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 Kleijnen1 and M Westwood1

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

Health Technology Assessment 2007; Vol. 11: No. 20
**How to obtain copies of this and other HTA Programme reports.**

An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public and private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

- fax (with credit card or official purchase order)
- post (with credit card or official purchase order or cheque)
- phone during office hours (credit card only).

Additionally the HTA website allows you either to pay securely by credit card or to print out your order and then post or fax it.

**Contact details are as follows:**

HTA Despatch

c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

**Payment methods**

**Paying by cheque**
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to Direct Mail Works Ltd and drawn on a bank with a UK address.

**Paying by credit card**
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

**Paying by official purchase order**
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

**How do I get a copy of HTA on CD?**

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. HTA on CD is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.
**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**

The Health Technology Assessment (HTA) programme, now part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the costs, effectiveness and broader impact of health technologies for those who use, manage and provide care in the NHS. ‘Health technologies’ are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Secondly, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Thirdly, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer-reviewed by a number of independent expert referees before publication in the widely read monograph series *Health Technology Assessment*.

---

**Criteria for inclusion in the HTA monograph series**

Reports are published in the HTA monograph series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed ‘systematic’ when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

---

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.

**Editor-in-Chief:** Professor Tom Walley  
**Series Editors:** Dr Aileen Clarke, Dr Peter Davidson, Dr Chris Hyde, Dr John Powell, Dr Rob Riemsma and Dr Ken Stein  
**Managing Editors:** Sally Bailey and Sarah Llewellyn Lloyd