8

NON-INVASIVE IMAGING OF CORONARY ARTERIES

Shun Kohsaka, MD

Norman Lepor, MD

EXECUTIVE SUMMARY

Noninvasive angiography could provide valuable coronary anatomic information in an important segment of the population at risk for heart disease. Computed tomographic (CT) angiography offers excellent negative predictive value (≥ 95%) for the absence of coronary artery disease and has shown promising results in evaluating allograft vasculopathy, bypass grafts, and degenerative aortic valve disease. A single multidetector (MD) CT scan in the emergency department may also become valuable in ruling out both cardiac and noncardiac causes of acute chest pain. While MDCT can quantify plaque volume, magnetic resonance (MR) imaging has great potential for characterizing coronary plaques, as well as following their progression and regression. Cardiac MR currently lacks the spatial resolution of MDCT, limiting its assessment of the coronary vasculature, but the proximal coronary arteries can be evaluated along with myocardial function and viability without exposure to contrast dye or ionizing radiation.

Introduction

Cardiac imaging is evolving rapidly. Cardiac computed tomography (CT) and magnetic resonance (MR) imaging hold great promise as tools for the assessment of coronary artery atherosclerosis. Once used primarily as research tools, these modalities are increasingly being used in routine clinical practice, particularly for direct imaging of the coronary vasculature.

Coronary CT Angiography

Contemporary multislice/multidetector CT (MSCT/MDCT) techniques, which allow noninvasive evaluation of coronary arteries and bypass grafts, continue to evolve as alternatives to invasive coronary angiography. Modern MDCT systems can provide electrocardiogram-gated acquisition with adequate temporal resolution (100-220 ms) and the submillimeter spatial resolution needed to visualize the lumen of the coronary arteries. Currently, 64-slice MDCT has a spatial resolution in the range of 0.6-1.0 mm in all three dimensions (compared with 0.3 mm for conventional angiography). A spatial resolution of 1.0 mm is sufficient for imaging most of the coronary vascular tree, except for distal and calcified segments, which require a spatial resolution of 0.5 mm.

Numerous studies have evaluated the potential of CT coronary angiography to define focal coronary stenoses (Table 1). Compared with cardiac MR, MDCT has similar reliability for ruling out disease in non-diseased patients and is superior for detecting significant atherosclerotic lesions (1). In selected patients referred for invasive coronary angiography, the sensitivity of 16- and 64-slice CT coronary angiography was 95% or higher in most studies, after exclusion of arteries whose image quality was considered to be subdiagnostic. The 64-slice MDCT also has shown value in correctly identifying the absence of any atheromatous plaque among patients deemed to be at intermediate-to-high risk of coronary artery disease (CAD), with a negative predictive value of 98% to 99% in most recent studies. In addition, as the number of detectors has increased, so has the number of coronary artery segments that can be evaluated. In a recent meta-analysis, 78%, 91%, and 100% of segments could be evaluated with a 8-, 16-, and 64-slice MDCT, respectively (2).

Although these applications of cardiac MDCT are promising, there is still room for improvement in coronary MDCT image acquisition and post-processing techniques. Current technological limitations still prevent exact quantification of the degree of stenosis and reliable visualization of all small segments. In addition, image quality is compromised when the heart rate is too rapid (≥ 65 beats/min for 16-slice MDCT or ≥ 75 beats/min for 64-slice MDCT), the patient is morbidly obese (> 350 lbs), or the cardiac rhythm is irregular because of atrial fibrillation, frequent premature atrial or ventricular contractions, or exaggerated sinus arrhythmia (Figure 1). Also, calcium is a frequent feature of the coronary arteries (found in 70-80% of the population), and complete assessment by MDCT can be hindered by dense, focal calcium deposits in the vessel wall, leading to an overestimation of the severity of stenosis. Coronary artery calcium scores >1000 Agatston units are associated with an inability to perform an optimal diagnostic CT coronary angiogram. Finally, IV contrast and radiation limit the use of MDCT. The typical IV contrast dose is 80-100 cc, and the usual radiation dose is 10-15 mSv (3). The radiation dose is equivalent to what is absorbed during a stress nuclear perfusion examination and nearly twice as high as conventional coronary angiography without ventriculography or graft imaging. The risk of malignancy and other radiation-related complications is low with this level of radiation, but raises a concern about using MDCT for routine serial testing.

