Eur J Vasc Endovasc Surg **35**, 405–412 (2008)
doi:10.1016/j.ejvs.2007.12.008, available online at http://www.sciencedirect.com on ScienceDirect

Assessment of Apparent Internal Carotid Occlusion on Ultrasound: Prospective Comparison of Contrast-enhanced Ultrasound, Magnetic Resonance Angiography and Digital Subtraction Angiography

C.J. Hammond,[1] S.J. McPherson,[1*] J.V. Patel[1] and M.J. Gough[2]

Departments of [1]Radiology, and [2]Vascular Surgery, Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK

Objectives. *Modern conventional ultrasound is sensitive to slow flow, but may misclassify some tight stenoses as occlusion. Symptomatic patients with tight proximal internal carotid artery stenoses may benefit from carotid endarterectomy but those with occlusion or long-segment disease do not.*
Design. *A prospective study of the diagnostic accuracy of contrast-enhanced ultrasound (CE-US), 2D time-of-flight magnetic resonance angiography (2D-TOF MRA) and contrast-enhanced magnetic resonance angiography (CE-MRA) against a reference standard of digital subtraction angiography (DSA) in patients with apparent carotid occlusion on conventional ultrasound.*
Materials and methods. *Thirty-one patients with apparent carotid occlusion on conventional ultrasound and with recent ispilateral hemispheric transient ischaemeic attacks (TIAs) were studied. The primary endpoint was confirmation of occlusion with a secondary endpoint of identification of a surgically correctible lesion.*
Results. *The sensitivity and specificity of CE-US, 2D-TOF MRA and CE-MRA for patency were 1 & 1, 0.33 & 1 and 0.6 & 1 respectively and for the detection of a surgically correctible lesion were 1 & 0.96, 0.67 & 1 and 1 and 0.96 respectively. CE-US was difficult to interpret, precluding confident diagnosis in 5 cases.*
Conclusions. *2D-TOF MRA had poor sensitivity for patency and cannot be recommended as a second-line investigation to assess vessels apparently occluded on conventional ultrasound. Confident diagnosis on CE-US and CE-MRA accurately identified occlusion. If occlusion is confirmed by either of these modalities, no further imaging is required. The relative advantages of CE-US or CE-MRA in this situation are uncertain.*

Keywords: Carotid stenosis; Diagnosis; Ultrasonography; Magnetic resonance angiography; Angiography; Endarterectomy, carotid.

Introduction

The role of carotid endarterectomy (CEA) in reducing the stroke and death rates in patients with a significant (>70%) symptomatic internal carotid artery (ICA) stenosis is well established.[1–3] Patient selection in these trials was based upon selective carotid digital-subtraction angiography (DSA). Patients with an ipsilateral carotid occlusion were considered unsuitable for surgery. In theory, with a stenosis of ≥95% the likelihood of distal embolization is reduced because of low flow, although the risk of watershed ischaemia may increase. CEA in these patients remains controversial, conferring only a marginal benefit over best medical therapy in the short term (up to 5 years).[3] Further, the annual incidence of ipsilateral stroke in patients with an occluded ICA on conventional US (in the absence of ongoing symptoms) is only 2%.[4] Nevertheless, many clinicians would offer surgery to patients with apparent carotid occlusion on conventional US if near-occlusion (rather than true occlusion) was found on confirmatory DSA[5,6] in the face of recent ipsilateral hemispheric TIAs despite maximal medical therapy[7] and evidence of hemispheric perfusion from the ipsilateral ICA. It remains critical therefore, to establish whether the ICA is occluded or has a tight stenosis. If the ICA is patent, clarification as to whether the ICA stenosis is focal, affects a long

*Corresponding author. Dr. S. J. McPherson (Consultant Vascular and Interventional Radiologist), BSc, MRCP, FRCR, Department of Radiology, Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK.
E-mail address: simon.mcpherson@leedsth.nhs.uk

length of the extracranial ICA or is associated with a tandem lesion of the distal ICA is required.

The presence of flow in the cervical ICA on conventional ultrasound (including 2D, colour and power Doppler ultrasound) is a sensitive marker for patency in this vessel.[8] The reference standard for assessing carotid stenotic lesions (and confirming occlusion) has been selective digital-subtraction angiography but this is an invasive procedure and is associated with a small risk of post-angiography stroke.[9] The ability of contrast-enhanced ultrasound and magnetic-resonance angiography to distinguish occlusion from near-occlusion and surgical from non-surgical lesions has not been investigated in the group of patients with apparent ICA occlusion on conventional US, despite the fact that about 3% of symptomatic patients attending for US of the ICA will fall into this group.[4]

This study prospectively examines the accuracy of contrast-enhanced ultrasound (CE-US), 2D time-of-flight (2D-TOF MRA) and contrast-enhanced MRA (CE-MRA) against a reference standard of selective contrast angiography in symptomatic patients whose ipsilateral ICA was apparently occluded on conventional US. Our primary criterion for accuracy was the assessment of patency, with a secondary criterion of detecting a stenosis suitable for CEA as defined by DSA.

