RESEARCH

Duplex ultrasonography, magnetic resonance angiography, and computed tomography angiography for diagnosis and assessment of symptomatic, lower limb peripheral arterial disease: systematic review

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ABSTRACT

Objectives To determine the diagnostic accuracy of duplex ultrasonography, magnetic resonance angiography, and computed tomography angiography, alone or in combination, for the assessment of lower limb peripheral arterial disease; to evaluate the impact of these assessment methods on management of patients and outcomes; and to evaluate the evidence regarding attitudes of patients to these technologies and summarise available data on adverse events.

Design Systematic review.

Methods Searches of 11 electronic databases (to April 2005), six journals, and reference lists of included papers for relevant studies. Two reviewers independently selected studies, extracted data, and assessed quality. Diagnostic accuracy studies were assessed for quality with the QUADAS checklist.

Results 107 studies met the inclusion criteria; 58 studies provided data on diagnostic accuracy, one on outcomes in patients, four on attitudes of patients, and 44 on adverse events. Quality assessment highlighted limitations in the methods and quality of reporting. Most of the included studies reported results by arterial segment, rather than by limb or by patient, which does not account for the clustering of segments within patients, so specificities may be overstated. For the detection of stenosis of 50% or more in a lower limb vessel, contrast enhanced magnetic resonance angiography had the highest diagnostic accuracy with a median sensitivity of 95% (range 92-99.5%) and median specificity of 97% (64-99%). The results were 91% (89-99%) and 91% (83-97%) for computed tomography angiography and 88% (80-98%) and 96% (89-99%) for duplex ultrasonography. A controlled trial reported no significant differences in outcomes in patients after treatment plans based on duplex ultrasonography alone or conventional contrast angiography alone, though in 22% of patients supplementary contrast angiography was needed to form a treatment plan. The limited evidence available suggested that patients preferred magnetic resonance angiography (with or without contrast) to contrast angiography, with half expressing no preference between magnetic resonance angiography or duplex ultrasonography (among patients with no contraindications for magnetic resonance angiography, such as claustrophobia). Where data on adverse events were available, magnetic resonance angiography was associated with the highest proportion of adverse events, but these were mild. The most severe adverse events, although rare, were mainly associated with contrast angiography.

Conclusions Contrast enhanced magnetic resonance angiography seems to be more specific than computed tomography angiography (that is, better at ruling out stenosis over 50%) and more sensitive than duplex ultrasonography (that is, better at ruling in stenosis over 50%) and was generally preferred by patients over contrast angiography. Computed tomography angiography was also preferred by patients over contrast angiography; no data on patients' preference between duplex ultrasonography and contrast angiography were available. Where available, contrast enhanced magnetic resonance angiography might be a viable alternative to contrast angiography.

INTRODUCTION

Management strategies differ for patients with differing severity of lower limb peripheral arterial disease, so detailed assessment is needed to develop a suitable treatment plan. Assessment by intra-arterial contrast angiography is regarded as the reference standard. Drawbacks are associated with arterial puncture, ionising radiation, and potential nephrotoxicity of iodinated contrast agents. Several alternative imaging techniques are available. We carried out a systematic review to look at the performance of magnetic resonance angiography, computed tomography angiography, and duplex ultrasonography as alternatives to contrast angiography to try to identify a technique that is safer and more acceptable to patients but as effective as contrast angiography for the assessment of symptomatic peripheral arterial disease. Here we present the systematic review of the evidence on effectiveness. The full report with economic evaluation is available elsewhere.[1]

METHODS

We searched 11 databases, six key journals, and reference lists of included studies for published and unpublished data. No language restrictions were applied. Two reviewers conducted each stage of the review process. Disagreements were resolved by consensus or referral to a third reviewer. See bmj.com.

We used the QUADAS checklist to assess the quality of diagnostic accuracy studies.[2] The results of diagnostic accuracy studies were analysed according to the imaging tests assessed. Magnetic resonance angiography technologies were further grouped by specific technique (2D phase contrast, 2D time of flight, or contrast enhanced). We derived the sensitivity and specificity for the detection of stenosis in arterial segments from the 2×2 tables reported in each study. Heterogeneity was assessed with the Q statistic and graphically with forest plots. Most studies provided data for more than one anatomical area (above knee, below knee, foot) or more than one threshold of stenosis (50%, 70%, occlusion). The number of arterial segments assessed per patient and their anatomical distribution varied and was sometimes incompletely reported.