No clear scientific evidence is available to justify widespread use of MDCT in broad clinical populations, and indiscriminant testing can lead to further unnecessary testing and escalating costs (4). Long-term studies to determine the predictive value of MDCT are also necessary, similar to what has been done with electron-beam CT and coronary artery calcification (5). Still, several specific situations have emerged beyond simple coronary artery imaging in which MDCT may be particularly valuable.

Bypass Grafts

Most early (<1 month) graft occlusion, which occurs in up to 10% of patients, is attributable to a mechanical cause, whereas the late (5-10 years) stenosis or occlusion that occurs in the majority of grafts results from an accelerated atherosclerotic process. Because many vein graft occlusions are asymptomatic, being able to identify early saphenous vein graft degeneration using CT coronary angiography may allow earlier intervention when graft patency makes revascularization feasible. Bypass grafts are excellent targets for visualization with MDCT because of their reduced overall motion and their large lumens. Graft diameter typically ranges from 4 to 6 mm throughout the conduit, whereas the native vessel can taper to a diameter as small as 1 mm in the distal portion. In a study by Schlosser et al. (6), MDCT showed good accuracy in assessing graft patency, with a sensitivity of 96% and a specificity of 95%. However, it was less well suited to evaluating areas adjacent to surgical clips, and the distal bypass anastomosis could not be visualized in nearly 25% of cases.

Cardiac Allograft Vasculopathy

Conventional coronary angiography is the current gold standard for the serial detection and follow-up of cardiac allograft vasculopathy in heart transplant patients. However, MDCT may offer a non-invasive alternative. In a series of 53 patients who underwent both routine invasive coronary angiography and MDCT, MDCT's sensitivity and specificity for detecting coronary stenoses >50% were 83% and 95%, respectively (7). It was felt that MDCT may offer an advantage over conventional coronary angiography by showing coronary wall thickening as well as luminal narrowing. However, visual assessment was noted to be limited by small caliber vessels, tachycardia, and the presence of stents.

Degenerative Aortic Valve Disease

Advanced imaging applications enable 3-dimensional depiction of a stenotic aortic valve and provide quantitative estimates of valve area, while determining the presence or absence of coronary artery disease. A study of MDCT for patients with degenerative aortic stenosis (AS) demonstrated that using retrospective electrocardiographic gating provides accurate architectural delineation of the aortic valve (8). The sensitivity of the 16-slice MDCT to detect degenerative AS was 100%, and the specificity was 94%. Aortic valve area quantification with MDCT also had good correlation to transthoracic echocardiography (r = 0.89).

Functional Assessment

The data acquired from MDCT angiography of the coronary arteries can be used to create volumetric cine loops of cardiac function. This simultaneous acquisition of angiographic and functional data avoids the need for repeat scanning and for administering additional contrast material (1). Furthermore, MDCT allows assessment of first-pass perfusion and delayed enhancement imaging in patients with subacute infarction.

Computed Tomography Scans for a Triple Rule-out

The feasibility of using MDCT for comprehensive assessment of cardiac and noncardiac causes of chest pain in patients presenting to the emergency room is being evaluated. In particular, a single MDCT scan could be used to rule out coronary artery disease, pulmonary embolism, and aortic dissection. A feasibility study of MDCT in evaluating cardiac and noncardiac causes of acute chest pain in 69 patients presenting to the emergency department showed that MDCT evaluation was comprehensive and produced a false-negative rate of only 3% (9). Further investigation is needed to determine whether and how patients with low-to-intermediate risk can be triaged effectively using a MDCT algorithm. Application of CT coronary angiography in the emergency department may be limited by the skills required for performing 3-dimensional reconstructions, which most radiologists and technicians do not have, and by the time it takes to produce diagnostic-quality images.

Plaque Characterization

MDCT can provide valuable quantitative information on coronary atherosclerotic plaques. In terms of plaque volume measurement, its results correlate highly with those of intravascular ultrasonography (10). In 41 proximal coronary segments imaged using IVUS and MDCT, sensitivity and specificity for MDCT were 95% and 91%, respectively, for calcified plaque, and 91% and 89%, respectively, for noncalcified plaque. However, MDCT cannot provide the qualitative plaque information obtained by MR imaging.

Coronary MR Angiography

Cardiac MR allows assessment of proximal coronary anatomy, global and regional cardiac function, cardiac volumes, and myocardial viability without exposing patients to intravenous contrast or ionizing radiation (11). Individually, various cardiac MR techniques have shown promise as alternatives to established noninvasive tools for detecting coronary stenosis and myocardial ischemia.