Materials and Methods

The study group was recruited from patients referred for carotid ultrasound because of focal hemispheric neurological symptoms (TIA or minor stroke) within the previous six months. Symptomatic patients with non-disabling neurology and an apparent carotid occlusion on US (technique as described in Table 1) ipsilateral to the symptomatic cerebral hemisphere who were fit for CEA were invited to participate in the study provided that informed consent was obtainable and there was no contraindication to MRI or angiography (eg. metallic implants, absent femoral access, allergy to iodinated contrast medium).

The study group underwent further carotid imaging as described below. All tests were completed within 14 days using the methods described in Table 1. Patients failing to undergo their investigations within this time frame were excluded from the study.

1. Repeat conventional US 'confirm' ICA occlusion (technique identical to that for first scan)
2. Contrast enhanced US
3. 2D time-of-flight MRA
4. 3D contrast-enhanced MRA
5. Selective digital-subtraction angiography

Tests 1 and 2 (US) were dual reported at the time of scanning by an experienced vascular sonographer and a consultant vascular radiologist in an unblinded manner. Vessels were characterised as definitely occluded (if no flow was seen anywhere within the cervical ICA) or definitely patent (if a flow channel was seen throughout the cervical ICA). Disagreement was resolved at the time of scanning by consensus and was not recorded.

Tests 3 and 4 (MRA) were dual reported by two consultant vascular radiologists in a blinded manner. Image review occurred at a workstation, making reference to source data, whole-volume and sub-volume maximum-intensity-projections, operator defined multi-planar reformats and other post-processing as required. Vessels were characterised as definitely patent if signal could be identified within the cervical ICA in continuity with the siphon (small focal flow gaps were allowed as long as distal signal was preserved) or definitely occluded if no signal could be identified in the line of the cervical ICA. Vessels characterised as definitely patent were further classified into four groups on the basis of their apparent suitability for CEA: (a) probably suitable for CEA (proximal stenosis with good calibre distal ICA); (b) possibly suitable for CEA (proximal stenosis with reduced calibre distal ICA); (c) probably unsuitable for CEA (reduced calibre ICA, possible tandem lesions); (d) not suitable for CEA (diffuse narrowing, multicentric stenoses). Both the 2D-TOF and CE-MRA datasets were used for this subjective assessment.

Inter-observer error for these 2 assessments was assessed by using the kappa statistic. Disagreement regarding patency *versus* occlusion was resolved by consensus review of the images.

Test 5 (DSA) was singly reported by a consultant vascular radiologist at a workstation with reference to digital data and hardcopy film. Vessels were characterised as definitely patent if a linear contrast column of any thickness could be seen from the origin of the cervical ICA to the siphon in the absence of backfilling from intracranial vessels. Vessels were characterised as definitely occluded if no contrast could be identified in the line of the cervical ICA or if there was significant discontinuity with backfilling of the siphon and distal ICA from the intracranial vessels. The suitability of patent vessels for CEA was defined using the same criteria as those for MRA, with the addition of the assessment of filling of intracerebral vasculature from the ipsilateral side.

CEA was performed when an isolated focal proximal stenosis was demonstrated with a good or moderate calibre smooth distal ICA in symptomatic patients. The patency of the vessel at surgery was recorded.

