Editorial

Will CT coronary angiography revolutionise emergency department chest pain evaluation?

電腦掃描冠狀動脈造影術會否在急症室胸痛的評估中起革命?

Anne-Maree Kelly

Professor of Emergency Medicine/Director, Joseph Epstein Centre for Emergency Medicine Research, Western Health and The University of Melbourne, Melbourne, Australia

Assessment and investigation of patients presenting to emergency departments (ED) with chest pain is an increasing challenge world-wide. In the US, non-traumatic chest pain contributes to approximately 4.6 million ED visits, an average of 22.7 visits per 1000 people.[1] Extrapolating this to developed and developing countries gives a frightening estimation of the magnitude of the problem.

The dual challenges in the ED are to identify patients who have sustained myocardial infarction so that emergent treatment can be given and the group who have significant coronary artery disease (CAD) without infarction (at least not yet) so that interventions to minimise morbidity/mortality can be undertaken. The former group relies on biomarkers and ECG analysis while the latter has, until recently, relied on functional tests and selective coronary angiography (SCA). Multi-slice CT coronary angiography (MSCT-CA) is an emerging technology for the assessment of coronary arteries. Most of the data are from higher risk populations, but what role does it have, if any, in the ED evaluation of chest pain patients?

Correspondence to:
Anne-Maree Kelly, MD, MClinEd, FACEM
Sunshine Hospital, Joseph Epstein Centre for Emergency Medicine Research, Furlong Road, St Albans 3021, Australia
Email: Anne-Maree.Kelly@wh.org.au

For me, the fundamental questions are:

- Is it sensitive for the detection of CAD?
- Is it suitable for the patient cohort in question?
- Is it feasible and safe in an ED chest pain population?
- How does it perform in comparison to alternative investigation strategies?
- What are the up and down sides?

Diagnostic accuracy

The diagnostic accuracy of MSCT-CA has been improving steadily with advances in technology that have improved image quality and minimised artefact. A 16-slice CT has better sensitivity than a 4-slice and preliminary data suggests that a 64-slice CT may be better still. The use of rate control agents such as beta-blockers and calcium channel blockers coupled with ECG-gating of images has overcome most of the issues with motion artefact.

The gold standard for comparison is fluoroscopic SCA. Sensitivity can be assessed at the segment level (i.e. in a given coronary segment, does MSCT-CA accurately identify CAD) or at the patient level (i.e. does MSCT-CA accurately identify the presence of or rule out CAD). Emergency physicians are probably more interested in the latter, as our question is *'is there*

significant CAD?' more than *'where is it?'* Cardiologists might prefer the former definition, with its potential relationship to planning intervention.

A recent review of the performance of 16-slice MSCT-CA reported pooled sensitivity (at the segment level) of 89% with specificity of 96%. Variation in sensitivity was in large part due to whether studies included small coronary branches or not. Negative predictive value ranged from 95-99%.[2] A more recent observational study reported similar sensitivity/specificity performance with a negative predictive value of 100%.[3] It is also very accurate for the evaluation of coronary artery bypass graft patency.[3] Based on the available data, it would seem that diagnostic performance is satisfactory for answering the key ED question: CAD or no CAD? It is important however to remember that MSCT-CA is an anatomical test. It provides no information about the presence of an acute coronary syndrome (ACS) or the functional significance of any lesions found.

Suitability for the patient cohort

One of the major challenges is defining the patient cohort of relevance. Studies to date have concentrated on low risk chest pain patients, often defined as TIMI risk score ≤2. This is a diverse group, with those with TIMI score of zero having much lower risk regarding outcomes than those with scores of 1 or 2.[4] This approach also discounts clinical suspicion for patients with atypical chest pain and high risk factors such as isolated diabetes or strongly positive family history. It also does not include patients with cardiac marker levels that seem incongruent with the clinical assessment, particularly those with minor troponin abnormalities on the new sensitive assays. I would prefer to see the relevant cohort defined by moderate clinical suspicion/risk. While clinically practical, this group will be difficult to define with precision for research purposes.

