64-Slice or higher CT angiography for the investigation of coronary artery disease

Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease

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Executive summary

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Executive summary

Background

Coronary artery disease (CAD) is a major cause of mortality and ill-health. Coronary angiography (CA) is the gold standard for diagnosing CAD. However, CA is an invasive and expensive procedure, with a small (0.1–0.2%) risk of major complications such as death, myocardial infarction and stroke. A primary non-invasive technique for the diagnosis of CAD is therefore highly desirable.

The emergence of multislice computed tomography (MSCT) in the past decade and the introduction of 64-slice systems in 2004 have overcome many of the image quality issues that affected conventional CT systems. The technical factors that enhance image quality in 64-slice CT also result in a higher radiation dose, although the use of electrocardiogram (ECG)-dependent dose modulation can reduce this by 30–50%.

Objectives

This review aims to assess the clinical effectiveness and cost-effectiveness, in different patient groups, of the use of 64-slice or higher CT angiography, instead of invasive CA, for diagnosing people with suspected CAD and assessing people with known CAD.

Methods

Electronic searches were undertaken to identify published and unpublished reports. Searches were restricted to the years 2002 onwards and to English-language reports. The date of the last searches was December 2006.

The types of studies considered were randomised controlled trials, non-randomised comparative studies or case series in which adults received 64-slice or higher CT angiography, with invasive CA or long-term follow-up as the reference standard. Myocardial perfusion scintigraphy (MPS) was considered as a comparator test. Diagnostic accuracy studies had to report the absolute numbers of true and false positives and negatives, or sensitivity and specificity. Prognostic studies had to provide information on the likelihood of future cardiac events.

One reviewer screened the titles (and abstracts if available) of all reports identified by the search strategy. Two reviewers independently extracted details from the included full-text studies and assessed their quality using a modified version of the QUADAS instrument.

The results of the individual studies were tabulated and sensitivity, specificity, positive and negative predictive values calculated. Separate summary receiver operating characteristic (SROC) curves were derived for various levels of analysis. Meta-analysis models were fitted using hierarchical summary receiver operating characteristic (HSROC) curves. A symmetric SROC model was used. Summary sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios (DORs) for each model were reported as a median and 95% credible interval (CrI).

Searches were also carried out for studies on the cost-effectiveness of 64-slice CT in the assessment of CAD.

Results

Twenty-one diagnostic accuracy studies reported as full-text papers and 20 reported as abstracts, along with one prognostic study reported as a full-text paper and four reported as abstracts, met the inclusion criteria for the review. The diagnostic accuracy and prognostic studies enrolled over 2500 and 1700 people, respectively. As measured by the modified QUADAS checklist, the overall quality of the full-text diagnostic accuracy studies was reasonably good.

In the pooled estimates, 64-slice CT angiography was highly sensitive (99%, 95% CrI 97 to 99%) for patient-based detection of significant CAD (defined as >50% or ⩾50% stenosis), while across studies the negative predictive value (NPV) was very high (median 100%, range 86 to 100%). In the 13 full-text studies included in the pooled estimates, in terms of patient-based detection, 11 (2%) of 718 patients could not be assessed ▶

owing to unevaluable CT scans (median across studies 0%, range 0 to 6%). Three studies reported that all vessels smaller than 1.5 mm were excluded from analysis.

In segment-level analysis compared with patient-based detection, sensitivity was lower (90%, 95% CrI 85 to 94%, versus 99%, 95% CrI 97 to 99%) and specificity higher (97%, 95% CrI 95 to 98%, versus 89%, 95% CrI 83 to 94%), while across studies the median NPV was similar (99%, range 95 to 100%, versus 100%, range 86 to 100%). At individual coronary artery level the pooled estimates for sensitivity ranged from 85% (95% CrI 69 to 94%) for the left circumflex (LCX) artery to 95% (95% CI 84 to 99%) for the left main artery, specificity ranged from 96% for both the left anterior descending (LAD) artery (95% CrI 91 to 98%) and LCX (95% CrI 92 to 99%) to 100% (95% CrI 99 to 100%) for the left main artery, while across studies the positive predictive value (PPV) ranged from 81% (range 56 to 100%) for the LCX to 100% (range 90 to 100%) for the left main artery and NPV was very high, ranging from 98% for the LAD (range 95 to 100%), LCX (range 93 to 100%) and right coronary artery (range 94 to 100%) to 100% (all five studies) for the left main artery. The pooled estimates for bypass graft analysis were 99% (95% CrI 95 to 100%) sensitivity, 96% (95% CrI 86 to 99%) specificity, with median PPV and NPV values across studies of 93% (range 90 to 95%) and 99% (range 98 to 100%), respectively. This compares with, for stent analysis, a pooled sensitivity of 89% (95% CrI 68 to 97%), specificity 94% (95% CrI 83 to 98%), and median PPV and NPV values across studies of 77% (range 33 to 100%) and 96% (range 71 to 100%), respectively.