Table 1. Details of techniques used

Test	Details
Conventional US (test 1)	**Acuson 128 XP10 US machine** **7 MHz linear array transducer** B mode and colour and power Doppler images used for superimposed simultaneous flow information on greyscale images. Beam focussing at level of vessel being investigated. Lowest possible pulse repetition frequency (PRF) without aliasing. Maximum colour and power gain without background noise. Adjustments to gain and transmission power (increased) and wall filter and PRF (decreased) if no flow seen under standard conditions. Pulsed Doppler for velocity profile assessment using angle of insonation <60 degrees. Standardised sequential longitudinal and axial views of the entire extracranial carotid system using greyscale, colour and spectral modalities
Contrast enhanced US (test 2)	**US contrast agent: Levovist (Schering, UK) − 99.9% galactose, 0.1% palmitic acid, as granules** **Otherwise equipment as for test 1** 2.5 g vial of Levovist prepared according to manufacturers instructions with 5 ml water for injections, reconstituting to make 6.5 ml Levovist 400 Solution injected at 1 ml/second via indwelling 18 or 20 G iv cannula in the antecubital vein Scan protocol thereafter as per conventional US
2D-TOF MRA (test 3)	**Philips ACS NT MRI scanner at 1.5 Tesla** **Quadrature neck coil** 2D FFE inflow technique **Scan parameters:** TR 25 ms, TE 7 ms, Flip angle 25deg, FoV 22 cm, RFoV 80%, Matrix 256 × 256, Slice thickness 3/1, axial scan plane
CE-MRA (test 4)	**MR contrast agent: Magnevist (Schering,** UK) − gadopentetic acid in solution **Otherwise equipment as for test 3** 30 ml Magnevist (14.1 g), followed by 20 ml saline chaser injected by automated injector at 1 ml/second via indwelling 18 or 20 G iv cannula in the antecubital vein **Scan parameters:** Spoiled GE sequence: TR 5 ms, TE 1.5 ms, Flip angle 40deg, FoV 22 cm, RFoV 80%, Matrix 512 × 200, Slice thickness 1/0.5, Phase order low-high (centric k-space filling), Scan initiation Bolus-Trak, coronal scan plane.
DSA (test 5)	**Siemens Angiostar vascular suite** **Angiographic catheters as available/needed** **Angiographic contrast agent: Ultravist 370 − lopromide 370 mg/ml** Outpatient examination unless contraindicated 1 l normal saline as prehydration via iv cannula 4Fr puncture into common femoral artery. Insertion of 4Fr sheath. Pigtail catheter advanced to arch. Arch injection (25 ml contrast at 15 ml/min) to assess ostia of carotids followed by selective cannulation of common carotid artery with various catheters (as appropriate) over soft hydrophilic guidewire. Assessment of cervical carotid (at least 2 views) and intracranial circulation following selective injection of 10 ml diluted contrast (to approx. 300 mg/ml). Imaging rate of 2 frames/sec with prolonged runs to detect faint antegrade flow in carotid. Patient discharged home after two hours observation in recovery area and if puncture site and neurology satisfactory. Data archived electronically onto compact disc and stored.

Sensitivity and specificity were calculated for each technique against DSA for its ability to detect patency and a surgically correctible lesion. Calculations were made using pre-prepared worksheets in Microsoft® Excel®.

The study had local ethical committee approval.

Results

Between April 2001 and August 2004, 56 patients agreed to participate. Three of these 56 patients had apparent bilateral ICA occlusions diagnosed on their initial conventional US, making a total of 59 vessels enrolled into the study. Nineteen vessels were excluded on the basis of incomplete imaging due to patient failure to attend (8 vessels), claustrophobia and inability to tolerate MRA (10 vessels), or refusal to consent to DSA (1 vessel). A further 9 vessels were excluded because there was a delay of >14 days in completing of their imaging. Thus 31 vessels (in 30 patients) underwent all 5 imaging tests with a median delay (from initial confirmatory US) of 1 day (range 0−9 days) to MRA and 0 days (range 0−9 days) to DSA.

Reference standard − DSA and decision to operate

DSA confirmed carotid occlusion in 25/31 (81%) vessels (Fig. 1a). Of the remaining 6 patent vessels, 2 were very irregular, with filling of the intracranial vessels from the contralateral side or from external carotid artery (ECA) collaterals via the ophthalmic artery. These vessels were considered unsuitable for CEA. A third patent vessel with an irregular distal lumen was also classified as unsuitable for CEA.

