Peripheral arterial disease: meta-analysis of the diagnostic performance of MR angiography

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Authors' objectives
To summarise the overall diagnostic performance of magnetic resonance (MR) angiography in the evaluation of peripheral arteriosclerotic occlusive disease, and to identify the important sources of variation in diagnostic accuracy between the studies.

Searching
MEDLINE was searched from January 1991 to June 1999 for publications in the English language. The search terms were 'peripheral vascular disease', 'peripheral arterial disease', 'arterial occlusive disease', 'intermittent claudication', 'arterial insufficiency', 'lower limb ischemia', 'lower extremity ischemia', 'peripheral' and 'lower extremity', combined with 'magnetic resonance angiography', 'MR angiography' or 'MRA'. Citations in reviews and identified studies were also examined.

Study selection
Study designs of evaluations included in the review
The inclusion criteria were not defined in terms of the study design. The included studies selected the participants (where stated) randomly and as consecutive and non-consecutive series.

Specific interventions included in the review
Studies of MR angiography were eligible. Studies that evaluated two- dimensional (2D) gadolinium-enhanced or phase-contrast MR angiography were excluded. The specific tests in the included studies were 2D time-of-flight MR angiography and three-dimensional (3D) gadolinium-enhanced MR angiography. The processing techniques used in the primary studies were maximum intensity projection (MIP) with and without transverse source images, multiplanar reformation, or coronal source images. The percentage of patients with aortoiliac segments included in the trajectory ranged (where stated) from 0 to 100% across the studies.

Reference standard test against which the new test was compared
The studies had to use conventional angiography as the reference standard. The cut-off point was the detection of a haemodynamically significant lesion. This was defined as either a stenosis of 50 to 99% or as an occlusion.

Participants included in the review
Studies of patients with peripheral vascular disease were eligible. Across the included studies (where stated), the mean age of the participants ranged from 50 to 74 years, the percentage of males ranged from 43 to 100%, the percentage of patients with claudication ranged from 4 to 100%, and the percentage with critical ischaemia ranged from 0 to 96%.

Outcomes assessed in the review
Studies that either presented the absolute numbers of true-positive, false-positive, false-negative and true-negatives, or allowed their derivation, were eligible.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Validity was assessed using the following criteria: blinding of the readers of the MR angiographic images to the results of conventional angiography and vice versa (yes or no), sample size, and low potential for verification bias (yes or no). The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.
**Data extraction**
The data were extracted using a standard form, but the authors do not state how many of the reviewers performed the data extraction.

The data extracted related to the year of publication, examination, patient characteristics, study design characteristics and results. Details of the examination included the type of MR angiography, extent of image evaluation and use of cardiac synchronisation. The patient characteristics were the mean age, percentage of males, the percentage with clinical indications, anatomical sites and the percentage of aortoiliac segments included. Where the studies reported data from more than one anatomical level, the data were pooled into aortoiliac arteries, femoropopliteal arteries and the below-knee arteries. Site-specific results were extracted where possible. Where the results were reported by more than one observer, the results from the first observer were used. It was generally assumed there was no data overlap between the studies.

**Methods of synthesis**
How were the studies combined?
Summary receiver operating characteristic (ROC) curves were fitted using the methods described by Littenberg and Moses (see Other Publications of Related Interest nos.1-2).

How were differences between studies investigated?
Linear regression models were explored using the diagnostic odds ratio (DOR) as the dependent variable and potentially relevant study design characteristics as covariates. The analyses were conducted separately for the following covariates: type of MR angiographic examination (3D versus 2D); use of cardiac synchronisation; year of publication (before versus after 1995); processing technique (maximum intensity projection (MIP) in combination with review of transverse source images or multiplaner versus MIP alone); mean age (65 years versus less than 65 years); percentage male (greater than 25% versus 25%); prevalence of stenosed segments (greater than 25% versus 25%); presence of aortoiliac segments in the evaluation trajectory; and sample size (greater than 30 versus 30 or less). The characteristics with the largest DORs were evaluated simultaneously in a multiple variable model.

**Results of the review**
Twenty-one articles reported on 23 studies. Of these, 13 studies (344 patients) evaluated 2D MR angiography and 10 studies (253 patients) evaluated 3D MR angiography.

There was a wide range of sensitivity and specificity values that could not be explained by differences in the threshold for a positive result.

2D MR angiography: the sensitivity ranged from 64% (specificity 73%) to 100% (specificity 90%), while the specificity ranged from 68% (sensitivity 83%) to 96% (sensitivity 87%). The prevalence of stenosed segments ranged from 13 to 73%. 3D MR angiography: the sensitivity ranged from 92% (specificity 93%) to 100% (specificity 95 to 99%), while the specificity ranged from 91% (sensitivity 81 to 96%) to 99% (sensitivity 100%). The prevalence of stenosed segments ranged from 13 to 36%.

The final univariate model included two variables in addition to the variable S (sum of the logit transformations). The relative adjusted DOR (in multivariate analysis using these 3 covariates) was 7.46 (95% confidence interval, CI: 2.48, 22.20) for 3D versus 2D MR angiography, and 4.53 (95% CI: 1.46, 13.87) for MIP alone versus MIP plus additional processing.

Methodological quality.

Most studies described the MR angiographic and the conventional angiographic examination, and in almost all of the studies the MR and conventional angiography readers were blinded to the results of the other examination. Seven studies did not state the clinical indication and the majority of the studies did not provide adequate information to assess verification bias. Ten studies did not report the methods used to select the patients, while only two studies reported the number of eligible patients and the reasons for exclusion.
Authors' conclusions
The diagnostic accuracy of 3D gadolinium-enhanced MR angiography was superior to that of 2D time-of-flight MR angiography. Significantly better diagnostic performance is achieved when reviewing the transverse source images, or when using additional processing techniques such as multiplanar reformation.

CRD commentary
The aims of the review were stated and the inclusion criteria were defined in terms of the index and standard reference test and outcome. The inclusion criteria were not defined in terms of the study design or participants. The search was limited to English language publications identified in one database and this strategy may have missed other relevant studies. The methods used to select the studies for inclusion were not described. Validity was assessed using a limited number of criteria, but the methods used to assess validity were not described. The experience of the MR angiography reader and the extent of inter-observer variability were not mentioned. Relevant data were extracted and presented in tabular format. The data were pooled and some potential sources of heterogeneity (determined a priori) were explored, but considerable unexplained heterogeneity remained. The influence of validity factors on the results was not explored.

Conclusions based on such heterogeneous studies must be interpreted with caution.

Implications of the review for practice and research
Practice: The authors state that the review supports the use of 3D gadolinium-enhanced MR angiography rather than 2D time-of-flight MR angiography.

Research: The authors did not state any implications for further research.

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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.