Coronary magnetic resonance angiography (MRA) has a longer scan time and lower spatial resolution (1.2-1.4 mm) than MDCT, limiting its use in detecting CAD. The overall sensitivity and specificity of MRA is as high as 90% for proximal and mid-coronary disease (Table 2). The most promising MRA technique currently seems to be whole-heart acquisition, in which the entire heart is scanned in a fashion similar to that used in cardiac CT protocols (12). Other methods that have been investigated include the use of intravascular gadolinium-based agents and 3-dimensional acquisition strategies (13) (Figure 2).

Plaque Characterization

MR imaging has technical limitations that make it unsuitable for plaque volume measurements, but it has great potential for noninvasive quality assessment, using a variety of sequencing techniques (eg, T1, T2, fat saturation). In addition to being used to study atherosclerotic plaques in the human carotids and aorta (14), MR appears particularly promising for identifying vulnerable coronary plaques (15). Coronary arteries are relatively deeply located and create motion artifact, but in a study using a porcine model of CAD, MR imaging was found to sufficiently differentiate among fibrocellular, lipid-rich, and calcified coronary plaques, and its findings correlated significantly with histopathologic findings (16). For more precise quantification, contrast agents that target specific molecules (e.g., adhesion molecules) or other substances are being developed (17,18). In animal models, MR has also been a powerful tool in serially investigating in vivo the progression and regression of atherosclerotic lesions (19). Given the rapid development of this field, the ability to identify, aggressively treat, and serially monitor patients with high-risk plaques will probably improve significantly in the near future.

Conclusion

Despite existing limitations, noninvasive imaging can provide coronary anatomic information with sufficient diagnostic quality in certain segments of the population. Furthermore, various noninvasive techniques offer potential advantages over traditional invasive coronary angiography, such as characterizing coronary plaque, providing both structural and functional information about the left ventricle and heart valves, and not exposing patients to a risk of vascular injury. In the near future MDCT may be used routinely to evaluate coronary anatomy in symptomatic and high-risk asymptomatic patients as an alternative to conventional coronary angiography. On the horizon, combined CT and MR imaging may provide information not available from other imaging modalities, including lesion localization along with structural and biological plaque characterization.

Acknowledgments

We would like to thank Scott D Flamm, MD, for his thoughtful reviews of an earlier draft of this manuscript.

References

1. Schuijf JD, Bax JJ, Salm LP, Jukema JW, Lamb HJ, van der Wall EE, de Roos A. Noninvasive coronary imaging and assessment of left ventricular function using 16-slice computed tomography. *Am J Cardiol.* 2005;95:571-574.
2. Stein PD, Beemath A, Kayali F, Skaf E, Sanchez J, Olson RE. Multidetector computed tomography for the diagnosis of coronary artery disease: a systematic review. *Am J Med.* 2006;119:203-216.
3. Martuscelli E, Romagnoli A, D'Eliseo A, Razzini C, Tomassini M, Sperandio M, Simonetti G, Romeo F. Accuracy of thin-slice computed tomography in the detection of coronary stenoses. *Eur Heart J.* 2004;25:1043-1048.
4. Gibbons RJ, Eckel RH, Jacobs AK. The utilization of cardiac imaging. *Circulation.* 2006;113:1715-1716.
5. Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. *J Am Coll Cardiol.* 2005;46:807-814.
6. Schlosser T, Konorza T, Hunold P, Kuhl H, Schmermund A, Barkhausen J. Noninvasive visualization of coronary artery bypass grafts using 16-detector row computed tomography. *J Am Coll Cardiol.* 2004;44:1224-1229.
7. Romeo G, Houyel L, Angel CY, Brenot P, Riou JY, Paul JF. Coronary stenosis detection by 16-slice computed tomography in heart transplant patients: comparison with conventional angiography and impact on clinical management. *J Am Coll Cardiol.* 2005;45:1826-1831.
8. Feuchtner GM, Dichtl W, Friedrich GJ, Frick M, Alber H, Schachner T, Bonatti J, Mallouhi A, Frede T, Pachinger O, zur Nedden D, Muller S. Multislice computed tomography for detection of patients with aortic valve stenosis and quantification of severity. *J Am Coll Cardiol.* 2006;47:1410-1417.
9. White CS, Kuo D, Kelemen M, Jain V, Musk A, Zaidi E, Read K, Sliker C, Prasad R. Chest pain evaluation in the emergency department: can MDCT provide a comprehensive evaluation? *AJR Am J Roentgenol.* 2005;185:533-540.
10. Achenbach S, Moselewski F, Ropers D, Ferencik M, Hoffmann U, MacNeill B, Pohle K, Baum U, Anders K, Jang IK, Daniel WG, Brady TJ. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: a segment-based comparison with intravascular ultrasound. *Circulation.* 2004;109:14-17.
11. Plein S, Ridgway JP, Jones TR, Bloomer TN, Sivananthan MU. Coronary artery disease: assessment with a comprehensive MR imaging protocol--initial results. *Radiology.* 2002;225:300-307.
12. Sakuma H, Ichikawa Y, Suzawa N, Hirano T, Makino K, Koyama N, Van Cauteren M, Takeda K. Assessment of coronary arteries with total study time of less than 30 minutes by using whole-heart coronary MR angiography. *Radiology.* 2005;237:316-321.
13. Larose E, Yeghiazarians Y, Libby P, Yucel EK, Aikawa M, Kacher DF, Aikawa E, Kinlay S, Schoen FJ, Selwyn AP, Ganz P. Characterization of human