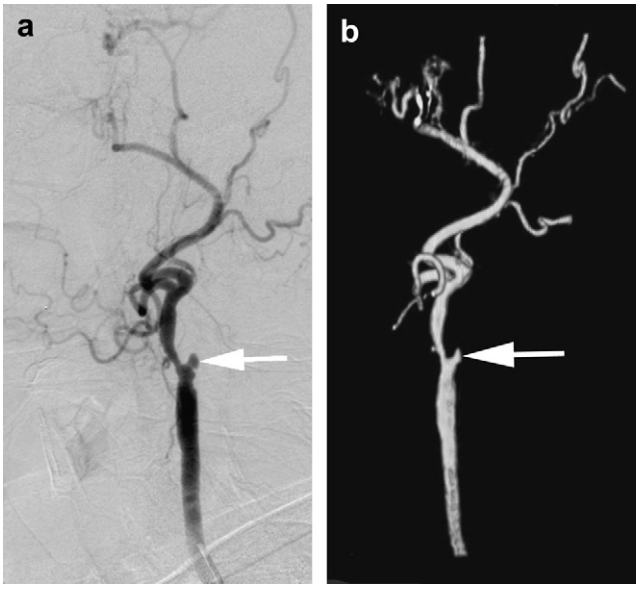

Fig. 1. a: DSA following left common carotid artery injection demonstrating a small stump of proximal ICA (arrow) with no demonstrable flow beyond it, indicating a proximal ICA occlusion. b: Surface shaded maximum-intensity projection CE-MRA of the left CCA, ICA and ECA, demonstrating a small stump of proximal ICA (arrow) with no demonstrable signal beyond it, indicating proximal ICA occlusion (same patient as Fig. 1a).

Three remaining vessels had tight focal origin stenoses with smooth collapsed lumens beyond these, with flow into the ipsilateral middle cerebral artery. These were considered suitable for CEA (Fig. 2a) and 2 patients with recurrent ipsilateral hemispheric symptoms underwent surgery. The third patient in this group did not undergo surgery as his on-going symptoms were related to the contralateral cerebral hemisphere. No other patients underwent CEA. At surgery, both operated vessels were found to be patent.

Conventional-US

All patients enrolled into the study had their apparent carotid occlusion confirmed at confirmatory conventional US (test 1).

CE-US

A confident diagnosis could not be made in 5/31 (16%) vessels. Two investigations were technically inadequate due to patient movement or contrast flooding. In 3 vessels there was uncertainty in distinguishing between patency and occlusion. These investigations were classified as non-diagnostic. In the 26 remaining vessels, 24 were classified as definitely occluded and 2 as definitely patent.

Table 2 compares assessment of patency by CE-US with DSA. When the diagnosis of patency or occlusion was confident, this agreed with DSA in all cases. The sensitivity of a confident diagnosis of patency or occlusion *versus* DSA is therefore 1, with a specificity of 1. When patent but non-surgically correctible lesions are accounted for the sensitivity of confident CE-US diagnosis this *versus* DSA is 1, with a specificity of 0.96.

2D-TOF MRA

All 2D TOF MRA examinations were technically adequate. Inter-observer agreement of assessment of patency was substantial ($\kappa = 0.65$). There was a single vessel over which there was disagreement. The consensus was that the vessel was patent on 2D-TOF MRA. This vessel was suitable for CEA on DSA. Following consensus, 2 ICAs were characterized as patent and 29 as occluded. Four of these were patent on DSA including 1 which was suitable for CEA. These results are summarised in Table 3a.

The sensitivity of 2D-TOF MRA to detect patency is therefore 0.33 with a specificity of 1. Even for identifying arteries with a surgically correctible lesion, the sensitivity was 0.67, again with a specificity of 1. Exclusion of the vessel over which there was disagreement would have *reduced* sensitivity further.

CE-MRA

A single CE-MRA examination was abandoned due to coil failure after the 2D-TOF images had been obtained. This vessel was suitable for CEA on DSA.

Inter-observer agreement of assessment of patency was good ($\kappa = 0.78$). There was a single vessel over which there was disagreement. The consensus was that the vessel was patent on CE-MRA. Although this vessel was patent on DSA, it was unsuitable for CEA. Following consensus, 3 ICAs were characterized as patent (Fig. 2b) and 27 as occluded (Fig. 1b), 2 of which were patent on DSA. Neither of these vessels was suitable for CEA. Thus CE-MRA correctly identified 3 patent vessels, 2 of which were suitable for CEA on DSA.

The sensitivity of CE-MRA to detect patency *versus* DSA is therefore 0.6 with a specificity of 1, and 1 and 0.96 respectively for identifying a surgically correctible lesion (Table 3b).

Interobserver assessment of suitability of ICA stenosis for CEA on MRA

There was no agreement ($\kappa = 0$) regarding the suitability for CEA of the three vessels characterised as patent on

