Multislice computed tomography coronary angiography for triaging patients with positive radionuclide myocardial perfusion imaging

Sir,

Myocardial perfusion imaging using single-photon emission computed tomography (SPECT) is the most commonly applied diagnostic imaging modality in patients with suspected coronary artery disease in the US, with more than 9 million procedures performed annually.1 The positive predictive value of SPECT is limited, and in a considerable number of patients with suspected perfusion deficits conventional coronary angiography shows no significant coronary stenoses. Multislice computed tomography (MSCT) coronary angiography allows the non-invasive assessment of coronary artery stenoses, and has a high negative predictive value.2–4 Thus, MSCT might be applied as a secondary gate-keeper in patients with positive SPECT, prior to deciding whether to perform conventional coronary angiography in these patients.

We aimed to investigate the role of MSCT (Aquilion, Toshiba), using 16 simultaneous detector rows (according to a previously described protocol)3 to triage 38 patients (63±8 years) with positive SPECT myocardial perfusion imaging (99mTc, n=24; 201TI, n=14; both rest and stress) who were scheduled for conventional coronary angiography. Patients with an equivocal SPECT examination (e.g. examinations in which neither the target heart rate nor a perfusion deficit was achieved) were not included in the study, and SPECT was considered positive when at least either the rest or the stress examination showed a significant perfusion deficit in any myocardial area. Readers of the three tests were blinded against the results of the other tests. The 17 myocardial segments/areas on SPECT were assigned to one of the three coronary arteries seen on MSCT, with post-hoc adjustment for the coronary artery distribution type as defined by conventional coronary angiography according to the detailed recommendations in the American Heart Association segmentation scheme publication.5 The study was approved by the institutional review board, and all patients gave written informed consent. A contingency analysis with a χ2 or Fisher’s exact test was used to compare the per-patient positive predictive value and per-artery/territory diagnostic performance of SPECT and MSCT with conventional coronary angiography as the reference standard.

Twenty-one of the 38 patients (55%, Figure 1) with a positive SPECT result showed significant coronary artery disease (at least 50% diameter stenosis on the worst view) on quantitative analysis of conventional coronary angiography. MSCT correctly identified 90% (19/21) of the patients with coronary disease, while the positive predictive value was significantly superior to that of SPECT: 95% (19/20) vs. 55% (21/38), p<0.002. The triage of patients with positive SPECT was significantly influenced by using MSCT, which would have avoided 15 of 17 unnecessary conventional coronary angiographies (specificity 88%, 15/17) (Figure 1). One of the false-negative patients with MSCT did not undergo revascularization because this patient had single-vessel disease with a 50% stenosis of the right coronary artery, which was considered not to require revascularization. One patient who had no significant disease on conventional coronary angiography was nondiagnostic on MSCT because of a singular motion artifact in the right coronary artery.

In the per-coronary artery analysis, MSCT also had significantly higher diagnostic accuracy (85% [97/114] vs. 66% [75/114], p<0.001), specificity (90% [62/69] vs. 62% [43/69], p<0.001), and positive and negative predictive values (92% [35/38] vs. 55% [32/58], p<0.001 and 91% [62/68] vs. 77% [43/56], p<0.05, respectively) than SPECT. Of the 45 significant stenoses on conventional coronary angiography, 13 were not correctly detected using SPECT. The mean percentage diameter stenosis of these 13 false-negative lesions was 87±7% (range: 72–100%), and 11 (85%) of these required subsequent revascularization with coronary artery bypass surgery (n=7) or stent placement (n=4), indicating that these lesions missed by SPECT were considered clinically relevant. None of the 26 false-positive myocardial territories on SPECT showed borderline or significant stenoses of the respective territory.

<table>
<thead>
<tr>
<th>Positive SPECT</th>
<th>MSCT</th>
<th>Nondiagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=38</td>
<td>n=38</td>
<td>n=1</td>
</tr>
<tr>
<td>Positive, n=20</td>
<td></td>
<td>True positive, n=19, False positive, n=1</td>
</tr>
<tr>
<td>Negative, n=17</td>
<td></td>
<td>True negative, n=15, False negative, n=2</td>
</tr>
</tbody>
</table>

Figure 1. Possible clinical triage of patients with positive SPECT using MSCT.
arteries (mean percentage diameter stenosis of the corresponding arteries 2 ± 7%, range 0–30%), and none was revascularized, indicating that these lesions were truly false-positive on SPECT myocardial perfusion imaging.

In a recent report comparing SPECT myocardial perfusion imaging and coronary artery imaging using MSCT, the positive predictive value of significant coronary stenoses to detect reversible myocardial ischaemia with MSCT was 29%, but no conventional coronary angiography was performed in this retrospective study.6 Hacker et al. have recently added a comparison of MSCT with a combined reference standard of SPECT and conventional coronary angiography, and have suggested that MSCT fails to predict the functional relevance of lesions.7 However, all patients who were classified as false-positive on CT (7 patients) were considered ‘false’ because of no perfusion deficit on SPECT, but all had significant stenoses on conventional coronary angiography (personal communication with the authors). Another recent study has shown that MSCT is at least as accurate as SPECT for the prediction of an acute coronary syndrome or cardiac event in patients with low-risk chest pain.8 In contrast, patients included in the present study had a higher likelihood of disease and a positive SPECT test. In this group of patients, MSCT coronary angiography might identify those patients who are false-positive on SPECT.

