Effectiveness and cost-effectiveness of echocardiography and carotid imaging in the management of stroke

Authors' objectives
To investigate a number of 'key questions' relating to the effectiveness and cost-effectiveness of imaging strategies for evaluating and managing patients presenting with new ischaemic brain syndromes (stroke or transient ischaemic attack).

Searching
MEDLINE, HealthSTAR, the Cochrane Controlled Trials Register, the Cochrane Database of Systematic Reviews, DARE and HTA were searched from 1966 or inception for papers published in English; the search terms were reported. In addition, reference lists were checked and experts in the area contacted.

Study selection
Study designs of evaluations included in the review
It appears that randomised controlled trials (RCTs), cohort studies, case-control studies and case series were included in the review.

Specific interventions included in the review
Studies of imaging strategies were eligible for inclusion: transthoracic echocardiography (TTE), transoesophageal echocardiography (TEE), carotid ultrasound (CUS), magnetic resonance imaging (MRA) and cerebral angiography. Other ultrasonic strategies and noninvasive carotid imaging techniques were excluded. The review also investigated the efficacy and safety of carotid endarterectomy (CEA) following carotid imaging.

Participants included in the review
Studies of patients with stroke or transient ischaemic attack were eligible for inclusion. Patients with coronary artery disease, subarachnoid or cerebral hemorrhage of non-ischaemic non-embolic origin, and patients with asymptomatic carotid artery stenosis were excluded.

Outcomes assessed in the review
A number of outcomes were assessed: stroke, echocardiographic lesions, complications requiring intervention, haemorrhage, death, diagnostic accuracy of the available tests and harms associated with these tests.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected papers for inclusion in the review using predefined inclusion criteria; any differences were resolved through discussion.

Assessment of study quality
The validity of studies relating to all questions except those relating to echocardiographic yield, complications of testing and treatment, and cost-analysis was assessed using criteria developed by the third U.S. Preventive Services Task Force (USPSTF). Each study was rated as good, fair or poor, based on specific criteria for that study design. A similar rating was given to the overall evidence for each question area. A modified version of the USPSTF was used for diagnostic accuracy studies and those reporting complication rates for CEA, cerebral angiography and TEE.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were abstracted onto forms developed by the investigator for each key question. In addition to standard study and patient characteristics, information specific to each of the study questions was also extracted; this included incidence rates, efficacy estimates and operating characteristics (sensitivity, specificity and likelihood ratios).

**Methods of synthesis**

How were the studies combined?
Where possible, the studies were pooled to provide summary estimates using meta-analytic statistical methods. Where this was not possible, the studies were combined in a narrative.

How were differences between studies investigated?
The chi-squared test was used to assess statistical heterogeneity. A sensitivity analysis investigating study quality (good, fair and poor) was performed. Differences between the studies were also highlighted in the tables and text.

**Results of the review**

It is unclear how many studies were included in the review.

Echocardiography.

With current estimates of echocardiographic accuracy and prevalence of intracardiac thrombus, the review found that testing all stroke patients with echocardiography is likely to result in false positives at least as often as true positives. The sensitivity and specificity corresponding to fixed points of accuracy on summary receiver operating characteristic (ROC) curves were 90.0 and 27.8. Mortality rates for TEE did not differ when study quality was considered.

Carotid imaging.

The accuracy of CUS varied across centres. MRA (sensitivity 90.2% and specificity 93.0%) may be more accurate than CUS (sensitivity 78.2% and specificity 88.8%), but few high-quality studies addressed its accuracy. When poor-quality studies were excluded, the sensitivity of MRA was 90.0% and its specificity was 96.4%. The combination of MRA and CUS has high reported sensitivity (94.5%) and specificity (96.4%), but the studies were limited by verification bias and were of fair to poor quality. RCT evidence indicated that CEA reduces the risk of disabling stroke or death for patients with severe or moderate stenosis. Evidence from fair-quality non-randomised studies indicated that early CEA is not associated with an increased risk of major complications compared with delayed CEA.

**Cost information**

TEE and TTE cost over $290,000 per quality-adjusted life-year (QALY) saved at thrombus prevalence of 5% or less, assuming that anticoagulation reduces the risk of recurrent stroke from intracardiac thrombus by 33% over one year. Cost-effectiveness ratios dropped to less than $50,000 per QALY if the relative risk reduction with anticoagulation was 86% and the prevalence of thrombus at least 6%. All carotid imaging testing strategies cost at least $250,000 per QALY when the prevalence of severe stenosis was assumed to be 15%. Cost-effectiveness ratios were below $75,000 per QALY when the prevalence of severe stenosis was above 20% for two testing strategies: initial CUS with angiographic confirmation and CEA for those with severe stenosis, and MRA with direct referral to CEA for those with severe stenosis.

**Authors’ conclusions**

Overall, evidence for the effectiveness of echocardiography in the management of patients with stroke is weak. There is insufficient evidence to draw conclusions about whether echocardiographically identifiable lesions are associated with increased risk of recurrent stroke, or whether treatment for reducing recurrent stroke is associated with intracardiac thrombus or other lesions.

The accuracy of CUS varied across centres; MRA may be more accurate than CUS but few high-quality trials have addressed its accuracy. The combination of MRA and CUS has high reported sensitivity, but the studies were limited by verification bias and were of fair to poor quality.
CRD commentary
The review questions were clearly stated and the risk of missing relevant studies was minimised by searching a wide range of sources for published and unpublished data. The search was limited to English language material, which introduces a possible risk of language bias. Appropriate review methods were used to reduce error and bias at the study selection stage, although it is unclear whether similar methods were applied for the data extraction. The quality of the included studies was assessed and results reported. Primary study characteristics were reported and the analysis seemed appropriate. The authors’ conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors suggested a number of research requirements. They stated that there are a number of knowledge gaps, notably the presence and degree of risk of stroke conveyed by echocardiographically identified lesions, and the efficacy of treatment for reducing that risk. Further studies assessing complication rates of TEE in patients with stroke are required, as are high-quality studies on the diagnostic accuracy of CUS and MRA. In addition, studies assessing the efficacy and safety of early versus late CEA are needed to determine the most appropriate timing of carotid imaging. More accurate estimates of the cost of TTE and TEE would help future economic evaluations. Comparisons of outcomes of CEA with the latest nonsurgical treatments for carotid stenosis across clinical and demographic patient groups would also help future evaluations of carotid imaging studies.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract
contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.