Imaging of the carotid arteries: the role of duplex ultrasonography, magnetic resonance arteriography, and computerized tomographic arteriography

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Abstract: Stenosis of the internal carotid artery represents a major cause of stroke, with atherosclerosis representing the major pathophysiology of this stenosis. It is estimated that over 700,000 Americans suffer a stroke annually. A prompt and accurate diagnosis of carotid artery disease is critical when planning a therapeutic strategy. Physical examination is inaccurate in determining the presence and severity of carotid artery disease. Therefore, reliable imaging tests which offer little risk to the patient are required.

Key words: carotid artery diseases; diagnostic; imaging

Indications for non-invasive imaging

Stroke represents a major health hazard, with over 700,000 events occurring annually in the United States along.[1] Non-invasive imaging of the internal carotid arteries (ICA) is indicated in several clinical settings. Patients undergoing evaluation for acute stroke should have carotid imaging due to the large proportion of embolic strokes (20–25%) that originate from the carotid artery.[2] Transient ischemic attacks (TIA) are also an indication for ICA imaging, as there is a significantly increased risk of stroke in the months following a TIA.[3–5] While cervical bruits are neither a sensitive nor specific indicator of severe carotid artery disease, as many as one-third of patients with bruits have severe ICA stenosis,[6] and therefore patients with cervical bruits should undergo evaluation for carotid artery stenosis. Although carotid artery imaging prior to coronary artery bypass graft surgery is controversial and beyond the scope of this manuscript, it remains an important area of debate among clinicians.[7] A recent review of the literature suggests that a carefully planned approach using non-invasive imaging can replace invasive angiography for carotid artery assessment in a cost-effective and safe manner.[8]

Currently, indications for carotid duplex ultrasonography (DUS) which are acceptable for reimbursement include: cervical bruit; amaurosis fugax; focal or cerebral transient ischemic attacks; drop attacks or syncope; episodic dizziness with symptoms characteristics of transient ischemic attacks; evaluation and follow-up of cervical bruits (http://www.empiremedicare.com/newypolicy/policy/l3743_final.htm).

Diagnostic algorithms

The choice of modality for non-invasive carotid artery assessment depends largely on the clinical indications for imaging and the skills available in individual centers. For emergency patients with a high likelihood of neurovascular disease requiring immediate therapy, such as those with acute stroke, computerized tomographic arteriography (CTA) is an appropriate first exam. For screening of patients with a lower probability of neurovascular disease requiring urgent or surgical intervention, including those with TIA, carotid DUS followed by magnetic resonance angiography (MRA) is routinely obtained along with parenchymal brain imaging. If significant stenotic disease of the ICA is detected, DUS or CTA can be used to confirm the diagnosis and more accurately determine the precise degree of stenosis.[6,9] For asymptomatic patients, such as those with an audible bruit or in those patients scheduled for coronary artery bypass graft

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Figure 4 is available to view in color online at http://vmj.sagepub.com

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Table 1 Duplex ultrasound criteria for *de novo* carotid artery stenosis

Stenosis severity	Peak systolic velocity (PSV) (cm/s)	End-diastolic velocity (EDV) (cm/s)	Spectral broadening
1–14%	<125	N/A	None
15–49%	<125	N/A	Present
50–79%	>125	<140	Present
80–99%	>125	>140	Diffuse
Occluded	0	0	N/A

N/A, not applicable.
Data from ref. 11.

surgery, DUS is an accurate and cost-effective non-invasive screening tool. If significant ICA stenosis is identified based on the DUS results, some authors suggest further testing with MRA to add specificity and exclude tandem intracranial lesions or other anatomic variants that may affect surgery. Until recently, CTA has been reserved as a problem-solving tool for cases in which DUS and MRA results are discordant or inconclusive. Intra-arterial digital subtraction arteriography (IADSA) is rarely required in cases of severe multi-vessel disease, for which assessment of flow direction and collateral patterns may be desirable, or when the quality of non-invasive imaging is of limited value (Figure 1).[10]

Duplex ultrasonography

Carotid duplex ultrasonography (CDUS) is the standard of care for the initial diagnosis of carotid artery bifurcation disease. Initial Doppler criteria proposed by Strandness, *et al.*[11] utilized measurements of the spectral waveform to predict ICA stenosis (Table 1). Subsequently, alternative criteria were developed which have resulted in excellent sensitivity and specificity of DUS to determine high-grade stenosis.[12] Meta-analyses of published criteria for CDUS have demonstrated sensitivities of 98% and specificities of 88% for detecting > 50% ICA stenosis; and 94% and 90% respectively for detecting > 70% ICA stenosis.[13] Given the multitude of diagnostic criteria, a multi-specialty consensus conference convened and developed criteria based on review of the published literature[14] (Table 2).

