Multimodality Imaging of Anatomy and Function in Coronary Artery Disease

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Chapter 15

Changing Paradigm: Atherosclerosis versus Ischemia

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Editorial in response to the article:
"64-slice spiral CT angiography does not predict the hemodynamical relevance of coronary artery stenoses in patients with stable angina."
by Hacker M. et al

Eur J Nucl Med Mol Imaging 2007; 34: 1-3

Traditionally, imaging is used for the non-invasive detection of coronary artery disease (CAD) in patients with an intermediate likelihood of disease [1]. Various imaging modalities are currently available for this purpose, including nuclear imaging with PET and SPECT, echocardiography and magnetic resonance imaging [1]. These tests rely on the demonstration of stress-inducible ischemia, evidenced by the induction of perfusion abnormalities or systolic dysfunction, as a surrogate marker for CAD. Based on the location, extent and severity of ischemia, patients may be referred for invasive coronary angiography followed by interventional therapy [2].

Recently, this algorithm has been challenged by the introduction of non-invasive anatomical imaging (i.e. non-invasive coronary angiography), using multi-slice computed tomography (MSCT). Thus far MSCT has only been validated against the anatomical gold standard for CAD, being invasive coronary angiography, and in selected patient populations the technique has been demonstrated to provide reliable detection of significant coronary artery stenoses [3-5]. The most important contribution of MSCT however, is the exclusion of CAD, since the likelihood of CAD is virtually nihil in the presence of a normal MSCT examination.

Substantial data on the performance of MSCT in relation to other imaging techniques (e.g. SPECT) however, are currently not available. In this issue of the *Journal*, Hacker and colleagues report their results of a direct comparison between 64-slice MSCT and gated SPECT imaging in 38 (74% male) patients presenting with stable angina [6]. CAD was suspected in 26 (68%), whereas 12 patients presented with a previous history of CAD (7 previous coronary artery bypass surgery, 8 previous percutaneous coronary intervention). Coronary arteries on MSCT were evaluated for the presence of significant (≥ 50% luminal diameter narrowing) stenoses and results were compared to myocardial perfusion assessed with SPECT. In total, 152 coronary arteries were evaluated, with 43 (28%) showing at least 1 significant stenosis.

Only 7 of 109 coronary arteries without significant stenoses on MSCT were associated with abnormal myocardial perfusion on SPECT, resulting in a negative predictive value of 94%. Thus, in the absence of significant lesions on MSCT, perfusion will be normal. These findings indicate that MSCT may allow accurate exclusion of flow-limiting coronary stenoses.

Conversely, abnormal perfusion on SPECT (including both fixed and reversible defects) was noted in only 23 of 43 (53%) of coronary arteries with significant lesions on MSCT. Moreover, only 12 of 38 coronary arteries with significant CAD revealed ischemia (reversible perfusion abnormalities) on SPECT. As a consequence, the corresponding positive predictive value of MSCT to detect hemodynamically relevant stenoses was only 32%.

Similar observations have been reported by the same authors when 16-slice MSCT was compared to SPECT imaging [7]. Data obtained in 99 coronary arteries of 25 patients with known (n=14) or suspected CAD (n=11) revealed that all 82 coronary arteries without significant (≥ 50% diameter narrowing) lesions were associated with normal perfusion on SPECT, yielding a negative predictive value of 100%. On the other hand, a positive MSCT was not consistently associated with abnormal perfusion and only 8 of 17 (47%) stenotic coronary arteries on MSCT were associated with abnormal perfusion on SPECT.

Thus, only half of the significant lesions on MSCT appear to have hemodynamical consequences, indicating that the presence of coronary atherosclerosis with luminal obstruction does not invariably imply the presence of ischemia. Accordingly, a non-invasive angiographic imaging technique such as MSCT cannot be used to predict the hemodynamical importance of observed lesions.

This discrepancy between anatomical and functional imaging was noted already in direct comparisons between invasive angiography and myocardial perfusion imaging. Particularly, lesions with an intermediate stenosis severity (40% to 70% luminal narrowing) have been demonstrated to show a wide variation in hemodynamic relevance [8]. For example, Heller et al [8] demonstrated that only 48% of 67 intermediate lesions on invasive angiography (with on average 59±12% luminal narrowing) were associated with ischemia on myocardial perfusion imaging. An even lower percentage was reported by Chamuleau et al, who performed SPECT and invasive coronary angiography in 191 patients with at least 1 severe (>70% diameter narrowing) and 1 intermediate (defined as between 40% to 70% diameter narrowing) lesion on invasive angiography [9]. In particular, 153 (80%) patients showed ischemia on SPECT in the vascular territory corresponding to the severe lesion, but only 30 (16%) patients exhibited ischemia in the territory of the intermediate lesion. These observations underscore that anatomical imaging does not provide information on the hemodynamic consequences of the lesions, and functional testing remains required to provide this information.

