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Use of magnetic resonance angiography to select candidates with recently symptomatic carotid stenosis for surgery: systematic review

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Abstract

Objective To determine if sufficient evidence exists to support the use of magnetic resonance angiography as a means of selecting patients with recently symptomatic high grade carotid stenosis for surgery.
Design Systematic review of published research on the diagnostic performance of magnetic resonance angiography, 1990-9.
Main outcome measures Performance characteristics of diagnostic test.
Results 126 potentially relevant articles were identified, but many articles failed to examine the performance of magnetic resonance angiography as a diagnostic test at the surgical decision thresholds used in major clinical trials on endarterectomy. 26 articles were included in a meta-analysis that showed a maximal joint sensitivity and specificity of 99% (95% confidence interval 98% to 100%) for identifying 70-99% stenosis and 90% (81% to 99%) for identifying 50-99% stenosis. Only four articles evaluated contrast enhanced magnetic resonance angiography.
Conclusions Magnetic resonance angiography is accurate for selecting patients for carotid endarterectomy at the surgical decision thresholds established in the major endarterectomy trials, but the evidence is not very robust because of the heterogeneity of the studies included. Research is needed to determine the diagnostic performance of the most recent developments in magnetic resonance angiography, including contrast enhanced techniques, as well as to assess the impact of magnetic resonance angiography on surgical decision making and outcomes.

Introduction

Patients with arteriosclerosis, particularly those with recent carotid territory stroke or transient ischaemic attack who might benefit from carotid endarterectomy, may be investigated with conventional angiography, ultrasonography, or magnetic resonance angiography.[1 2] Although conventional catheter angiography remains the definitive imaging technique, it is an invasive procedure for which the patient must be admitted to hospital, it involves the use of ionising radiation, and when used in the carotid circulation it is accompanied by serious complications, including a 0.5-2% risk of stroke.[3] Magnetic resonance angiography may be more acceptable to patients and may be of particular use in patients not suitable for conventional angiography—for example, patients with an allergy to iodinated contrast medium, frail and elderly patients, and patients with severe peripheral vascular disease. These potential benefits may be offset by poor performance as a diagnostic test.

This systematic review examines the evidence on the performance of magnetic resonance angiography in evaluating patients with recently symptomatic internal carotid artery stenosis. The North American symptomatic carotid endarterectomy trial (NASCET) and the European carotid surgery trial (ECST) found a clear benefit of surgery in patients with recently symptomatic stenoses of 70-99% as measured by conventional angiography with the NASCET criteria.[4 5] We therefore evaluated the evidence on the diagnostic performance of magnetic resonance angiography in comparison with conventional angiography at this threshold.

NASCET and ECST found a smaller benefit of surgery in patients with symptomatic 50-99% stenosis; ECST also showed a clear downward trend in the benefit of surgery for stenoses less than 70%.[5] The benefit in this group also depended on the age and sex of the patients. However, a recent Cochrane review concluded that surgery was beneficial for patients with 50-69% stenosis,[6] so we also evaluated the evidence on the diagnostic performance of magnetic resonance angiography when these more moderate stenoses were included (that is, for patients with 50-99% stenosis).

For each diagnostic threshold, we aimed to answer the question "What are the sensitivity and specificity of magnetic resonance angiography, in comparison with the gold standard of conventional angiography, in distinguishing severely stenosed arteries suitable for surgery, from either occluded or minimally stenosed arteries?"

Methods

We searched the electronic databases Medline, Embase, HealthSTAR, Science Citation Index, Index to Scientific and Technical Proceedings, Cochrane Library, Inside (British Library), and Online Computer Library Centre for articles published between January 1990 and December 1999. We used the keywords magnetic resonance angiography and MRA (or accepted synonyms and abbreviations).[7] We also conducted a hand search of 10 key journals in the fields of imaging and vascular disease. We examined the reference lists of all articles retrieved from the above sources.

We included original research articles satisfying criteria A-D in the quantitative meta-analysis (table). Primary data (true positive, true negative, false positive, and false negative values) were extracted independently by two reviewers, and agreed by consensus, for the following clinical decision thresholds measured by using the NASCET criteria or similar[4]: 70-99% stenosed vessel (suitable for carotid endarterectomy) versus 0-69% stenosed or 100% occluded vessel (not suitable for carotid endarterectomy); 50-99% stenosed vessel (suitable for carotid endarterectomy) versus

Exclusions on application of final inclusion criteria. Only eight articles remained when all criteria A-H were applied. When only criteria A-D were used, 26 articles satisfied the criteria.[14-39] References for the excluded articles are available from the authors

