Assessment of Coronary Stenosis Severity and Plaque Characterization with Multislice CT Angiography

By David Kandzari, M.D.

Each year in the U.S., approximately one million individuals experience a myocardial infarction, contributing to over 300,000 cardiovascular-related deaths. In more than half of these fatal events, myocardial infarction and sudden cardiac death will be the first and only presenting symptom of coronary artery disease. Considering that the common denominator for nearly all adverse cardiovascular events is coronary artery disease, the need for early identification and intervention of vulnerable coronary plaques is paramount. Against a background of increasing prevalence of coronary artery disease, the practice of clinical cardiovascular medicine has rapidly evolved into a field characterized by dramatic advances in our understanding of the pathophysiology, therapeutic applications, and likely clinical outcomes for patients considered at high risk for initial or subsequent adverse events that include infarction and cardiovascular death. Recent discoveries have identified systemic inflammation and biomarkers predictive of future adverse events.1,2 To evaluate the presence of significant (>50% luminal obstruction) coronary artery disease, the clinical practitioner must determine which coronary segments without prior angiographic evidence of significant occlusive disease.1-3 In many instances, imaging modalities intended to characterize atherosclerotic disease and vessel wall anatomy require invasive measures, including cardiac catheterization and conventional angiography. More than 1.4 million invasive coronary angiographic procedures are performed annually in the U.S. to evaluate the presence of significant (>50% luminal obstruction) coronary artery disease. To identify “vulnerable” or unstable atherosclerotic plaque activity.4-6 The need to identify lesions prone to rupture and clinical sequelae is particularly urgent given that in most instances, atherosclerotic plaque rupture and thrombosis leading to myocardial infarction occurs in a vulnerable or unstable plaque type.4-6

The year 2005 marked a significant milestone in our understanding of the clinical impact of coronary plaque characterization. According to the American Heart Association (AHA) and the American College of Cardiology (ACC), vascular imaging can provide critical data to identify “vulnerable” or unstable coronary plaques and help stratify patients at higher risk in the setting of preprocedure multislice computed tomography (MSCT) coronary angiography.5-7 In contrast to invasive measurements, MSCT coronary angiography offers a noninvasive alternative to identify areas of high-risk coronary plaque.5-7 In addition to disease screening and prevention, ongoing studies will likely further define the role of MSCT coronary angiography in clinical decision-making. In the Comparison of Noninvasive CT Angiography for Epicardial Coronary Imaging with Catheter-based Angiography (CINEMA) trial comparing MSCT with conventional coronary angiography, the ability to make decisions regarding revascularization and medical therapy following blinded review of both CT and catheterization studies will be independently evaluated. Multislice coronary imaging may also assist in determining the method of revascularization and help predict procedural success.8 Further, ongoing studies evaluating the combination of MSCT coronary angiography with PET imaging for myocardial ischemia may prove to be the most complete assessment of both coronary anatomy and coronary functional significance (Figure 1). While unresolved issues mandate further clinical trials to refine the place of MSCT coronary angiography in routine clinical practice, clinicians can apply the presently available evidence on MSCT imaging not only to enable easier noninvasive identification of ath erosclerotic disease but also to provide treatment to patients at risk for vascular events.

Assessment of Coronary Stenosis Severity and Plaque Characterization with Multislice CT Angiography

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

• Explain the diagnostic accuracy of MSCT coronary angiography for the detection of significant coronary artery disease compared with conventional coronary angiography.

• List the limitations of current MSCT coronary angiography for disease screening.

• Discuss the ability of MSCT coronary imaging to assess the components of coronary atherosclerotic plaque.

• Describe ongoing and forthcoming trials with MSCT imaging to refine its role in the detection of coronary stenoses and plaque characterization.

For questions about this CME activity, please contact: onlinemcme@CME.com

OBJECTIVES


whether coronary revascularization is indicated. Aside from its expense, as an invasive procedure coronary angiography is associated with a mortality rate of 0.07%, 78% of which are due to complications, or cardiac arrest (sudden death).

Figure 2. MSCT coronary angiography of a right dominant coronary artery located in the proximal right coronary artery in longitudinal and cross-sectional views. Attenuation of 20 to 30 HU is consistent with hard-risk plaque.

held constant, athero-

angiography. The purpose of this review is to examine the results of recent trials with coronary CT angiography designed to characterize coronary atherosclerotic plaque and disease severity and present future directions for clinical investigation.