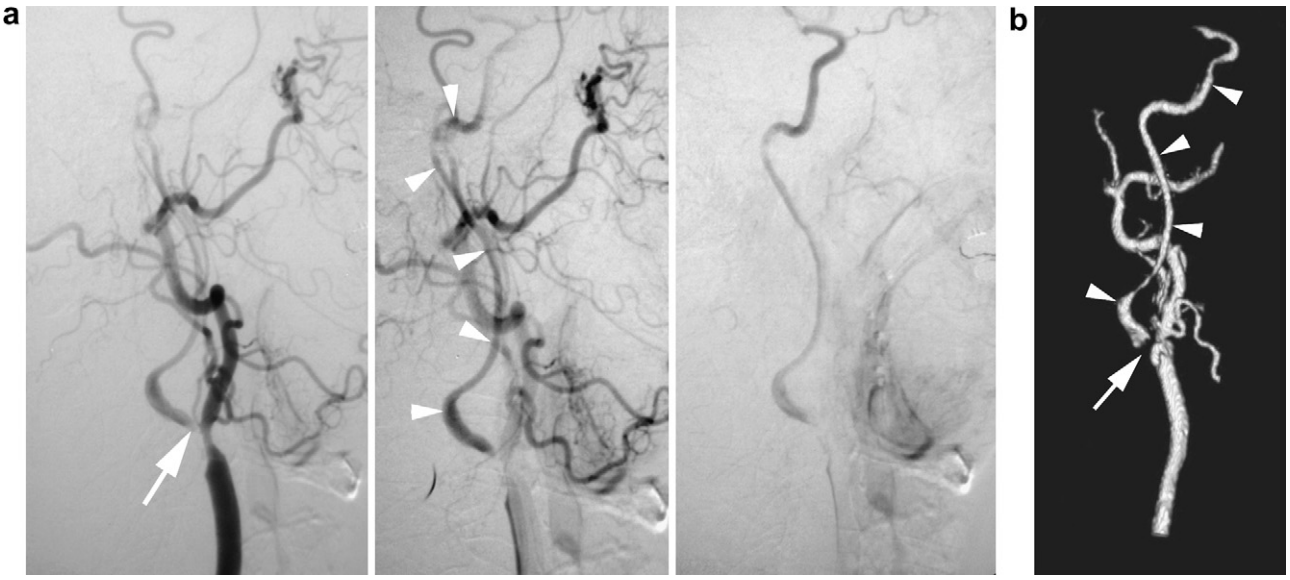

Fig. 2. a: DSA immediately following left common carotid injection (left hand pane) with subsequent (middle pane) and delayed (right hand pane) images of the same region. There is a tight focal stenosis of the proximal ICA (arrow) with forward flow of contrast along a smooth walled distal ICA (arrowheads) beyond the stenosis. The delayed image shows contrast arriving at the siphon with no evidence of backfilling of unopacified blood from the other side. The left middle cerebral artery filled from the left CCA injection. This patient underwent CEA. b: Surface shaded maximum-intensity projection CE-MRA of the left CCA, ICA and ECA, demonstrating a tight proximal ICA stenosis within which there is no discernible signal (arrow) but with good filling of the ICA distal to this (arrowheads) up to the carotid siphon (same patient as Fig. 2a).

CE-MRA. It was felt that the lack of dynamic flow information, inability to assess filling of the cerebral vasculature and the lower spatial resolution of MRA, compared with DSA, made this assessment very difficult.

Discussion

Modern duplex ultrasound is very sensitive to flow. Mansour *et al.*[8] reported a sensitivity of over 99% for detecting ICA patency relative to a reference standard of selective DSA. Others have described similar results for US in patients known to have a tight stenoses on DSA.[10] The relatively small size of our study stems from this high sensitivity of US to flow since patients with a patent ICA on US were never candidates for inclusion.

Of the 31 vessels in our study, only 6 were subsequently found (on DSA) to be patent, of which 3 (10%) were suitable for CEA. In the face of this low incidence of surgically correctible lesions in arteries said to be occluded on conventional US, and the potential risks of DSA, particularly in patients with severe carotid disease,[6] the question arises as to how to identify patients who might benefit from CEA whilst minimising the number undergoing angiography. A pre-angiography screening test is required with a false-negative rate of zero (thereby identifying *all* potential surgical candidates). An occluded vessel would therefore require no further imaging. If apparently patent vessels then proceed to angiography, the false-positive rate need not be zero, but should be as close to this as possible. In other words, the *sensitivity* of the test for patency (or for a surgically correctible lesion) should be unity relative to DSA, with a secondary requirement that it is to be *specific enough* to render it clinically useful. This is important when

Table 2. Performance of CE-US versus DSA in assessing patency of ICA

		CE-US		
		Patent	Occluded	Non diagnostic
DSA	Patent	2	0	4
	Occluded	0	24	1
DSA (suitability for CEA)	Suitable	1	0	3
	Unsuitable	1	24	2

Table 3a. Performance of 2D-TOF MRA *versus* DSA in assessing patency of ICA

		2D-TOF MRA	
		Patent	Occluded
DSA	Patent	2	4
	Occluded	0	25
DSA (suitability for CEA)	Suitable	2	1
	Unsuitable	0	28

Table 3b. Performance of CE-MRA *versus* DSA in assessing patency of ICA

		CE-MRA	
		Patent	Occluded
DSA	Patent	3	2
	Occluded	0	25
DSA (suitability for CEA)	Suitable	2	0
	Unsuitable	1	27

The 1 patient with coil failure is not included.

considering the performance of CE-US, 2D-TOF MRA and CE-MRA.