	Inclusion criterion	No of articles excluded
A	Study compared magnetic resonance angiography with digital subtraction angiography or cut film angiography	32
B	Sufficient data reported for the construction of a 2×2 contingency table	44
C	Performance at 50-99% or 70-99% or 100% stenosis reported	20
D	Not a duplicate study of same patient group. Where more than one study was found, the one using the largest patient group was included.	5
E	All patients in study received selective carotid intra-arterial digital subtraction or cut film angiography	13
F	The method used to determine the degree of stenosis was described	4
G	No asymptomatic patients were included	5
H	No time delays of over 1 month occurred between examinations	1
Total No of articles excluded		124

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0-49% stenosed or 100% occluded vessel (not suitable for carotid endarterectomy). Results derived with the very different ECST criteria were excluded from the meta-analysis.[5]

We plotted results from the independent studies on sensitivity versus 1 – specificity axes to illustrate the scatter of results. We then combined the sensitivity and specificity results for independent studies into a summary receiver operating characteristic curve.[8–11] The summary receiver operating characteristic curve is an excellent graphical summary, but for comparison purposes we calculated a further statistic—Q* and its 95% confidence interval.[8] Q* is the point on the summary receiver operating characteristic curve where sensitivity and specificity have the same value; it represents the maximal joint sensitivity and specificity. Q* is a good summary value in this application as there is no particular disadvantage to sensitivity and specificity being equal: patients with false positive results needlessly undergo the risks of surgery, but patients with false negative results are denied the benefits of surgery.

We then performed a multiple linear regression analysis at the line fitting phase of the summary receiver operating characteristic analysis, to determine if any of five covariates had a significant effect, at the 95% level, on the fitted summary receiver operating characteristic curve.[12] The five covariates were technique of magnetic resonance angiography, inclusion of articles that did not satisfy the inclusion criteria E-H, the risk of test or diagnostic review bias, the risk of verification bias, and the risk of withdrawal bias.[13]

Results

We identified 16 185 articles with the initial broad search strategy. After we had removed duplicates, 7183 unique articles remained. The exclusion criteria reduced the number of candidate articles on carotid artery stenosis to 26 satisfying the inclusion criteria A to D.[14–39] Only eight articles satisfied all the inclusion criteria A to H.[15 18 20 21 23 33 34 37]

For the diagnosis of 70-99% stenosis (fig 1), four sets of results obtained by using contrast enhanced techniques were included,[24 30 32 34] together with 11 sets of results (from nine articles[17 21 23 25 27 32 33 35 39]) obtained by using three dimensional time of flight and 10 sets of results[14–36] obtained by using two dimensional time of flight techniques. Q* was 99% (95% confidence interval 98% to 100%). None of the variables tested in the multiple linear regression, including magnetic resonance angiography technique, was significant at the 95% level.

For the diagnosis of 50-99% stenosis (fig 2), no results obtained by using contrast enhanced techniques were included. Results from four studies using three dimensional time of flight techniques were included,[19 27 37 38] together with six sets of results (from five articles[18 22 26 29 31]) obtained by using two dimensional time of flight. Q* was 90% (81% to 99%). None of the variables tested in the multiple linear regression was significant at the 95% level.

The patient populations of studies included in the quantitative meta-analysis were heterogeneous. Patient numbers ranged from 11 to 101 (mean = 40). In all articles where sex distribution was reported most patients were men; in these articles the proportion of men ranged from 55% to 100% (mean = 69%). Six articles did not report sex distribution.[15 20 24 27 28 33] The lower limit for age of patients ranged from 18 to 63 years (mean = 43 years), and the upper limit ranged from 73 to 87 years (mean = 80 years). Six articles did not report age range.[23 25 27 32 33 36] Eight articles stated that asymptomatic patients were included,[14 16 25–27 29 30 38] and 18 articles gave no information about symptoms.[14 15 17–24 26–28 31–35]

Discussion

Although many articles have been written about magnetic resonance angiography and carotid disease, little

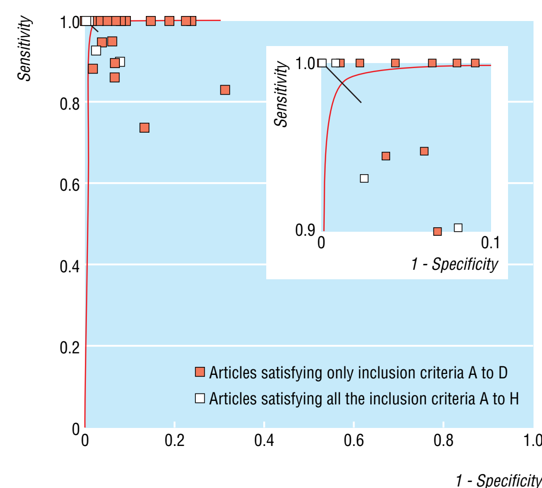

Fig 1 Summary receiver operating characteristic curve for magnetic resonance angiography: 70-99% stenosis is a positive result, and 0-69% stenosis and 100% occlusion are negative results. Straight line shows 95% confidence interval of Q*. Enlargement of region of sensitivity and specificity 90-100% shown for clarity

rigorous research has been conducted on the performance of magnetic resonance angiography in evaluating carotid artery stenosis. Small numbers of participants and inadequate details of study design mean that many studies included in this review have a potential for bias, but none of the factors tested in the multiple linear regression analysis had a significant effect on the results. Further sources of heterogeneity in patient populations (age, sex distribution, presenting symptoms) may influence patients' suitability for carotid endarterectomy,[5 40] and differences existed between the study groups included in the review, even among those that satisfied all the inclusion criteria.