None of the studies reporting the diagnostic accuracy of 64-slice CT included MPS as a comparator. In two systematic reviews of single-photon emission computed tomography (SPECT) MPS, sensitivity was reported as a median of 81% across studies (range 63 to 93%) or pooled estimate of 87% [fixed-effect model, 95% confidence interval (CI) 86 to 88%], while specificity was reported as a median of 65% across studies (range 10 to 90%) or pooled estimate of 64% (fixed-effect model, 95% CI 60 to 68%).

Three of the five prognostic studies included low-risk patients with suspected acute coronary syndrome and all reported that 64-slice CT angiography had very good NPV in short-term (mostly 30-day) follow-up. Of the other two studies, one reported that in the year following the introduction of 64-slice CT the rates of increase in diagnostic catheterisation volume and percutaneous coronary interventions had not been significantly affected, while the other reported that in the 6 months following the introduction of 64-slice CT invasive CA was avoided in 398 (82%) of 486 patients who would have received the test.

Cost-effectiveness

No studies of the cost-effectiveness of 64-slice CT in assessing CAD were found. However, some of the reviews and previous health technology assessments did identify some of the cost-effectiveness issues that are likely to arise. Other studies examined the cost-effectiveness of other investigations against angiography, such as exercise testing and positron emission tomography scanning, and these provided useful background.

Sixty-four-slice CT appears to be as good as but cheaper than MPS for the diagnosis of CAD. Consequently, 64-slice CT is likely to be a cost-effective replacement for MPS in diagnosing CAD.

Sixty-four-slice CT is almost as good as invasive CA in terms of detecting true positives. However, it is somewhat poorer in its rate of false positives. Consequently, diagnostic strategies involving 64-slice CT angiography will result in a number of false positives (not in terms of whether CAD is present, but in terms of quantifying the degree of stenosis). It seems likely that diagnostic strategies involving 64-slice CT will still require invasive CA for CT test positives, partly to identify CT false positives, but also because CA provides other information that CT currently does not, notably details of insertion site and distal run-off for possible coronary artery bypass graft (CABG).

The high sensitivity of 64-slice CT avoids the costs of unnecessary CA in those referred for investigation but who do not have CAD. Given the possible although small associated death rate, avoiding these unnecessary CAs through the use of 64-slice CT may also confer a small immediate survival advantage on the presenting population. This in itself may be sufficient to outweigh the very marginally inferior rates of detection of true positives by strategies involving 64-slice CT.

The avoidance of unnecessary CA through the use of 64-slice CT also appears likely to result in overall cost savings in the diagnostic pathway. Only if both the cost of CA is relatively low and the prevalence of CAD in the presenting ▶

population is relatively high (so that most patients will go on to CA) will the use of 64-slice CT be likely to result in a higher overall diagnostic cost per patient.

Conclusions

Implications for practice

The proportion of CA that could be replaced by 64-slice CT is currently uncertain. Reduction in CA would be mainly at the diagnostic end of the pathway, in both elective assessment of chest pain of possibly anginal origin, and assessment of suspected acute coronary syndromes in some patients with normal or equivocal ECGs and negative troponin tests. In the emergency situation, some hospital admissions might be avoided. However, to do so, 64-slice CT would need to be readily available, ideally on a 24-hour basis, which is unlikely to be the case in most hospitals. Some perfusion studies could also be replaced by 64-slice CT angiography.

In summary, the main value of 64-slice CT may at present be to rule out significant CAD. It is unlikely to replace CA in assessment for revascularisation of patients, particularly as angiography and angioplasty are often done on the same occasion.

One issue is whether to acquire 64-slice CT systems or wait until 256-slice systems become available. Evidence on 256-slice CT is currently sparse and mostly commercial in origin. However, it is unlikely that performance would be less good, and if the cost difference between 64- and 256-slice machines were small, it could be argued that the NHS should bypass 64-slice machines in favour of 256-slice ones. However, there must come a time when the extra data do not provide additional clinical benefit, although it is as yet unclear when that point will be reached.

Recommendations for research

The following areas should be addressed by further research.

- The marginal advantages and costs of 256-slice machines compared with 64-slice CT.
- The usefulness of 64-slice CT in people with suspected ACS. This review identified only a few studies, mostly reported as abstracts, containing small numbers of patients, most of whom were low risk and would be expected to have relatively low event rates.
- The potential of MSCT to examine plaque morphology.
- The role of CT in identifying patients suitable for CABG. CT can identify stenoses, but research is needed into its ability to identify distal insertion sites and adequacy of run-off. Such research could be done by conducting CT in a large group of patients before CABG (with preceding invasive CA), with assessment of suitability for CABG by observers unaware of the invasive CA results and arterial findings at CABG.
- Concerns raised about repetitive use, or use of 64-slice or higher CT angiography in younger individuals or women of childbearing age.

Publication

Mowatt G, Cummins E, Waugh N, Walker S, Cook J, Jia X, *et al*. Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease. *Health Technol Assess* 2008;**12**(17).

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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 06/15/01. The contractual start date was in July 2006. The draft report began editorial review in October 2007 and was accepted for publication in November 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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