We present a narrative synthesis for studies evaluating the impact of the method of assessment on management and outcome of patients, attitudes of patients, and studies of adverse events.

RESULTS

The search strategy generated 8590 references, of which 650 were considered to be potentially relevant; ultimately 107 met the inclusion criteria (see bmj.com).

Quality of diagnostic accuracy studies—All included studies were diagnostic cohorts and were conducted in secondary or tertiary care settings. There were several potential sources of bias: spectrum bias where the accuracy of a test may be underestimated or overestimated by investigating a selected population with regard to the severity of disease, demographics, or comorbidity; bias due to delay between the index test and reference standard being long enough for the disease to have progressed naturally; and bias due to the results of the

Diagnostic accuracy for detection of stenosis 50% or more or occlusion with different assessment methods

Study	No of patients	Fontaine stage II/III/IV* (%)	No of segments	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Contrast enhanced magnetic resonance angiography					
Cronberg[w13]	35	9/3/89	418	91.9 (87.8 to 95.0)	63.7 (56.1 to 70.9)
Laissy[w16]	20	100/0/0	520	92.0 (85.4 to 96.3)	96.6 (94.3 to 98.1)
Lenhart[w17]	45	NR	220	95.2 (88.1 to 98.7)	94.2 (88.8 to 97.4)
Schafer[w19]	30	NR	576	93.9 (88.7 to 97.2)	97.0 (94.9 to 98.4)
Steffens[w21]	50	NR	900	99.5 (97.0 to 100)	98.9 (97.8 to 99.5)
Sueyoshi[w22]	23	83/17/0	423	97.1 (89.9 to 99.6)	99.2 (97.5 to 99.8)
Winterer[w23]	76	87/13/0	1780	96.3 (93.8 to 97.9)	96.9 (95.9 to 97.8)
2D time of flight magnetic resonance angiography					
Baum[w2]	155	NR	1188	84.1 (80.9 to 86.8)	82.0 (78.6 to 85.1)
Hoch[w6]	20	NR	544	78.5 (72.3 to 84.0)	89.1 (85.3 to 92.2)
Hoch[w7]	45	18/20/62	352	93.5 (88.9 to 96.6)	92.3 (87.1 to 95.8)
Snidow[w10]	42	NR	378	92.0 (84.1 to 96.7)	73.9 (68.4 to 78.8)
Yucel[w12]	25	0/84/16	206	91.5 (82.5 to 96.8)	88.1 (81.5 to 93.1)
2D phase contrast magnetic resonance angiography					
Steffens[w1]	115	100/0/0	253	97.9 (95.1 to 99.3)	73.7 (48.8 to 90.9)
Computed tomography angiography					
Heuschmid[w27]	23	78/13/9	568	89.3 (83.1 to 93.7)	90.5 (87.2 to 93.1)
Martin[w28]	41	NR	1312	89.6 (86.0 to 92.5)	93.6 (91.8 to 95.0)
Puls[w30]	31	97/3/0	186	88.9 (78.4 to 95.4)	86.2 (78.8 to 91.7)
Rieker[w31]	50	74/12/14	327	97.4 (92.5 to 99.5)	90.6 (85.9 to 94.2)
Catalano[w26]	50	6/48/46	1137	98.8 (96.6 to 99.8)	97.4 (96.1 to 98.3)
Portugaller[w29]	50	62/4/34	740	92.0 (88.0 to 95.0)	83.3 (79.7 to 86.5)
Duplex ultrasonography					
Aly[w33]	90	90/9/1	3108	92.2 (89.3 to 94.6)	99.0 (98.5 to 99.3)
Bergamini[w35]	44	NR	404	79.7 (71.3 to 86.5)	95.5 (92.4 to 97.6)
Hatsukami[w40]	29	NR	243	85.9 (76.6 to 92.5)	96.2 (91.9 to 98.6)
Linke[w48]	25	100/0/0	134	95.3 (84.2 to 99.4)	95.6 (89.1 to 98.8)
Sensier[w50]	76	88/0/12	469	88.4 (83.7 to 92.2)	88.5 (83.7 to 92.4)
El-Kayali[w55]	44	NR	357	97.6 (93.2 to 99.5)	93.5 (89.5 to 96.3)
Legemate[w58]	61	80/16/3	918	84.4 (78.8 to 89.0)	95.8 (94.0 to 97.1)

NR=not reported.
*Stage II=intermittent claudication; stage III=ischaemic rest pain; stage IV=tissue loss.

index test being interpreted by someone with prior knowledge of the results of the reference test and vice versa. Finally the availability of clinical data when interpreting imaging results was poorly reported.