To be able to determine whether a patient is a suitable candidate for carotid endarterectomy, a diagnostic test must distinguish severely (>70%) stenosed or moderately (>50%) stenosed arteries (which are suitable for carotid endarterectomy) from both minimally stenosed (0-69% or 0-49%) and occluded arteries (100%), which are not suitable for carotid endarterectomy.[4 5] Candidate articles often failed to assess magnetic resonance angiography in these terms.

Our review does not support the use of magnetic resonance angiography to select surgical candidates with 50-99% stenosis. The 95% confidence interval for Q* extended from 81% to 99%, and only two of the articles whose results were included in the meta-analysis satisfied the inclusion criteria related to validity. It would be advisable for users of magnetic resonance angiography to ensure that rigorous training and audit are in place, including feedback from surgeons and continuing quality control comparisons with ultrasonography.

Our results indicate that magnetic resonance angiography is very effective for detecting 70-99% stenosis as defined by conventional angiography. Although there is a promising trend towards better performance from contrast enhanced methods, further research is essential as only four articles were included in this review and no significant difference was found between the results obtained by using the three main techniques.

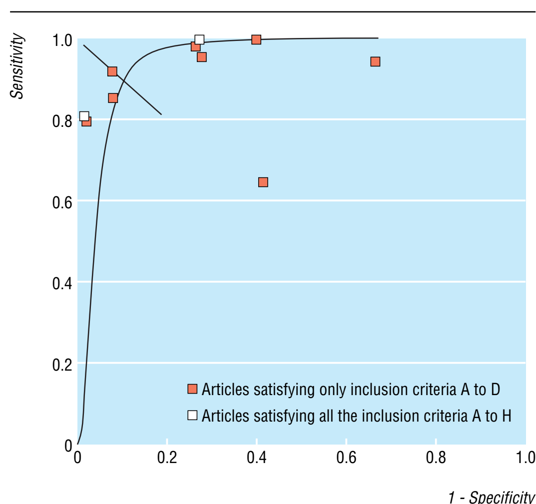

Fig 2 Summary receiver operating characteristic curve for magnetic resonance angiography: 50-99% stenosis is a positive result, and 0-49% stenosis and 100% occlusion are negative results. Straight line shows 95% confidence interval of Q*

What is already known on this topic

Carotid endarterectomy for recently symptomatic carotid stenosis is beneficial in patients with 70-99% stenosis as measured by conventional angiography

It is not known whether the less invasive imaging technique of magnetic resonance angiography can accurately identify patients who will benefit from surgery

What this study adds

Magnetic resonance angiography is highly sensitive and specific in diagnosing 70-99% carotid stenosis

However, the studies on which this conclusion is based are of low quality and high heterogeneity

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Contributors: See bmj.com

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Time trends in survival and readmission following coronary artery bypass grafting in Scotland, 1981-96: retrospective observational study

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Improvements in coronary revascularisation techniques and an increase in the use of percutaneous interventions[1] have led to a rise in the number of coronary artery bypass grafting operations in older patients with more severe cardiac disease and worse comorbidity and who have previously undergone revascularisation procedures.[2 3] Advances in surgical and anaesthetic techniques have prevented a worsening risk profile from being translated into an increase in perioperative deaths.[2 3] The aim of our study was to examine time trends in major outcomes up to two years after coronary artery bypass grafting.

Participants, methods, and results

We used the Scottish morbidity record (SMR1) system to identify all operations for coronary artery bypass grafting performed in Scottish NHS hospitals from 1981 to 1996. We excluded operations that included other procedures. Information was obtained on age, sex, urgency of the operation, and Carstairs socioeconomic deprivation category derived from postcode of residence.[4] Record linkage to subsequent SMR1 and registrar general records provided follow up information on readmission, repeat procedures, and death, both inside and outside of hospital, up to two years after the operation.

The study cohort comprised 25 229 coronary artery bypass operations; 19 687 (78%) were performed in men and 5542 (22%) in women. The number of operations overall increased from 68 to 490 per million population per year (see table A on the *BMJ*'s website for details). The percentage of operations performed on patients aged over 65 increased from 2% to 30% in men (7/289 *v* 582/1950, $P<0.0001$) and from 16% to 45% in women (10/61 *v*

See the BMJ's website for more data on coronary artery grafts 1981-96