Anatomical and functional imaging techniques: basically similar or fundamentally different?

J.D. Schuijf, J.J. Bax, E.E. van der Wall

Accurate and early detection of coronary artery disease (CAD) is essential, as the disease remains one of the leading causes of death in the industrialised world. For this purpose, several invasive as well as non-invasive modalities are available. The current gold standard to detect significant narrowing of the coronary arteries is invasive coronary angiography, which allows direct visualisation of the coronary arteries with high spatial and temporal resolution. In addition, if abnormalities are demonstrated, direct intervention is possible. However, it is also an invasive technique that is associated with substantial patient discomfort, costs and a small but distinct risk of potentially life-threatening complications.

Accordingly, only patients with a high-pretest likelihood of having CAD are directly referred for this procedure. In patients with a lower pretest likelihood, initial noninvasive testing is preferred. For this purpose, myocardial perfusion imaging by single-photon emission computed tomography (SPECT) is most frequently used, while more recently also stress echocardiography and magnetic resonance imaging have become available.¹ These techniques have in common that they detect the presence of ischaemia through induction of either perfusion or wall motion abnormalities during stress conditions. As a result, the presence and extent of ischaemia has long served as the basis for referral to invasive coronary angiography.

However, this paradigm has become challenged by the introduction of noninvasive coronary angiography

by means of multislice computed tomography (MSCT). The technique, which has witnessed an enormously rapid development, allows direct visualisation of both obstructive and nonobstructive coronary artery stenoses with excellent diagnostic accuracy.

Pooled analysis of 11 studies in 663 patients utilising 64-slice MSCT showed an average weighted sensitivity and specificity of 91 and 96%, respectively for the detection of lesions with $\geq 50\%$ luminal narrowing as determined on invasive coronary angiography.²⁻¹² The corresponding negative predictive value is particularly high (99%), and the likelihood of CAD is extremely low in a patient with normal coronary arteries on MSCT. Accordingly, the technique appears to be extremely suited to rule out CAD.

However, management in patients with an abnormal MSCT examination may be less straightforward. Since no direct information on the haemodynamic relevance of the observed lesions is obtained, the potential benefit of either revascularisation or medical therapy remains undetermined. In order to design evaluation algorithms that allow optimal integration of MSCT, investigations comparing MSCT with other noninvasive *functional* modalities are mandatory.

An initial comparison was published by Hacker and colleagues, who evaluated 38 patients (74% male) with both 64-slice MSCT coronary angiography and SPECT imaging.¹³ An excellent agreement was observed between a negative MSCT coronary angiogram and myocardial perfusion, with 102 of 109 (94%) coronary arteries without significant obstructions also having a normal SPECT study. On the other hand, only 23 of 43 (53%) significantly diseased coronary arteries resulted in haemodynamic consequences, as reflected by abnormal SPECT, suggesting a large discrepancy between these techniques. An important limitation of this study, besides the small number of patients included, was the fact that patients with suspected CAD as well as patients with a previous history of myocardial infarction and/or revascularisation were included.

Recently, results have been published on a larger prospective investigation, specifically addressing the

J.D. Schuijf

Department of Cardiology, Leiden University Medical Centre, Leiden, the Netherlands, the Netherlands Heart Foundation (grant number 2002B105), The Hague, the Netherlands and the Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands

J.J. Bax

E.E. van der Wall

Leiden University Medical Centre, Leiden, the Netherlands

Correspondence to: J.D. Schuijf
Department of Cardiology, Leiden University Medical Centre,
PO Box 9600, 2300 RC Leiden, the Netherlands
E-mail j.d.schuijf@lumc.nl

potential target population of MSCT, namely patients with an intermediate pretest likelihood.¹⁴ MSCT coronary angiograms of 114 patients (56% male, average age 60 ± 11 years) without previous history of CAD were evaluated for the presence of no CAD, non-obstructive CAD or obstructive CAD (defined as at least one significant stenosis of $\geq 50\%$ luminal narrowing). In addition, all patients underwent stress-rest gated SPECT to evaluate the presence of either reversible or irreversible defects. The majority of patients without evidence of CAD also showed normal myocardial perfusion, 37 of 41 (90%). However, in line with the study by Hacker et al., only a modest relation was noted between abnormal SPECT and abnormal MSCT studies. Only 45% of patients with atherosclerosis showed abnormal perfusion; considering only patients with at least one significant stenosis, this percentage was still only 50%. Accordingly, a substantial portion of the detected lesions on MSCT appear to have no haemodynamic consequences, indicating the need for further evaluation by means of functional imaging in patients with significant CAD on MSCT.