Contrast-enhanced ultrasound

Echo enhancement agents such as Levovist consist of microbubbles suspended in the plasma and increase the strength of echoes returned from blood by up to 30 dB.[11] Several studies have evaluated the use of ultrasound contrast agents in the assessment of severe carotid stenosis and occlusion[12–15] confirming ease of use and increased visualization of flow compared to conventional US. Sensitivities of CE-US for patency of 0.83–1 are reported. However, none of these studies are comparable to ours as they included patients with a patent but tightly stenosed ICA on conventional US. Such patients were excluded from the present study which is confined to a population with more extreme disease. This may explain the relatively high rate of non-diagnostic/equivocal investigations in this group.

Ferrer *et al.*[16] have reported a further study of 85 patients with apparent ICA occlusion on conventional US with a reference standard of DSA or surgical exploration. A confident diagnosis of patency (7 vessels) or occlusion on CE-US was made in all cases, with no cases in which patency was uncertain and no technical failures. Further, CE-US agreed with the reference standard in all patients (sensitivity and specificity of 1) and the authors concluded that DSA need only be used in exceptional cases. To some extent, these findings mirror the results reported here with all patent and all occluded vessels correctly identified by CE-US when the operator was confident of the diagnosis. However, in our study, of 2 vessels identified as patent by CE-US only 1 was suitable for CEA, an outcome not reported by Ferrer *et al.* Thus we cannot recommend CEA simply on CE-US confirmed ICA patency. In addition, CE-US did not make a conclusive diagnosis in 5 vessels. This occurred despite CE-US being performed independently by 2 highly experienced vascular sonographers.

As a result 7/31 vessels (23%) in this study would require further investigation to reach a definitive conclusion as to the suitability of the vessel for CEA. Although a protocol of CE-US followed by DSA in vessels not definitely occluded would ensure that no vessels suitable for CEA are missed, 1 in 4 vessels would require DSA.

2D-TOF magnetic resonance angiography

A 2D- rather than 3D-TOF sequence was selected as it is more sensitive to slow flow in highly stenotic arteries due to the lack of in-volume flow-saturation effects.[12,17] Despite this 2D-TOF MRA was insensitive (sensitivity = 0.33) for the detection of patency in this cohort of patients. This low sensitivity may reflect very slow flow through a tight stenosis, resulting in decreased inflow of unsaturated blood into the imaging slice and consequent loss of signal, or in-stenosis and post-stenotic turbulent flow also which contributes to signal loss in TOF-MRA.[18]

Prospective studies of near-occlusion on DSA report sensitivities for patency of 2D-TOF MRI of 0.65–0.95.[12,17] These are better than those reported here but again reflect the proportion of study patients who had a patent ICA on conventional US. It is expected that the more advanced atherosclerosis in our study group would be associated with slower flow and an increased likelihood of signal loss and misclassification. There have been no previous studies evaluating the performance of 2D-TOF MRI in a population such as the one reported here. The low sensitivity of 2D-TOF MRA for both vessel patency and a surgically correctible lesion means that this modality cannot be recommended as a screening tool, following conventional US, to reduce the requirement for DSA. Such a policy would result in 1 in 3 vessels with a correctible lesion being misclassified as occluded and not investigated further.

CE-MRA

Contrast enhanced MRA relies on contrast agent mediated T1 shortening of blood to define vessel anatomy. It overcomes the problem of signal loss due to slow-flow and turbulence and is less likely to overestimate stenoses.[19] This is confirmed by its improved performance over 2D-TOF MRA in detecting patency in the present study.

Although numerous studies have assessed the performance of CE-MRA versus DSA in unselected populations, with reported sensitivities for the detection of near-occlusion (as opposed to occlusion) of 0.78–1,[17,20–22] none have evaluated its performance in patients with apparent ICA occlusion on conventional US. Our sensitivity of 0.6 (for the detection of patency) is outwith this range but, is again likely to reflect the

more severe disease in our patient group. Despite this apparently disappointing result we found that CE-MRA successfully identified all patients in whom a patent ICA was suitable for CEA. This finding is crucial.