atherosclerotic plaques by intravascular magnetic resonance imaging. *Circulation.* 2005;112:2324-2331.

14. Fayad ZA, Fuster V, Nikolaou K, Becker C. Computed tomography and magnetic resonance imaging for noninvasive coronary angiography and plaque imaging: current and potential future concepts. *Circulation.* 2002;106:2026-2034.
15. Fuster V, Kim RJ. Frontiers in cardiovascular magnetic resonance. *Circulation.* 2005;112:135-144.
16. Worthley SG, Helft G, Fuster V, Fayad ZA, Rodriguez OJ, Zaman AG, Fallon JT, Badimon JJ. Noninvasive in vivo magnetic resonance imaging of experimental coronary artery lesions in a porcine model. *Circulation.* 2000;101:2956-2961.
17. Jaffer FA, Weissleder R. Seeing within: molecular imaging of the cardiovascular system. *Circ Res.* 2004;94:433-445.
18. Sirol M, Itskovich VV, Mani V, Aguinaldo JG, Fallon JT, Misselwitz B, Weinmann HJ, Fuster V, Toussaint JF, Fayad ZA. Lipid-rich atherosclerotic plaques detected by gadofluorine-enhanced in vivo magnetic resonance imaging. *Circulation.* 2004;109:2890-2896.
19. Helft G, Worthley SG, Fuster V, Fayad ZA, Zaman AG, Corti R, Fallon JT, Badimon JJ. Progression and regression of atherosclerotic lesions: monitoring with serial noninvasive magnetic resonance imaging. *Circulation.* 2002;105:993-998.