Integrated PET/CT imaging has recently been suggested as an alternative in decision making in patients with known coronary artery disease,9 but was not analysed in the present study. Rather, we analyzed the potential role of MSCT in triaging patients with positive myocardial perfusion imaging, and used a strict approach to assign myocardial territories to coronary segments as described.5 Referral bias might have influenced our results and led to a low specificity of SPECT, especially since patients with a higher likelihood of disease and a positive SPECT might have been referred for conventional coronary angiography.

A recent expert panel report suggested that MSCT coronary angiography might gain a role in patients with unequivocal stress test response, but found no sufficient grounds to support the indication in patients with evidence of moderate to severe ischaemia.10 Our present study is, to our best knowledge, the first to examine the potential clinical usefulness of MSCT in this indication. We found that the application of MSCT in patients with positive SPECT could have had an important impact on the potential triage of these patients, because of a high false-positive rate in radionuclide imaging, and might have led to significant avoidance of unnecessary conventional coronary angiographies (Figure 1). This highlights a further important clinical indication for CT coronary angiography, which could also help to significantly reduce healthcare costs.11

M. Dewey
B. Hamm
Department of Radiology

H-P. Dübèl
W. Rutsch
Department of Cardiology
Charité Medical School
Humboldt University and Free University
Berlin
Germany
email: marc.dewey@charite.de

References


8. Gallagher MJ, Ross MA, Raff GL, et al. The Diagnostic Accuracy of 64-Slice Computed Tomography Coronary Angiography Compared With Stress Nuclear Imaging in
Antibiotic hypersensitivity mimicking recurrent endocarditis—identifying the culprit with the in vitro lymphocyte transformation test

Sir,

The drug hypersensitivity syndrome is characterized by fever and systemic abnormalities including lymphopenia, lymphadenopathy, skin and visceral involvement mimicking systemic sepsis. The following case illustrates how the in vitro lymphocyte transformation test can be used to confirm drug hypersensitivity in this scenario, differentiating it from deteriorating infective endocarditis, hence avoiding progression to inappropriate interventions.

A 62-year-old man was admitted as a result of his cardiac resynchronization pacemaker generator eroding through the skin. On admission he was systemically well, and blood cultures were sterile; treatment with intravenous flucloxacillin 1 g qds was commenced empirically. A transoesophageal echocardiogram showed two vegetations; on the tricuspid valve and the right ventricular pacing lead. The pacemaker was extracted and culture of the leads grew Staphylococcus aureus. Intravenous flucloxacillin was changed to gentamycin 80 mg and intravenous teicoplanin 400 mg once daily. Ten days later, the patient became systemically unwell with pyrexia; the C-reactive protein became raised together with lymphopenia and mild eosinophilia. There was concern that endocarditis had recurred despite appropriate antibiotics and sterile blood cultures. However, the alternative diagnosis of teicoplanin hypersensitivity was also considered; teicoplanin was changed to vancomycin, and the patient monitored closely. Within twenty-four hours, he felt better and the fever settled. A repeat transoesophageal echocardiogram showed no evidence of new infection. No further episodes of fever occurred following discontinuation of teicoplanin. A cardiac resynchronization pacemaker with defibrillator back up was implanted. Twelve months later the patients remains well.

The presence of hypersensitivity to teicoplanin was investigated. Epicutaneous patch tests with teicoplanin were negative, probably because teicoplanin (a complex mix of six compounds with molecular weights between 1584 and 1894 kDa) is too big to pass through the epidermal barrier. However, peripheral blood mononuclear cells (centrifuged isolated lymphocytes and monocytes) cultured with various concentrations of teicoplanin (0–1000 μM) for 6 days, showed significant dose-related lymphocyte proliferation. Proliferation was quantified by measurement of [3H]-thymidine incorporation, and expressed as the stimulation index (SI = counts per minute in presence of drug—c.p.m. in drug-free control cultures/c.p.m. in control cultures) (Figure 1a). Labelling cells with the fluorescent dye carboxyfluorescein succinimidyl ester showed that the proliferating teicoplanin-specific lymphocytes were exclusively CD4+ as reflected by dilution of the carboxyfluorescein succinimidyl ester in this cell population (Figure 1b). Supernatants that were collected from the peripheral blood mononuclear cell cultures on day 5, and analysed with a flow cytometry-based bead enzyme linked immunosorbent assay (Cytometric Bead Array Kit; BD Biosciences) contained high levels of interferon-γ, interleukin-5 and tumour necrosis factor-α, indicating a Th0 lymphocyte response. These results thus confirmed the presence of teicoplanin sensitivity mediated by T lymphocytes.

Antibiotic-induced hypersensitivity may give a similar clinical picture to systemic sepsis. Laboratory markers such as C-reactive protein and liver enzymes may be abnormal and eosinophilia is a helpful clue. The hypersensitivity results from T-cell sensitization and develops 10–14 days after exposure to the drug.

Hypersensitivity syndrome is most commonly reported with anticonvulsants and sulphonamides, but has been reported in association with teicoplanin frequently with associated pyrexia.1, 2 Peripheral blood mononuclear cells cultures, also

References


doi:10.1093/qjmed/hcm102