PATHOPHYSIOLOGY OF UNSTABLE Atherosclerotic PLAQUE

Although investiga-
tions to characterize and predict vulnerable, stable, atherosclerotic plaque activity are ongoing, a common histologic feature is a thin fibrous cap overlying a lipid-rich core and a dense inflammatory cell infiltrate. In many instances, deep ulceration may not be apparent on catheter-based angiography, and lesions underlying thrombus may be stenotic or nonstenotic, although nonstenotic lesions are much more common and are more frequently identified in culprit ruptured lesions. Accumulation of lipid-laden macrophages (“foam cells”), lymphocytes, matrix metalloproteinases, oxygen radicals, and even erythrocyte membranes contribute to the eventual destabilization and fissuring of the plaque, leading to thrombosis deposition and platelet aggregation. Plaque rupture is the most common type of atherosclerotic plaque complication, responsible for approximately 70% of cardiovascular infarctions and sudden cardiac deaths. However, the subsequent clinical presentation is ultimately determined by whether the thrombotic mass is occlusive, partially occlusive, or nonobstructive, and is influenced by collateral flow, baseline left ventricular function, the amount of jeopardized myocardiun, and other factors. As a result, patients may experience severe angina and electrocardiographic ST-segment elevation, non-ST-elevated myocardial infarction, or unstable angina without elevated cardiac markers.

Coronary calcification is also a common finding with atherosclerosis and may reflect total plaque burden. While the extent of calcification determined by the calcium score may predict future cardiovascular events, 22 distribution of calcification is often heterogeneous, and it is not possible to noninvasively assess coronary atherosclerotic burden, differentiate calcified from noncalcified (“soft”) plaques, and quantify disease progression is essential to the development of novel technologies for coronary artery imaging.

COMPARATIVE TRIALS

Faster gantry speeds, multislice acquisi-
tion scanners, and enhanced image recon-
struction techniques have improved the spatial and temporal resolution of noninvasive coronary an-

Figure 3. Scintillation MSCT coronary angiography and PET imaging for myocardial ischemia. MSCT identifies a stress-induced hypoperfusion of the left anterior descending artery (bottom left), while PET (bottom right) identifies a redistribution of 18F-FDG (bottom right). PET imaging further confirmed the functional significance of the stenosis, revealing atherosclerotic-induced ischemic (bottom left) and stable (bottom right) segments (Provided by Dr. Salvador Bogaert, Department of Cardiology)
whether coronary revascularization is indicated. Aside from its expense, as an invasive procedure coronary angiography is associated with a mortality of 0.1% and 0.28% for bleeding complications, or cardiac arrest (7rhythms) rate that may be as high as 2% to 3% and with a mortality rate of 0.4%. Accordingly, an accurate, noninvasive assessment of coronary artery plaque composition and stenosis severity would constitute an important advancement in the care of patients with known or suspected coronary artery disease.

Over the past five years, the introduction of contrast-enhanced coronary computed tomography (CT) angiography has represented a revolutionary advancement from conventional electron-beam technology, enabling high spatial and temporal resolution and coordination of gated cardiac imaging with the electrocardiogram and cardiac cycle. In many instances, the sensitivity and specificity of MSCT angiography to visualize significant coronary artery lesions may be comparable to cardiac catheterization (Figure 1). However, in some cases, pliable noninvasive coronary angiography, although, coronary CT angiography may not only identify luminal narrowing but also provide insight into atherosclerotic plaque composition. In many instances, CT angiography may enable the characterization of vulnerable coronary lesions even when disease is not visually apparent by conventional catheter-based angiography. The purpose of this review is to examine the results of recent trials with coronary CT angiography designed to characterize coronary atherosclerotic plaque and disease severity and present future directions for clinical investigation.

PATHOPHYSIOLOGY OF UNSTABLE ATHEROSCLEROTIC PLAQUE

Over the past five years, the introduction of contrast-enhanced coronary computed tomography angiography has represented a revolutionary advancement from conventional electron-beam technology, enabling high spatial and temporal resolution and coordination of gated cardiac imaging with the electrocardiogram and cardiac cycle. In many instances, the sensitivity and specificity of MSCT angiography to visualize significant coronary artery lesions may be comparable to cardiac catheterization (Figure 1).