Assessment of stenosis/occlusion—Fifty eight diagnostic accuracy studies met the inclusion criteria. One evaluated 2D phase contrast magnetic resonance angiography,[w1] 11 evaluated 2D time of flight magnetic resonance angiography,[w2-w12] 14 evaluated contrast enhanced magnetic resonance angiography,[w8 w13-w25] 7 evaluated computed tomography angiography,[w26-w32] and 28 evaluated duplex ultrasonography.[w4 w8 w33-w58] Contrast angiography was the reference standard in all studies. As there was significant heterogeneity between individual studies we did not pool data and have presented results as medians (range). Most of the included studies reported results by arterial segment, rather than by limb or by patient, which does not account for the clustering of segments within patients. Therefore, the increased number of segments assessed is likely to increase the number of true negative test results, and thus the specificities may be overstated. We report results only for studies where data were reported by arterial segment. Full results are available elsewhere.[1]

Whole leg—The table shows data for detection of stenosis 50% or more or occlusion. Contrast enhanced magnetic resonance angiography had the highest diagnostic accuracy. 2D time of flight magnetic resonance angiography was less accurate, although the use of time of flight magnetic resonance angiography has now largely been superseded by contrast enhanced magnetic resonance angiography. The median sensitivity and median specificity were 95% (range 92-99.5%) and 97% (64-99%) for contrast enhanced magnetic resonance angiography, 91% (89-99%) and 91% (83-97%) for computed tomography angiography and 88% (80-98%) and 96% (89-99%) for duplex ultrasonography. For detection of occlusion, median sensitivity and median specificity were 94% (85-100%) and 99.2% (97-99.8%) for contrast enhanced magnetic resonance angiography, lower sensitivity (median 86% (77-100%)) and comparable specificity (97% (85-98%)) for 2D time of flight magnetic resonance angiography, median sensitivity 97% (89-100%) and median specificity 99.6% (99-100%) for computed tomography angiography and median sensitivity 90% (74-94%), and median specificity 99% (96-100%) for duplex ultrasonography.

Above and below the knee—The accuracy of the different techniques was similar for the detection of stenosis of 50% or more above and below the knee: with contrast enhanced magnetic resonance angiography the median sensitivity and specificity were 87% and 93%, respectively, above the knee[w8 w14 w17 w20] and 83% and 92% below the knee;[w15 w17 w24] with duplex ultrasonography the median sensitivity and specificity were 88% and 95% above the knee[w8 w35 w39 w40 w47 w55 w56] and 84% and 93% below the knee.[w35 w40 w43 w55] Two studies assessed accuracy for the detection of occlusion in the foot: one evaluated 2D time of flight magnetic resonance angiography[w5] and the other contrast enhanced

magnetic resonance angiography.[w24] Sensitivities were 86% and 79%, respectively, and specificities 27% and 86%, respectively. One study assessed the accuracy of duplex ultrasonography for detecting target vessels suitable for surgery in the foot, with sensitivity and specificity of 64% and 80% respectively.[w42]

Impact of method of assessment on management and outcome—Only one controlled trial, a prospective assessment of duplex ultrasonography using a historical control group who underwent contrast angiography, met the inclusion criteria for assessing impact on management and outcome.[w59] In 78% of cases the management plan was based on duplex ultrasonography without the need for additional contrast angiography. There were no significant differences between the groups in terms of immediate and intermediate outcomes. As the trial used a historical control group, however, other factors occurring within the timeframe of the trial may have affected the results.