A significant proportion of chest pain patients with potential CAD are unsuitable for MSCT-CA because of irregular heart rhythms, established CAD, renal impairment or contraindications to rate reducing drugs or intravenous contrast. The proportion of suitable patients is yet to be delineated. Preliminary unpublished data from a study being conducted at my institution looking at patients undergoing a short-stay assessment for chest pain suggests that about 45% of the cohort may be suitable for MSCT-CA. If the moderate clinical suspicion criterion mentioned above was applied, the proportion would be lower, as some of these patients are clearly TIMI score zero. On one level this is disappointing, while at another, if CAD can be confidently ruled out with MSCT-CA in 30-40% of patients, that may be of benefit to patients and the health system.

Feasibility, safety and prognostic value in an ED population

To date, only a small number of studies have looked at the role of MSCT-CA in the ED chest pain population. Soon et al[5] reported a pilot study addressing questions of safety, practicality and accuracy. Although only including 34 patients, they showed that diagnostic quality scans could be achieved in 76% of patients and that there were no major safety issues.

There are now a small number of studies that have followed up ED chest pain patients with negative MSCT-CA. These reported a very low rate of adverse cardiovascular events (0% at 30 days,[6] 2.8% at ~15 months[7]).

Comparison with other diagnostic strategies

The main alternative to MSCT-CA is functional testing, usually with physiological stress applied. The principle of stress testing is mismatch between demand and supply of myocardial blood flow. In the presence of severe CAD (stenosis >70%), myocardial blood flow is compromised and myocardial ischaemia occurs. Functional stress tests include exercise ECG testing, nuclear myocardial perfusion imaging (MPI) or stress echocardiography.

The overall sensitivity and specificity of treadmill ECG testing have been reported as 68% and 77%, respectively.[8] That said, treadmill ECG has very good prognostic value. In the setting of ongoing chest pain, resting MPI has both diagnostic and prognostic value. Studies consistently report sensitivity of the order of 96% and specificity of 79%. Its clinical value is its high negative predictive value, 99-100%.[9] A negative MPI in this setting predicts a negligible rate of major cardiac events during 12 months follow up. Nevertheless, when it is performed after the resolution of chest pain, resting MPI has low sensitivity (65%) and moderate specificity (84%). Stress MPI has sensitivity of the order of 90% with specificity around 65%. A normal stress MPI also predicts a low rate of future cardiac events. Stress echocardiography has sensitivity and specificity of 85% and 77% in meta-analysis[10] and, similar to the other functional tests, a normal examination is associated with a low rate of future cardiac events. Preliminary data from the USA suggests that functional tests and MSCT-CA are comparable in terms of cost.

It should be noted that functional tests overall perform less well in women. A major issue for emergency departments is access to same day or next day tests.

Up and down sides

Clearly the main strength of MSCT-CA is its high negative predictive value. Another strength is that the test could be performed in centres that do not have access (either because of geography or high catheter laboratory case loads) to fluoroscopic SCA, potentially affording patients timely testing, avoiding long distance travel (an important issue for patients in more remote areas) and potentially acting as a triaging tool for SCA. An emerging strength is the possibility of investigating the small but significant proportion of chest pain patients in whom CAD or pulmonary embolism, pericarditis or aortic dissection are viable differential diagnoses with a single test. Available data is scarce but preliminary results are promising. Johnson et al reported that in a group of 41 patients for whom a cause of chest pain was eventually identified, MSCT-CA accurately identified 37 (90%, 95% CI 77-96%).[11]

The 'down sides' of MSCT-CA are radiation exposure – about 15 mSv for men and 23 mSv for women for a standard MSCT-CA (similar to a stress thallium scan) and about 25-35 mSv for a 'triple rule out' MSCT-CA; and the risk of contrast reactions. Other issues include access, as ED chest pain assessment is a round-the-clock function, as well as availability of skilled readers. I also have a concern that MSCT-CA could go the way that cranial CT and trauma CT have gone in some countries, where overuse is the norm. Although adverse events are uncommon, if a large population is exposed, they add up. Also, findings of minor levels of CAD that are not functionally significant may have negative impacts on patients in terms of insurance and employment.