Of the 3 patent vessels on CE-MRA, only 2 were deemed suitable for CEA on subsequent DSA and thus surgery cannot be recommended on the basis of patency alone. ICA flow and ipsilateral cerebral filling are important factors in assessing surgical suitability and this dynamic information is unavailable on non-time resolved MRA. 3/30 (10%) ICAs scanned with CE-MRA would therefore need DSA to ensure that the option of CEA is never missed. However, 10 vessels in the originally recruited cohort could not be scanned due to patient inability to tolerate MRA. If these vessels are taken into account then 13 of 59 vessels (22%) would require DSA.

Clinical utility of CE-US, 2D-TOF MRA and CE-MRA

2D-TOF cannot be recommended as a second line screening investigation following conventional US as it lacks sensitivity. CE-US and CE-MRA identified all potential candidates for CEA with about 1 in 5 patients requiring subsequent DSA. The relative advantages of a policy of CE-US or CE-MRA as a second line screening tool are unclear: CE-US can be performed at the same visit as the conventional US and is an alternative to CE-MRA if the patient cannot tolerate or has other contraindications to MRA. On the other hand, if a patient can tolerate CE-MRA then a greater proportion of studies are diagnostic.

Other techniques

It has been reported that carotid CT angiography (CTA) has an excellent correlation with angiography in differentiating total from near occlusion in an unselected population[23] although in a population with apparent US-detected carotid occlusion the sensitivity for patency of dual slice CTA is 0.96[24] indicating that a small proportion of patent vessels would be missed using this technique. At present it cannot be recommended as a second line screening tool. Modern multislice CTA may offer improved performance although dynamic flow information would be lacking and DSA would still be required for patent vessels. The current study did not assess the accuracy of CTA.

Limitations and applicability of the study

The results should be interpreted with some caution as the study size was small and the recruitment period prolonged. Further, our first patient was recruited in 2001 and advances in US and MR technology have made modern scanners more sensitive to slow flow. Nevertheless, confirmation of apparent carotid occlusion remains an important (albeit infrequent) clinical issue in patients with recent ipsilateral hemispheric symptoms. It is likely, but unproven, that improvements in scanning technology have improved the clinical utility of these modalities over that observed in the current study.

Conclusions

The small size of our study, lengthy recruitment period and the low number of patent vessels emphasises the sensitivity of modern conventional US to flow. When carotid occlusion is identified on conventional US, in the presence of ipsilateral hemispheric symptoms, confirmation of this diagnosis is required to prevent patients being denied the opportunity to benefit from surgery. In order to minimise the number of patients undergoing angiography, a second line investigation is required with sensitivity for patency equivalent to that of DSA, and which is specific enough to be clinically useful. Vessels that are not definitely occluded can then go on to DSA.

Our data suggest that symptomatic patients found to have an occluded ICA on conventional US confirmation of the diagnosis is reliably achieved by CE-US or CE-MRA. In patients in whom a patent ICA is identified, angiography is required to accurately assess its suitability for CEA. Definite occlusion on CE-US or CE-MRA requires no further investigation. The relative advantages of a policy of CE-US or CE-MRA as a second line screening tool are uncertain.

Acknowledgements

Thanks to Mrs Lesley Stead, Mrs Sandra Wood, Dr Jonathan Barber and Mr Demos Dellagrammaticas for their assistance in the execution of this study.

Conflict of interest statement

No conflicts of interest on the part of any of the authors in the preparation of this paper.

Funding source

No funding obtained.

References

1 North American symptomatic carotid endarterectomy trial collaborators. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *N Engl J Med* 1998;**339**:1415–1425.

2 European carotid surgery trialists' collaborative group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European carotid surgery trial (ECST). *Lancet* 1998;**351**:1379–1387.

3 Rothwell PM, Eliasziw M, Fox AJ, Taylor DW, Mayberg MR, Warlow CP *et al*, for the carotid endarterectomy trialists' collaboration. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet* 2003;**361**:107–116.

4 Verlato F, Camporese G, Bernardi E, Salmistraro G, Rocco S, Mayellaro V *et al*. Clinical outcome of patients with internal carotid occlusion: a prospective follow up study. *J Vasc Surg* 2000;**32**:293–298.

5 Archie Jr JP. Carotid endarterectomy when the distal internal carotid artery is small or poorly visualized. *J Vasc Surg* 1994;**19**:23–31.

6 O'Leary DH, Mattle H, Potter JE. Atheromatous pseudo-occlusion of the internal carotid artery. *Srtoke* 1989;**20**:1168–1173.