Patients' attitudes—Four studies reported results relating to patients' attitudes.[w60-w63] Significantly more patients (28/30 patients) stated that they would prefer contrast enhanced magnetic resonance angiography over contrast angiography if they had to undergo testing again in the future,[w60] and contrast enhanced magnetic resonance angiography scored significantly better on a scale that rated patients' experience of the test compared with contrast angiography (P=0.0001 and P=0.0002).[w60 w61] Contrast angiography was reported as the most uncomfortable, followed by contrast enhanced magnetic resonance angiography, with computed tomography angiography being the least uncomfortable (P=0.016).[w63] Fifty per cent of patients (who were not claustrophobic and had no metallic implants) had no preference between time of flight magnetic resonance angiography or duplex ultrasonography (49/98 patients). Of those who did express a preference, most preferred time of flight magnetic resonance angiography (40/49 patients).[w62] Within the same population there was no significant difference between time of flight magnetic resonance angiography and duplex ultrasonography on a scale that rated how "bothersome" the tests were.[w62]

Adverse events—Adverse event data were poorly reported, therefore these results should be regarded only as a guide to the spectrum of adverse events reported and not as an accurate assessment of their frequency. The most commonly reported adverse events were minor pain or discomfort during or immediately after the procedure (17% for 2D time of flight magnetic resonance angiography (2/12 patients), 22% for duplex ultrasonography (22/98 patients), and up to 10% for contrast enhanced magnetic resonance angiography (10/98 patients)); acute symptoms in the digestive system associated with contrast enhanced magnetic resonance angiography (up to 10% (2/20) patients); anxiety associated with 2D time of flight magnetic resonance angiography (10% (4/40) patients); and acute adverse events in the central and peripheral nervous system associated with contrast enhanced magnetic resonance

angiography (up to 10% (2/20) patients). The highest proportion of adverse events was reported for magnetic resonance angiography. Major adverse events (death and severe vascular adverse events), however, were reported in a higher proportion of patients who underwent contrast angiography, although the overall proportion who experienced major adverse events was low (severe vascular adverse events: contrast angiography 5% (1/19 patients); contrast enhanced magnetic resonance angiography 0.5% (2/435 patients)). There were two deaths: one with contrast angiography and one with contrast enhanced magnetic resonance angiography. Studies reported adverse events related to the contrast agent for a small proportion of patients in relation to contrast angiography (see bmj.com).

DISCUSSION

Key findings

Contrast enhanced magnetic resonance angiography is the most accurate diagnostic technique for the detection of (50% or more) stenosis or occlusion, with most studies reporting sensitivities and specificities of over 90% (based on a "per segment" rather than "per patient" analysis). Magnetic resonance angiography was associated with the highest proportion of adverse events, although these were generally mild, with the most severe events associated with contrast angiography. The results of three surveys on patients' attitudes showed that patients who had no contraindications for magnetic resonance angiography preferred magnetic resonance angiography to contrast angiography.

The use of computed tomography angiography for the assessment of peripheral arterial disease is a relatively recent development, and its contribution to effective surgical planning remains to be explored. Patients found computed tomography angiography less uncomfortable than contrast angiography or magnetic resonance angiography, and only a few mild adverse events were reported.

The only controlled trial of the effectiveness of imaging procedures, in terms of surgical planning and outcome of patients, found that duplex ultrasonography and contrast angiography were comparable, a result that is seemingly at odds with poor estimates of the diagnostic accuracy for duplex ultrasonography. The sensitivity of duplex ultrasonography seems to be inferior to both contrast enhanced magnetic resonance angiography and computed tomography angiography, which means that duplex ultrasonography may miss some significant stenoses. This may be of particular concern if duplex ultrasonography were to be used to screen patients before surgical planning. Duplex ultrasonography, however, is unlikely to misclassify a whole limb as "normal" and thus inappropriately screen out a patient from further investigation. Fifty per cent of patients expressed no preference between time of flight magnetic resonance angiography or duplex ultrasonography, and those who did generally preferred time of flight magnetic resonance angiography. Some studies reported minor adverse events associated with duplex ultrasonography.

The area of leg assessed probably affects diagnostic performance. Contrast enhanced magnetic resonance angiography and duplex ultrasonography were less accurate for detecting stenoses in the foot. There was insufficient evidence to judge computed tomography angiography. The assessment of potential outflow vessels in the foot is known to be problematic.[3] Separate data on calf vessels and foot vessels are required as the inclusion of foot vessels in below knee imaging may lower the accuracy of results.

Strengths and weaknesses of the review

The possibility of publication bias remains a potential problem for all systematic reviews. Our review was limited by the lack of high quality, well reported studies. We found only one controlled trial, which used a historical control group that could be subject to bias. Most studies that provided data on diagnostic accuracy had small sample sizes (median 41.5, range 20-183) and reported results on a per segment rather than per patient basis. Our review therefore provides information on the ability of these techniques to detect stenosis within particular arterial segments, rather than on a per patient or per limb basis. Analysis by segment also means that the estimates of the 95% confidence intervals for sensitivity and specificity do not account for the clustering of segments within patients. The estimates of specificity may be raised as increasing the number of segments assessed is likely to increase the number of true negatives.

