Non-invasive imaging compared with intra-arterial angiography in the diagnosis of symptomatic carotid stenosis: a meta-analysis

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CRD summary
This review determined the accuracy of noninvasive imaging for diagnosing carotid stenosis in patients with carotid territory ischaemic symptoms. The authors' cautious conclusions, that existing data might support the cautious use of noninvasive imaging to diagnose 70 to 99% stenosis by experts in carotid imaging, but more data are needed to determine the accuracy of the commonly used noninvasive imaging tests in routine practice, appear appropriate.

Authors' objectives
To determine the accuracy of noninvasive imaging compared with intra-arterial angiography (IAA) for diagnosing carotid stenosis in patients with carotid territory ischaemic symptoms.

Searching
MEDLINE and EMBASE were searched from January 1980 to April 2004; the search terms were reported. Six key journals were also searched (1990 to 2002): Radiology, Neuroradiology, American Journal of Radiology, American Journal of Roentgenology, Stroke, and European Journal of Vascular and Endovascular Surgery. The reference lists of primary studies and relevant reviews were checked. Studies published only in abstract form and pre-1986 were excluded.

Study selection
Study designs of evaluations included in the review
Prospective controlled studies with at least 20 participants, and which stated that the index test was interpreted blind to the reference standard, were eligible for inclusion. It appears that quasi-randomised controlled trials and randomised controlled trials (RCTs) were included in the review.

Specific interventions included in the review
Studies comparing Doppler ultrasound (DUS), computed tomographic angiography (CTA), magnetic resonance angiography (MRA) or contrast-enhanced MRA (CEMRA), either alone or in combination, with IAA were eligible for inclusion. The studies also had to provide sufficient detail of the imaging technique to enable repetition.

Reference standard test against which the new test was compared
Studies of IAA for diagnosing clinically relevant carotid stenosis according to a stated method for defining degree of stenosis (North American Symptomatic Endarterectomy Trial (NASCET) method, common carotid or European Carotid Surgery Trial) were eligible.

Participants included in the review
Studies of individuals with transient ischaemic attack or stroke in the carotid territory, amaurosis fugax, or retinal artery occlusion were eligible for inclusion. The included studies were required to have at least 70% symptomatic patients. Studies of carotid imaging in trauma, cancer, healthy volunteers, children, or test phantoms were excluded. The average age, where reported, ranged from 56 to 70 years (range: 34 to 89).

Outcomes assessed in the review
The studies had to report sufficient data to construct a 2x2 table of test performance to be eligible for inclusion.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the papers. Any disagreements were resolved through discussion with a third reviewer. A: Whilst all abstracts were assessed for relevance by two reviewers, any abstract that was considered relevant by at least one reviewer was included for full paper assessment. Each full paper was assessed by two reviewers,
with discrepancies referred to a third reviewer. A few foreign language papers were assessed by only one reviewer.]

**Assessment of study quality**
Studies were assessed for methodological quality using the Quality Assessment of Diagnostic Accuracy Studies criteria and Standards for Reporting of Diagnostic Accuracy criteria. Items assessed included patient spectrum, reference standard, disease progression bias, verification bias, review bias, clinical review bias, incorporation bias, test execution, study withdrawals and indeterminate results. The authors did not state how many reviewers performed the quality assessment. [A: Each paper was assessed by two reviewers, with discrepancies referred to a third reviewer. A few foreign language papers were assessed by only one reviewer.]

**Data extraction**
Two reviewers checked the extracted data. Any discrepancies were resolved by arbitration with a third reviewer. Accuracy data were extracted as 2x2 tables of test performance. Estimates of accuracy were extracted for each noninvasive imaging type and categorised by percentage stenosis: definitely operable (70 to 99% stenosis); possibly operable (50 to 69% stenosis); definitely not operable (0 to 49% stenosis, or 100% occluded) based on the NASCET stenosis criteria.

**Methods of synthesis**
**How were the studies combined?**
The sensitivity and specificity, along with 95% confidence intervals (CIs), were calculated using a random-effects model for each noninvasive imaging technique compared with IAA by stenosis band. The analysis was performed on a per-patient basis, and adjustments were made for studies that reported on the number of arteries per study. The distribution of individual studies was examined on receiver operating characteristic plots. Publication bias was assessed through funnel plots.

**How were differences between studies investigated?**
Chi-squared tests and the variance inflation factor were used to assess statistical heterogeneity between the studies. Predefined sensitivity analyses examined publication date, noninvasive imaging modality, image interpretation method, patient population, recruitment method, spectrum of disease, blinding of IAA results, and observer experience. Sensitivity analyses were restricted to 70 to 90% stenosis due to a shortage of data.

**Results of the review**
Forty-one studies were included in the review (2,541 patients and 4,876 arteries).

For 70 to 99% stenosis, CEMRA demonstrated the greatest sensitivity compared with IAA (0.94, 95% CI: 0.88, 0.97), followed by DUS (0.89, 95% CI: 0.85, 0.92), MRA (0.88, 95% CI: 0.82, 0.92) and CTA (0.77, 95% CI: 0.68, 0.84). Significant heterogeneity was shown for most noninvasive imaging modalities at most stenosis bands. The authors reported that neither the year of publication nor disease spectrum affected the diagnostic accuracy of any modality. There were insufficient data to make reliable comparisons for 50 to 69% stenosis, although the available data suggested that CEMRA had the highest sensitivity (0.77, 95% CI: 0.59, 0.89) and CTA the lowest specificity (0.79, 95% CI: 0.63, 0.89). Direct comparisons of test accuracy between noninvasive tests were not possible.

Data were too limited to explore possible sources of heterogeneity. The authors stated that forest plots for the meta-analyses of 70 to 99% stenosis were consistent with data missing from small studies, with small diagnostic odds suggesting some evidence of publication bias (data not presented).

**Authors' conclusions**
Existing data might support the cautious use of noninvasive imaging to diagnose 70 to 99% stenosis by experts in carotid imaging. However, more data are needed to determine the accuracy of the commonly used noninvasive imaging tests in routine practice where the balance of risk and benefit for carotid endarterectomy is narrow (especially for 50 to
69% stenosis) and when used in combination.

**CRD commentary**

The review question was supported by clear inclusion and exclusion criteria. The search strategy was not restricted by language, although the authors stated that not every non-English paper obtained could be assessed; publication bias was assessed. The methodologies used to identify primary papers and extract the data were likely to reduce the possibility of reviewer error or bias. In addition, the authors took steps to ensure that only studies providing the most reliable data were included in the review. The quality of the primary studies was assessed using appropriate criteria (see Other Publications of Related Interest no.1).

Although the authors did not report findings for individual studies, they discussed a number of methodological limitations, including poor description of patient populations and selection processes. They also acknowledged several additional limitations: the studies did not compare all noninvasive imaging tests on an equal footing, and most studies analysed the number of arteries imaged rather than patients, potentially inflating sample size. The authors' cautious conclusions appear appropriate given the limitations of the evidence available.

**Implications of the review for practice and research**

Practice: The authors stated that any increased use of noninvasive carotid imaging should be implemented cautiously.

Research: The authors listed a number of methodological, design and reporting issues that future studies should address. In addition, they stated that the methodology for evaluating imaging tests should be improved; practical, streamlined and reliable methods are needed to evaluate new technologies.

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**Other publications of related interest**


This additional published commentary may also be of interest. Kelly AG, Holloway RG. Review: noninvasive imaging techniques may be useful for diagnosing 70% to 99% carotid stenosis in symptomatic patients. ACP J Club 2006;145:77.

**Indexing Status**
Subject indexing assigned by NLM

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Record Status
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.