Techniques

The performance of high-quality and accurate CDUS requires excellent technical equipment; skilled vascular technologists; and knowledgeable physician interpreters. Prior to the performance of CDUS, technologists must obtain a brief patient history, including any previous vascular interventional procedures.

1) A bilateral examination is performed of the common carotid (CCA), internal carotid (ICA), external carotid (ECA) and the vertebral arteries (VA) (Figure 2).
2) Real-time B-mode imaging is conducted as a separate segment of the exam from the spectral Doppler evaluation to accommodate the optimal vessel to beam angles required for each component. The best B-mode images are obtained using a 90° angle. A Doppler angle of 60° or less is optimal for the spectral Doppler.
3) Gray-scale images are obtained throughout the course of the CCA and ICA, in both transverse and sagittal views. Evaluation includes identification of plaque location and composition (i.e. homogeneous, heterogeneous, calcific) (Figure 3).

Utilizing gray-scale B-mode imaging, color and Doppler flow provide all of the imaging tools required to determine the severity of ICA stenosis. The absence or presence of hemodynamically significant disease in the ICA is determined by an increase in Doppler-derived blood flow velocity. Therefore, the accuracy of the exam is dependent upon the accuracy of the spectral Doppler waveform interrogation (Figure 4). To minimize any potential errors

Table 2 Society for Radiology in Ultrasound criteria[14] for carotid artery stenosis grading with duplex ultrasonography

Degree of stenosis (%)	ICA PSV (cm/s)	Plaque estimate (%)	ICA/CCA PSV ratio	ICA EDV (cm/s)
Normal	<125	None	<2.0	<40
<50	<125	<50	<2.0	<40
50–69	125–230	>50	>4.0	<100
≥70 but less than near occlusion	>230	>50	>4.0	>100
Near occlusion	High, low, or undetectable	Visible	Variable	Variable
Total occlusion	Undetectable	Visible, no detectable lumen	N/A	N/A

ICA, internal carotid artery; PSV, peak systolic velocity; CCA, common carotid artery; EDV, end-diastolic velocity; N/A, not applicable.