Consequently, the question that emerges is: "What are the implications of these observations for the clinical use of MSCT in addition to SPECT?"

In fact, the combined use of anatomic and functional imaging may actually be preferred since this combination may allow better characterization of patients. In subjects with a normal SPECT, MSCT coronary angiography allows further differentiation into patients with atherosclerosis (but non-obstructive lesions, not resulting in ischemia), and patients with completely normal coronary arteries. This differentiation permits to identify CAD at an earlier stage, i.e. atherosclerosis present, but no ischemia yet. Accordingly, the availability of non-invasive visualization of the coronary arteries has resulted in a paradigm shift: the hallmark of CAD on non-invasive imaging is shifting from demonstration of ischemia to assessment of atherosclerosis.

In this respect, sequential use of MSCT and SPECT may provide a useful approach to patients presenting with an intermediate likelihood of CAD. As depicted in Figure 1, anatomic imaging with MSCT could be the initial test.

If the coronary arteries reveal no abnormalities on MSCT, the patient may be safely discharged without the need for further testing. The reliable exclusion of significant CAD by MSCT is supported by the extensive literature validating the technique against invasive coronary angiography [10] consistently showing that if the MSCT examination is normal, the likelihood of finding significant CAD on invasive coronary angiography is negligible.

Next, in the presence of atherosclerosis without significant lesions (<50% diameter narrowing), the likelihood of ischemia is low as demonstrated in the current study [6]. These patients need aggressive risk factor modification and medical therapy.

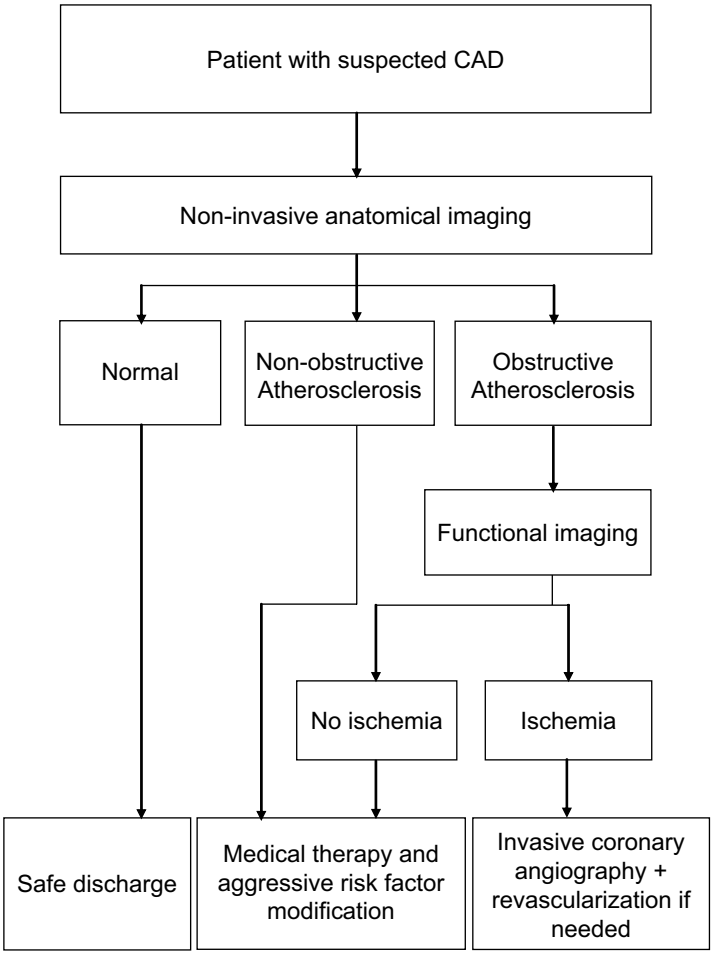

Figure 1. Potential algorithm for diagnostic imaging in patients with suspected CAD.

Finally, if obstructive lesions are demonstrated on MSCT, subsequent functional testing is needed to determine the presence and extent of ischemia, on which the decision for referral to invasive coronary angiography and possible revascularization is based.

Thus, rather than competing, MSCT and SPECT appear to be complementary techniques which each its valuable position in the diagnostic work-up of patients with suspected CAD. Still, before adopting these algorithms in clinical practice, more studies are needed, particularly focusing on long-term prognosis.

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