DUS, MRA and CTA for the diagnosis and assessment of lower limb peripheral arterial disease

A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease

R Collins,[1*] G Cranny,[1] J Burch,[1] R Aguiar-Ibáñez,[1] D Craig,[1] K Wright,[1] E Berry,[2] M Gough,[3] J Kleijnen[1] and M Westwood[1]

[1] Centre for Reviews and Dissemination, University of York, UK
[2] Academic Unit of Medical Physics, University of Leeds, UK
[3] Leeds Teaching Hospitals NHS Trust, UK

* Corresponding author

Executive summary

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Executive summary

Background

Lower limb peripheral arterial disease (PAD) is characterised by atheromatous narrowing or occlusion of one or more of the arteries of the leg. Symptoms include intermittent claudication (pain on walking), ischaemic rest pain, ulceration and gangrene. This review concerns the assessment of symptomatic PAD. Intervention decisions utilise information regarding the degree, length and location of stenoses or occlusions. This review summarises the evidence on the role of duplex ultrasound (DUS), magnetic resonance angiography (MRA), and computed tomography angiography (CTA), as alternatives to contrast angiography (CA), for the assessment of PAD.

Objectives

The objectives of this review were:

- to determine the diagnostic accuracy of DUS, MRA and CTA, alone or in combination, for the assessment of lower limb PAD
- to evaluate the impact of these assessment methods on patient management/outcome
- to evaluate the evidence regarding patient attitudes to these technologies
- to summarise available adverse event data associated with these technologies
- to analyse the cost-effectiveness of these technologies using a review of existing cost-effectiveness literature, and decision analysis.

Methods

Data sources

Studies were identified through extensive searches of electronic databases (carried out in April 2004, with update searches in May 2005), handsearching of journals, scanning reference lists of included papers and consultation with experts in the field.

Study selection

Two reviewers independently screened titles and abstracts for relevance. Full papers of potentially relevant studies were assessed for inclusion by one reviewer and checked by a second. Published and unpublished studies in any language were eligible for inclusion.

Inclusion criteria

Separate inclusion criteria, relating to study design, participant characteristics and outcome measures, were derived for each objective.

Data extraction

Data extraction and quality assessment were performed using standardised forms. The quality of the included studies was evaluated using published checklists and criteria. All data extraction was checked by a second reviewer.

Data synthesis

Assessment of stenosis/occlusion

Results were analysed according to test type (MRA, DUS, CTA) and diagnostic threshold (e.g. 50% stenosis, occlusion). Data for different MRA techniques [e.g. time-of-flight (TOF), phase-contrast (PC), contrast-enhanced (CE)] were grouped separately. Data were further grouped according to the area of the leg assessed (whole leg, above knee, below knee, foot). Sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios were calculated for each data set. Individual study results were presented graphically in receiver operating characteristic (ROC) space. Heterogeneity was investigated using the Q statistic and through visual examination of study results. Pooled estimates of diagnostic test performance were calculated where statistically and clinically meaningful; otherwise, median likelihood ratios and ranges were presented. Insufficient data were available to facilitate the use of subgroup or regression analyses to investigate potential sources of between study heterogeneity (e.g. aspects of methodological quality, presence of co-morbidities or risk factors, image postprocessing techniques, personnel involved in test interpretation).

Impact of assessment method on patient management/outcome

A narrative synthesis was presented.

Studies of patient attitudes

A narrative synthesis was presented.

Adverse events

Results were tabulated and, where more than one study reported a particular adverse event, the range of the proportion of patients experiencing that adverse event was presented.

Economic evaluations
Economic evaluations were described and critically appraised in a narrative summary.

Economic modelling
The objective of the economic analysis was to assess the relative cost-effectiveness of MRA, DUS and CTA compared with CA, from the UK NHS perspective, in order to identify the type and level of stenosis and subsequently formulate a treatment plan for patients with PAD. A decision tree was developed and a probabilistic sensitivity analysis performed to incorporate statistical uncertainty into the cost-effectiveness analysis.

Results

The searches identified 650 potentially relevant studies, of which 113 met the inclusion criteria (including six economic evaluations).