On the other hand, these observations also imply that in patients with a normal SPECT, MSCT may allow distinction between patients who have absolutely no CAD and patients with (considerable) atherosclerosis. This differentiation may allow identification of CAD at a much earlier stage, namely while atherosclerotic changes are present but as yet without haemodynamic consequences. Although these patients do not require immediate revascularisation, they might represent patients with an elevated long-term risk and probably warrant more aggressive medical therapy as well as closer monitoring as compared with those individuals with completely normal coronary arteries. Another advantage is the fact that MSCT, in contrast to functional imaging, is unlikely to miss severe, high-risk CAD, such as left main disease or three-vessel disease.

Thus, it is important to recognise that MSCT coronary angiography and functional imaging provide fundamentally different information and may be considered complementary rather than interchangeable. In contrast, integrated use of anatomical and functional imaging may in fact offer a promising opportunity to further optimise diagnosis and selection of therapy in patients with suspected CAD. Although hybrid or dual modality imaging techniques are under investigation for this purpose with encouraging results, sequential imaging strategies may be more practical and cost-effective.

In patients with low-to-intermediate likelihood of CAD, a first step could be to evaluate the presence of atherosclerosis with MSCT. If coronary atherosclerosis is shown to be absent, the patient may be discharged without the need for further testing. However, if considerable atherosclerosis is demonstrated, additional functional assessment is required to evaluate the presence and extent of ischaemia. Based on these ob-

servations one may decide between invasive coronary angiography (and possibly intervention) and medical therapy in combination with aggressive risk profile modification.

Potentially, the combination of both anatomical and functional information may allow superior evaluation of CAD, resulting in more individually targeted management as well as improved outcome. Still, data supporting such algorithms are currently lacking, and prospective studies addressing the accuracy, safety and cost-effectiveness of integrated imaging strategies in larger cohorts are required. ■

References

- Schuijff JD, Shaw LJ, Wijns W, Lamb HJ, Poldermans D, de Roos A, et al. Cardiac imaging in coronary artery disease: differing modalities. *Heart* 2005;91:1110-7.
- Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *J Am Coll Cardiol* 2005;46:552-7.
- Pugliese F, Mollet NR, Runza G, van Mieghem C, Meijboom WB, Malagutti P, et al. Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. *Eur Radiol* 2006;16:575-82.
- Ehara M, Surmely JF, Kawai M, Katoh O, Matsubara T, Terashima 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. *Circulation* 2006;70:564-71.
- Fine JJ, Hopkins CB, Ruff N, Newton FC. Comparison of accuracy of 64-slice cardiovascular computed tomography with coronary angiography in patients with suspected coronary artery disease. *Am J Cardiol* 2006;97:173-4.
- Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005;46:147-54.
- Leschka S, Alkadhi H, Plass A, Desbiolles L, Grunfelder J, Marincek B, et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. *Eur Heart J* 2005;26:1482-7.
- Malagutti P, Nieman K, Meijboom WB, van Mieghem CA, Pugliese F, Cademartiri F, et al. Use of 64-slice CT in symptomatic patients after coronary bypass surgery: evaluation of grafts and coronary arteries. *Eur Heart J* 2006 (Epub ahead of print).
- Mollet NR, Cademartiri F, van Mieghem CA, Runza G, McFadden EP, Baks T, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. *Circulation* 2005;112:2318-23.
- Plass A, Grunfelder J, Leschka S, Alkadhi H, Eberli FR, Wildermuth S, et al. Coronary artery imaging with 64-slice computed tomography from cardiac surgical perspective. *Eur J Cardiothorac Surg* 2006;30:109-16.
- Ropers D, Rixe J, Anders K, Kuttner A, Baum U, Bautz W, et al. Usefulness of multidetector row spiral computed tomography with 64- x 0.6-mm collimation and 330-ms rotation for the non-invasive detection of significant coronary artery stenoses. *Am J Cardiol* 2006;97:343-8.
- Schuijff JD, Pundziute G, Jukema JW, Lamb HJ, van der Hoeven BL, de Roos A, 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.
- Hacker M, Jakobs T, Hack N, Nikolaou K, Becker C, von Ziegler F, 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.
- Schuijff JD, Wijns W, Jukema JW, Atsma DE, Lamb HJ, Stokkel MP, et al. Relationship between non-invasive coronary angiography with multi-slice computed tomography and myocardial perfusion imaging. *J Am Coll Cardiol* 2006;48:2508-14.