Table 1. Computed Tomographic Angiography of the Coronary Arteries

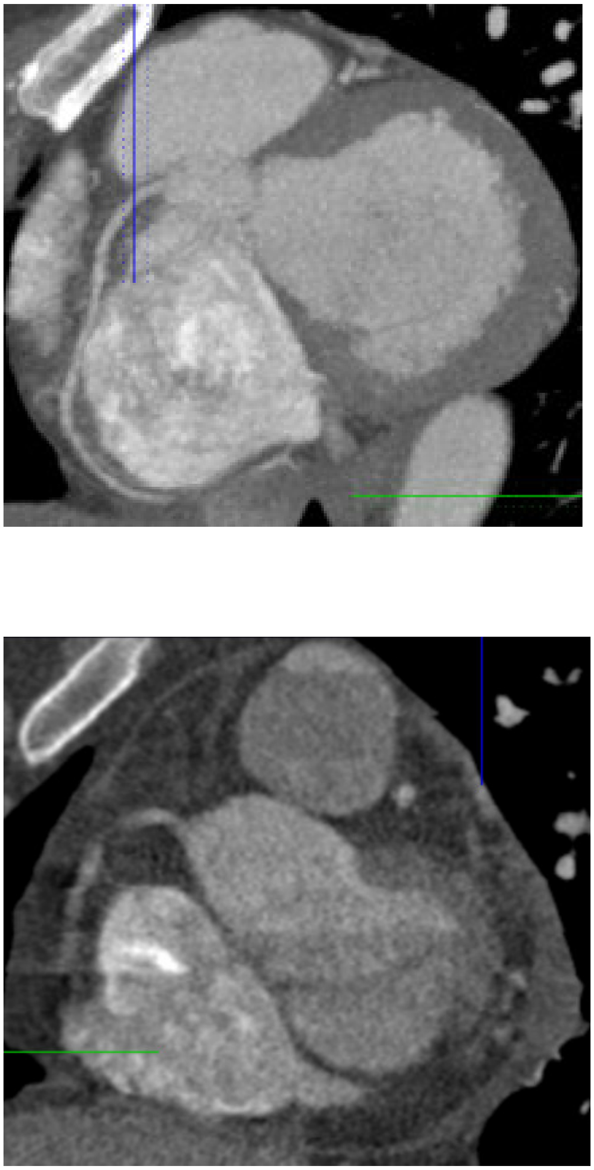
Technique	Reference	# Patients	Sensitivity	Specificity	Negative Predictive Value
16-slice MDCT (segments >2mm)	Nieman et al. Circulat. 2002;107:664	59	86%	95%	97%
	Ropers et al. Circulat. 2002;107:664	77	92%	93%	97%
	Mollet et al. JACC 2004;43:2265	128	95%	92%	98%
	Mollet et al. JACC 2005;45:128	51	98%	95%	99%
	Hoffmann et al. Circulat. 2004;110:2638	103	98%	95%	99%
16-slice MDCT (all-segment analysis)	Kuettner et al. JACC 2004;44:1230	60	97%	72%	97%
	Kuettner et al. JACC 2005;45:123	72	92%	82%	97%
	Schuijf et al. AJC 2005;95:571	45	91%	93%	98%
64-slice MDCT	Raff et al. JACC 2005;46:552	84	86%	95%	98%
	Mollet et al. Circulat. 2005;112:2318	52	95%	99%	99%
	Leber et al. JACC 2005;47:672	59	97%	80%	99%
	Leschka et al. EHJ 2005;26:1482	67	97%	94%	99%

Table 2. Magnetic Resonance Angiography of the Coronary Arteries

Technique	Reference	# Patients	Sensitivity	Specificity
2D breathhold	Manning et al. NEJM 1993;328:828	39	90%	92%
	Pennell et al. Heart 1993;70:315	30	85%	NA
	Post et al. EHJ 1997;18:426	35	35%	63%
3D navigator, retrospective-gating	Woodard et al. AJR 1998;170:883	10	70%	NA
	Kessler et al. Radiology 1992;210:566	73	65%	88%
	Sandstede et al. AJR 1999;172:135	30	81%	89%
	Sardanelli et al. Radiology 2000;214:808	42	82%	89%
3D navigator, prospective-gating	Weber et al. Eur Radiol 2002;12:718	15	88%	94%
3D breathhold and/or contrast-enhanced	Regenfus et al. AJC 2002;90:725	50	94%	57%
	Van Guens et al. Radiology 2002;217:270	38	68%	97%

Figure Legends

Figure 1. 64-slice MDCT Images: normal patient with heart rate of 52 bpm (A), heart rate of 70 bpm (B), and obese patient with body mass index of 36 (C). *Courtesy of Tuan D Nguyen, MD*



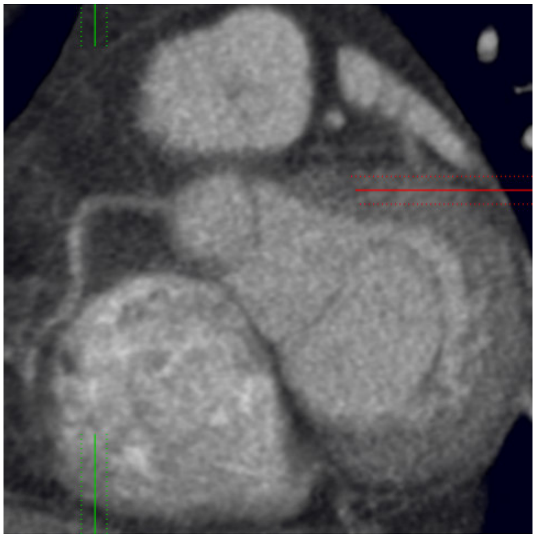


Figure 2. 3D Breathhold and Contrast-enhanced MR Angiogram Images