An interesting medico-political side issue is that of training and credentialing for interpretation of MSCT-CA. Currently, radiologists, cardiologists and nuclear medicine physicians all see it as 'their territory' and agreement regarding training and credentialing seems some way off.

Potential place of MSCT-CA

There is a lot of debate currently about the place of MSCT-CA in investigation of ED patients with chest pain of uncertain origin. Given its high negative predictive value, there is a school of thought that sees it as a first line investigation in suitable patients without known CAD. An alternative school of thought sees it as a test reserved for low to intermediate risk patients with equivocal functional tests, to determine the need for fluoroscopic SCA. Both approaches have strengths and weakness and will be, in part, governed by local expertise and test availability. Both seem reasonable, if tailored to individual patients. MSCT-CA may be the preferable test in women, in those who are unsuitable for stress testing and in patients where alternative diagnoses are reliably detectable on MSCT

angiography. The small but appreciable risks of MSCT-CA (radiation, contrast reaction) are probably too high for patients at very low risk of CAD, e.g. TIMI zero or age or aspirin use as the only risk features. Then there are the patients with CAD occluding ≤70% of vessel lumens who may require functional testing to determine if intervention is warranted.

Summary

The state of knowledge regarding MSCT-CA is rapidly evolving. Based on currently available evidence it appears to be a useful test for the investigation of selected ED patients with chest pain but I do not believe that it will revolutionise ED chest pain management. Careful patient evaluation, including assessment of CAD risk and viable alternative diagnoses, should guide an investigation strategy tailored to the individual patient. I fear that the pendulum will swing too far, resulting in over-use with little benefit for patients and potential harm. We shall have to wait and see.

References

1. Burt CW. Summary statistics for acute cardiac ischemia and chest pain visits to United States EDs, 1995-1996. Am J Emerg Med 1999;17(6):552-9.
2. Soon KH, Kelly AM, Cox N, Chaitowitz I, Bell K, Lim YL. Non-invasive multi-slice CT coronary angiography for imaging coronary arteries, stents and bypass grafts. Intern Med J 2006;36(1):43-50.
3. Soon KH, Chaitowitz I, Cox N, Macgregor L, Eccleston D, Bell KW, et al. Diagnostic accuracy of 16-slice CT coronary angiography in the evaluation of coronary artery disease. Austral Radiol 2007;51(3):365-9.
4. Chase M, Robey JL, Zogby KE, Sease KL, Shofer FS, Hollander JE. Prospective validation of the Thrombolysis in Myocardial Infarction Risk Score in the emergency department chest pain population. Ann Emerg Med 2006;48(3):252-9.
5. Soon KH, Kelly AM, Cox N, MacGregor L, Chaitowitz I, Bell K, et al. Practicality, safety and accuracy of computed tomography coronary angiography in the evaluation of low TIMI-risk score chest pain patients: a pilot study. Emerg Med Australas 2007;19(2):129-35.
6. Hollander JE, Litt HI, Chase M, Brown AM, Kim W, Baxt WG. Computed tomography coronary angiography for rapid disposition of low-risk emergency department patients with chest pain syndromes. Acad Emerg Med 2007;14(2):112-6.
7. Rubinshtein R, Halon DA, Gaspar T, Jaffe R, Karkabi B, Flugelman MY, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation 2007;115(13):1762-8.
8. Gianrossi R, Detrano R, Mulvihill D, Lehmann K, Dubach P, Colombo A, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease: a meta-analysis. Circulation 1989;80(1):87-98.
9. Abbott BG, Jain D. Nuclear cardiology in the evaluation of acute chest pain in the emergency department. Echocardiography 2000;17(6 Pt 1):597-604.
10. Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280(10):913-20.
11. Johnson TR, Nikolaou K, Wintersperger BJ, Knez A, Boekstegers P, Reiser MF, et al. ECG-gated 64-MDCT angiography in the differential diagnosis of acute chest pain. AJR Am J Roentgenol 2007;188(1):76-82.