: incidence, pathophysiology, and clinical relevance. Circulation. 2002;105:2449-2454.

21. Danias PG, Stuber M, McConnell MV, Manning WJ. The diagnosis of congenital coronary anomalies with magnetic resonance imaging. Coronary Artery Disease 2001;12:621-626.

22. Blankstein R, Shturman LD, Rogers IS, et al. Adenosine-induced stress myocardial perfusion imaging using dual-source cardiac computed tomography. J Am Coll Cardiol. 2009;54:1072-84.