7 Kniemeyer HW, Aulich A, Schlachetzki F, Steinmetz H, Sandmann W. Pseudo- and segmental occlusion of the internal carotid artery: a new classification, surgical treatment and results. *Eur J Vasc Endovasc Surg* 1996;**12**:310–320.

8 Mansour MA, Mattos MA, Hood DB, Hodgson KJ, Barkmeier LD, Ramsey DE *et al*. Detection of total occlusion, string sign, and preocclusive stenosis of the internal carotid artery by color-flow duplex scanning. *Am J Surg* 1995;**170**:154–158.

9 Leffers A-M, Wagner A. Neurologic complications of cerebral angiography. A retrospective study of complication rate and patient risk factors. *Acta Radiologica* 2000;**41**:204–210.

10 Berman SS, Devine JJ, Erdoes LS, Hunter GC. Distinguishing carotid artery pseudo-occlusion with color flow Doppler. *Stroke* 1995;**26**:434–438.

11 Droste DW, Kaps M, Navabi DG, Ringelstein EB. Ultrasound contrast enhancing agents in neurosonology: principles, methods, future possibilities. *Acta Neurol Scand* 2000;**102**:1–10.

12 Fürst G, Saleh A, Wenserski F, Malms J, Cohnen M, Aulich A *et al*. Reliability and validity of noninvasive imaging of internal carotid pseudo-occlusion. *Stroke* 1999;**30**:1444–1449.

13 Ohm C, Bendick PJ, Monash J, Bove PG, Brown W, Long GW *et al*. Diagnosis of total internal carotid occlusions with duplex ultrasound and ultrasound contrast. *Vasc Endovasc Surg* 2005;**39**:237–243.

14 Hofstee DJ, Hoogland PH, Schimsheimer RJ, de Weerd AW. Contrast enhanced color duplex for diagnosis of subtotal stenosis or occlusion of the internal carotid artery. *Clin Neurol Neurosurg* 2000;**102**:9–12.

15 Droste DW, Jürgens R, Nabavi DG, Schuierer G, Weber S, Ringelstein B. Echocontrast enhanced ultrasound of extracranial internal carotid artery high-grade stenosis and occlusion. *Stroke* 1999;**30**:2302–2306.

16 Ferrer JM, Samso JJ, Serrando JR, Valenzuela VF, Montoya SB, Docampo MM. Use of ultrasound contrast in the diagnosis of carotid artery occlusion. *J Vasc Surg* 2000;**31**:736–741.

17 El-Saden S, Grant EG, Hathout GM, Zimmerman PT, Cohen SN, Baker JD. Imaging of the internal carotid artery: the dilemma of total versus near occlusion. *Radiology* 2001; **221**:301–308.

18 Summers PE, Jarosz JM, Markus H. MR angiography in cerebrovascular disease. *Clin Radiol* 2001;**56**:437–456.

19 Sardanelli F, Zandrino F, Parodi RC, De Caro G. MR angiography of internal carotid arteries: breath-hold Gd-enhanced 3D fast imaging with steady-state precession verus unenhanced 2D and 3D time-of-flight techniques. *J Comput Assist Tomogr* 1999;**23**:208–215.

20 Johnson MB, Wilkinson ID, Wattam J, Venables GS, Griffiths PD. Comparison of Doppler ultrasound, magnetic resonance angiographic techniques and catheter angiography in evaluation of carotid stenosis. *Clin Radiol* 2000;**55**: 912–920.

21 Remonda L, Heid O, Schroth G. Carotid artery stenosis, occlusion and pseudo-occlusion: first-pass gadolinium-enhanced three-dimensional MR angiography – preliminary study. *Radiology* 1998;**209**:95–102.

22 Remonda L, Senn P, Barth A, Arnold M, Lövblad K-O, Schroth G. Contrast-enhanced 3D MR angiography of the carotid artery: comparison with conventional digital subtraction angiography. *AJNR Am J Neuroradiol* 2002;**23**:213–219.

23 Chen C-J, Lee T-H, Hsu H-L, Tseng Y-C, Lin S-K, Wang L-J *et al*. Multi-slice CT angiography in diagnosing total versus near occlusions of the internal carotid artery. Comparison with catheter angiography. *Stroke* 2004;**35**:83–85.

24 Lubezky N, Fajer S, Barmeir E, Karmeli R. Duplex scanning and CT angiography in the diagnosis of carotid artery occlusion: a prospective study. *Eur J Vasc Endovasc Surg* 1998;**16**: 133–136.

Accepted 16 December 2007
Available online 8 February 2008