Assessment of stenosis/occlusion (58 studies)
For the detection of stenosis greater than 50% in the whole leg, CE MRA (14 studies) had the highest diagnostic accuracy, with sensitivity ranging from 92 to 99.5% and specificity from 64 to 99%. Two-dimensional (2D) TOF MRA (11 studies) was less accurate, with sensitivity ranging from 79 to 94% and specificity from 74 to 92%. 2D PC MRA (one study) had a sensitivity of 98% and specificity of 74%. CTA (seven studies) also appeared slightly inferior to CE MRA, with a sensitivity ranging from 89 to 99% and specificity from 83 to 97%, but better than DUS (28 studies), which had a sensitivity ranging from 80 to 98% and specificity from 89 to 99%. There was some indication that CE MRA and DUS were more accurate for detecting stenoses/occlusions above the knee than below the knee or in the pedal artery.

Impact of assessment method on patient management/outcome (one study)
This historically controlled trial reported no statistically significant differences in immediate or intermediate-term patient outcomes, following treatment plans based on DUS alone or based on conventional CA alone. However, in a subgroup of 22% of patients having DUS supplementary CA was needed to form a treatment plan.

Studies of patient attitudes (four studies)
These studies strongly suggested that patients preferred CE MRA to CA. CA was considered the most uncomfortable test, followed by CE MRA, with CTA being the least uncomfortable. Half of the patients (from a sample who did not suffer from claustrophobia and had no metallic implants) expressed no preference between undergoing TOF MRA or DUS, while the majority of those who did express a preference favoured TOF MRA.

Adverse events (55 studies)
MRA was associated with the highest proportion of adverse events reported in the studies. However, the most severe adverse events were more common in patients undergoing CA than MRA; although these only occurred in a very small proportion of patients undergoing either test. The most commonly reported adverse events were acute digestive system symptoms associated with CE MRA, unspecified contrast agent-related adverse events associated with CE MRA, minor pain/discomfort during or immediately after DUS, 2D TOF MRA or CE MRA, anxiety associated with 2D TOF MRA, and acute central and peripheral nervous system adverse events associated with CE MRA.

Economic evaluations/modelling
When the whole leg was assessed by a preoperative diagnostic test, DUS dominated the other alternatives by presenting higher effectiveness at a lower cost per quality-adjusted life-year (QALY; i.e. £13,646 per QALY). When the assessment was limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA was the most cost-effective preoperative diagnostic strategy. The incremental cost per QALY for below-the-knee comparisons was equal to £37,024 when 2D TOF MRA was compared with DUS. For above-the-knee comparisons, 2D TOF MRA presented the lowest cost and slightly lower effectiveness compared with the most effective diagnostic strategy (i.e. CE MRA), with a cost per QALY equal to £13,442.

Conclusions

The results of the review suggest that CE MRA has a better overall diagnostic accuracy than CTA or DUS, and that CE MRA is generally preferred by patients over CA. Where available, CE MRA may be a viable alternative to CA.

The only controlled trial of the effectiveness of imaging procedures suggested that the results of DUS were comparable to those of CA, in terms of surgical planning and outcome. This finding conflicts with the results of diagnostic accuracy studies, which reported poor estimates of accuracy for DUS in comparison with CA. ▶

There was insufficient evidence to evaluate the usefulness of CTA for the assessment of PAD, particularly newer techniques.

The results of the economic modelling suggest that for PAD patients for whom the whole leg is evaluated by a preoperative diagnostic test DUS dominates the other alternatives by presenting higher effectiveness at a lower cost per QALY. However, when the analysis of stenosis is limited to a section of the leg, either above the knee or below the knee, 2D TOF MRA appears to be the most cost-effective preoperative diagnostic strategy.

Recommendations for future research

The following specific questions requiring further research were identified:

- What is the relative clinical effectiveness of the available imaging tests, in terms of surgical planning and postoperative outcome?
- What adverse events occur as a consequence of testing, and what is the relative incidence for the available tests?
- Which tests do patients prefer?
- What is the true diagnostic accuracy of DUS for the detection of 50% or greater stenoses and occlusions and how is this affected by timing of the test and operator skill?
- What are the effects of operator skill/training/experience on measures of test accuracy for all the imaging modalities of interest?
- What is the diagnostic accuracy and clinical effectiveness of tests to image arteries in different areas of the leg, particularly the foot?
- What is the diagnostic accuracy and clinical effectiveness of tests in particular patient subgroups, for example diabetes mellitus?
- Are the prognosis and quality of life of PAD patients different according to whether they have an accurate or an inaccurate treatment plan?

Publication

Collins R, Cranny G, Burch J, Aguiar-Ibáñez R, Craig D, Wright K, *et al*. A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease. *Health Technol Assess* 2007;**11**(20).

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The research reported in this monograph was commissioned by the HTA Programme as project number 03/07/04. The contractual start date was in May 2004. The draft report began editorial review in December 2005 and was accepted for publication in October 2006. 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.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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