We did not collect data on variability between observers and few studies directly measured such variability. This is an important issue in the evaluation of tests that require subjective interpretation.[4]

The field of vascular imaging research is evolving rapidly, particularly in relation to the use of computed tomography angiography. Our results represent the imaging techniques available at the time the primary studies were undertaken and will become out of date as new techniques emerge.

Implications for clinical practice

From data that reported the accuracy of the imaging tests at assessing arterial segments, rather than the whole limb

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WHAT IS ALREADY KNOWN ON THIS TOPIC

Severity of disease determines the management strategy for symptomatic lower limb peripheral arterial disease, so detailed assessment of patients is needed before a suitable treatment plan can be developed

Intra-arterial contrast angiography is regarded as the reference standard investigation for the assessment of peripheral arterial disease

WHAT THIS STUDY ADDS

Contrast enhanced magnetic resonance angiography has better overall diagnostic accuracy than computed tomography angiography or duplex ultrasonography and is generally preferred by patients over conventional contrast angiography

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or areas of the limb, contrast enhanced magnetic resonance angiography seemed to have better overall diagnostic accuracy than computed tomography angiography and duplex ultrasonography, and was preferred by patients over conventional angiography. It might therefore be a viable alternative to conventional contrast angiography for assessing patients with peripheral arterial disease before treatment. We could not identify enough data to assess the effectiveness of the imaging tests in terms of surgical planning and postoperative outcomes. In addition, the lack of data on severity of disease and comorbidities reported by the included studies reduces the generalisability of these findings.

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Diagnostic scope of and exposure to primary care physicians in Australia, New Zealand, and the United States: cross sectional analysis of results from three national surveys

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ABSTRACT

Objective To compare mix of patients, scope of practice, and duration of visit in primary care physicians in Australia, New Zealand, and the United States.
Design Comparison of three comparable cross sectional surveys performed in 2001-2. Physicians completed a questionnaire on patients' demographics, diagnoses, and duration of visit.
Setting Primary care practice.
Participants 79 790 office visits in Australia, 10 064 in New Zealand, and 25 838 in the US.
Main outcome measures Diagnostic codes were mapped to the Johns Hopkins expanded diagnostic clusters. Scope of practice was defined as the number of expanded diagnostic clusters accounting for 75% of all managed problems related to morbidity. Exposure to primary care was calculated from duration of visits recorded by the physician, and reports on rates of visits to primary care for each country.
Results In each country, primary care physicians managed an average of 1.4 morbidity related problems per visit. In the US, 46 expanded diagnostic clusters accounted for 75% of problems managed compared with 52 in Australia, and 57 in New Zealand. Correlations in the frequencies of managed health problems between countries were high (0.87-0.97 for pairwise comparisons). Though primary care visits were longer in the US than in New Zealand and Australia, the per capita annual exposure to primary care physicians in the US (29.7 minutes) was about half of that in New Zealand (55.5 minutes) and about a third of that in Australia (83.4 minutes) because of higher rates of visits to primary care in these countries.

Conclusions Despite differences in the supply and financing of primary care across countries, many aspects of the clinical practice of primary care physicians are remarkably similar in Australia, New Zealand, and the US.

INTRODUCTION

Previous studies show that the strength of a country's primary care infrastructure is positively associated with health outcomes and negatively associated with healthcare costs.[1] Limited research has been done on the clinical content and duration of visits in primary care across countries. We sought to characterise the diagnostic scope of and exposure to primary care in three countries—Australia, New Zealand, and the United States—that vary in the supply of primary care physicians, the accessibility to primary care through health insurance, and the role of primary care physicians as gatekeepers to specialty care.

Of the three countries, Australia has the greatest number of primary care physicians per 100 000 population and the largest proportion of physicians trained in primary care specialties (table). In Australia and New Zealand, primary care physicians are trained as general practitioners. In the US, general internists, general paediatricians, and family practitioners all contribute to the pool of primary care physicians.

During the study period about 41 million Americans, (15% of the total population) were uninsured and another 16 million adults aged 19-64 were underinsured. The national insurance benefits in New Zealand and Australia include cost sharing except for some low