The “white plaques” that present a high risk of clinical events are noncalcified and contain cholesterol, fibrous, and calcific components. The composition of the lipid, fibrous, and calcific components of coronary atherosclerotic plaque that may not be visually apparent by conventional coronary angiography. For example, MSCT may enable detection of non-significant coronary soft plaques responsible for acute myocardial infarction by providing information on plaque volume, eccentricity, and density. More complete characterization of atherosclerosis is particularly relevant since the extent of disease may be assessed by electron-beam CT can only represent one-fifth of the entire atherosclerotic plaque burden. However, trials of local treatment by means of vascular lesions may be differentiated according to the relative Hounsfield unit densities of the plaque constituents (Figure 2).

In general, systolic and diastolic blood pressure and heart rate were similar among all groups. The mean age of the 35 patients was 52 ± 11 years, and 26% of the patients were from the hospital coronary care unit. The mean angiographic calcium score was 132 ± 186, and 74% of the patients had a calcium score of 0. For the purpose of this study, as determined by the coronary stent groups, patients were divided into the following three groups: 1) non-obstructive coronary plaques defined as plaques with plaque area >50% but ≤90% of the lumen diameter; 2) plaques with plaque area ≤50% of the lumen diameter; and 3) non-calcified and calcified plaques, as defined by the presence of calcium on MSCT angiography. The mean calcium score for each group was 14 ± 18, 47 ± 24, and 85 ± 51, respectively. The sensitivity and specificity of MSCT to identify stent restenosis was 78% and 86%, respectively. Small stents and stents with lesions covered by the most common reasons for the inability to assess coronary stent segments.

TABLE 1. COMPARATIVE TRIALS OF 16-SLICE MSCT AND CONVENTIONAL CORONARY ANGIOGRAPHY

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of patients</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Negative predictive value</th>
<th>Positive predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nieni et al, Circulation 2002</td>
<td>59</td>
<td>95</td>
<td>86</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Mollet et al, JACC 2004</td>
<td>128</td>
<td>92</td>
<td>95</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Mollet et al, JACC 2005</td>
<td>51</td>
<td>95</td>
<td>92</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Martuscelli et al, ENI JACC 2004</td>
<td>64</td>
<td>89</td>
<td>98</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Rogers et al, Circulation 2004</td>
<td>77</td>
<td>92</td>
<td>93</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Krueter et al, Circulation 2005</td>
<td>72</td>
<td>97</td>
<td>98</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Krueter et al, JACC 2004</td>
<td>66</td>
<td>97</td>
<td>99</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Krueter et al, JACC 2004</td>
<td>60</td>
<td>72</td>
<td>97</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>Hoffmann et al, Circulation 2004</td>
<td>33</td>
<td>63</td>
<td>96</td>
<td>97</td>
<td></td>
</tr>
</tbody>
</table>
ASSESSMENT OF CORONARY STENOSIS SEVERITY AND PLAQUE CHARACTERIZATION WITH MULTISLICE CT ANGIOGRAPHY

FUTURE DIRECTIONS

In part due to marked heterogeneity in atherosclerotic plaque composition, the development of a noninvasive method that can reliably image coronary stenosis severity, assist disease burden, and characterize plaque composition represents an important advance in our understanding of vascular disease and risk stratification. Although further study is required to evaluate the prognostic impact of density-based characterization of coronary atherosclerosis, advances in CT technology and reconstruction algorithms have positioned MSCT angiography as the most promising noninvasive method for the assessment of significant coronary atherosclerosis. Combined with the enhanced spatial and temporal resolution achieved with newer generation 64-detector row scanners, novel software algorithms may not only enable more accurate assessment of lesion composition but also permit earlier treatment with preventive therapies and assess their effect on disease progression or regression.

In addition to disease screening and prevention, ongoing studies will likely further define the role of MSCT coronary angiography in clinical decision-making. In the Comparison of Noninvasive CT Angiography for Epicardial Coronary Imaging with Catheter-based Angiography (CINEMA) trial comparing MSCT with conventional coronary angiography, the ability to make decisions regarding revascularization and medical therapy following blinded review of both CT and catheterization studies will be independently evaluated. MSCT coronary imaging may also assist in determining the method of revascularization and help predict procedural success. Further, ongoing studies evaluating the combination of MSCT coronary angiography with PET imaging for myocardial ischemia may prove to be the most complete means of assessment of both coronary anatomy and coronary functional significance (Figure 3). While unresolved issues mandate further clinical trials to refine the place of MSCT coronary imaging in routine clinical practice, clinicians can apply the presently available evidence on MSCT imaging not only to enable earlier noninvasive identification of ath erosclerotic disease but also to provide treatment to patients at risk for vascular events.