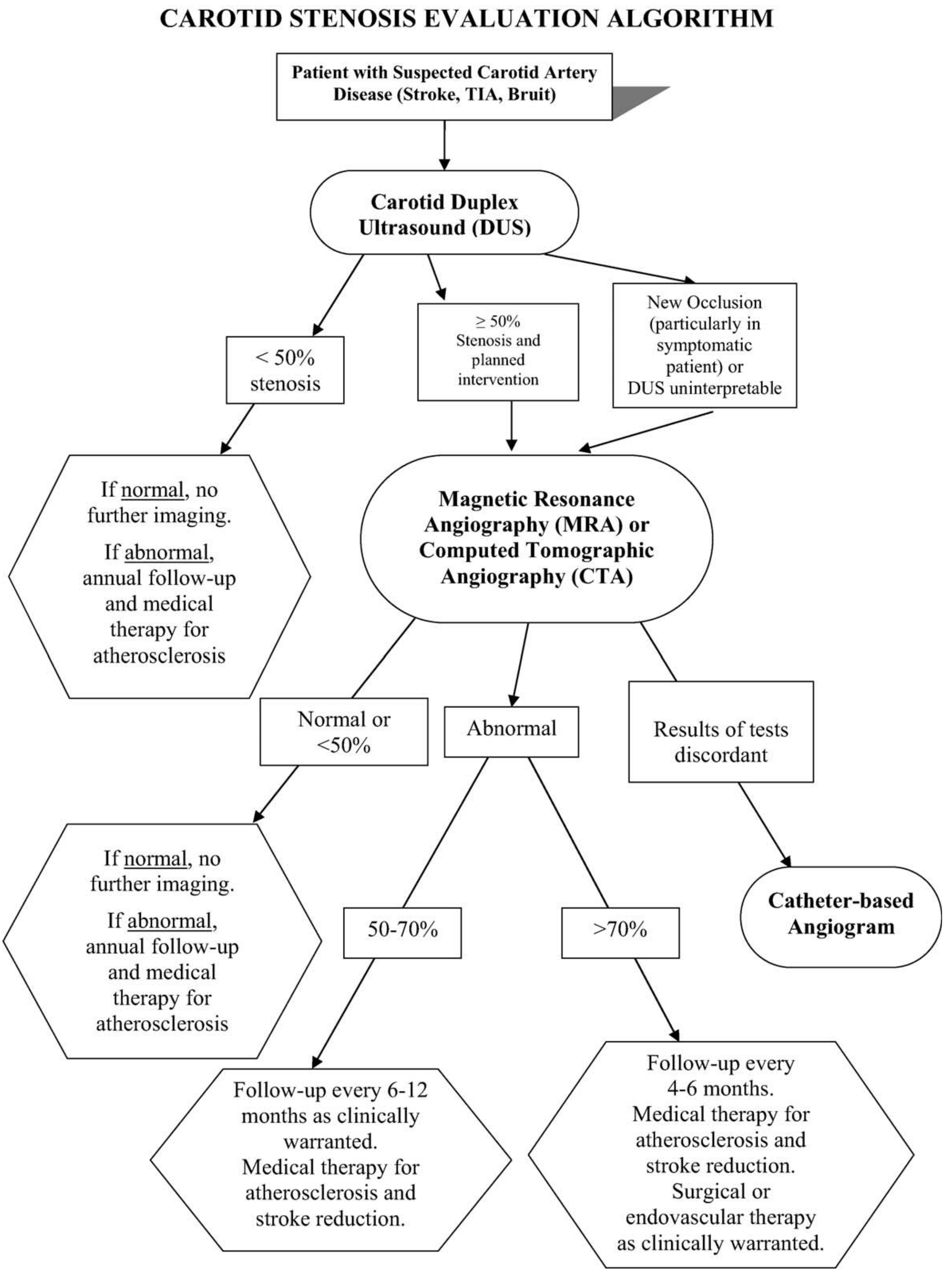

Figure 1 Diagnostic algorithm for asymptomatic carotid stenosis. A proposed diagnostic algorithm for the use of non-invasive imaging in evaluation of the carotid arteries in asymptomatic patients.[10] This algorithm reflects clinical practice at our institution, and is not based on published guidelines or level 1 evidence. A stroke workup should proceed directly to CTA, whereas TIA is initially evaluated with MRA, with CTA used to confirm/clarify findings.

in measuring the blood flow velocity it is essential to standardize the Doppler technique.

The standardized spectral Doppler technique includes the following elements.

1) Obtain waveforms from a long axis view of the artery, using a small sample volume placed in the center stream of flow or center to the flow ‘jet’.
2) Align the cursor parallel to the vessel wall.

Figure 2 Gray-scale duplex ultrasound image of the carotid bifurcation. This image demonstrates the distal CCA, and proximal ICA and ECA.

Figure 3 Gray-scale duplex ultrasound image of proximal ICA plaque. There is a partially calcific plaque with an area of homogeneity in the ICA, suggestive of a largely lipid-laden plaque on the posterior wall.

3) Standardize the Doppler angle, with the recommended Doppler angle of 60° or less. A correct Doppler angle is required to calculate the peak systolic velocity (PSV). If the angle measurement is correct, the cursor will be parallel to the vessel wall.
4) Survey the vessel to obtain the maximum PSV by 'walking or sweeping' the Doppler sample volume throughout the artery in specific areas of interest.

Spectral Doppler waveforms are obtained from standardized sites including the origin, proximal, mid, and distal CCA; proximal, mid, and distal ICA; proximal ECA; and proximal/mid vertebral artery.

Each vessel has a characteristic normal waveform pattern based on the vascular bed distal to the artery. The normal waveform pattern for each vessel is:

- CCA: low-resistance waveform with a brisk upstroke, continuous but less forward flow throughout diastole than the ICA. The CCA reflects flow in both the ICA (low-resistance vascular bed) and ECA (high-resistance vascular bed).
- ICA: low-resistance waveform with continuous forward flow throughout diastole.

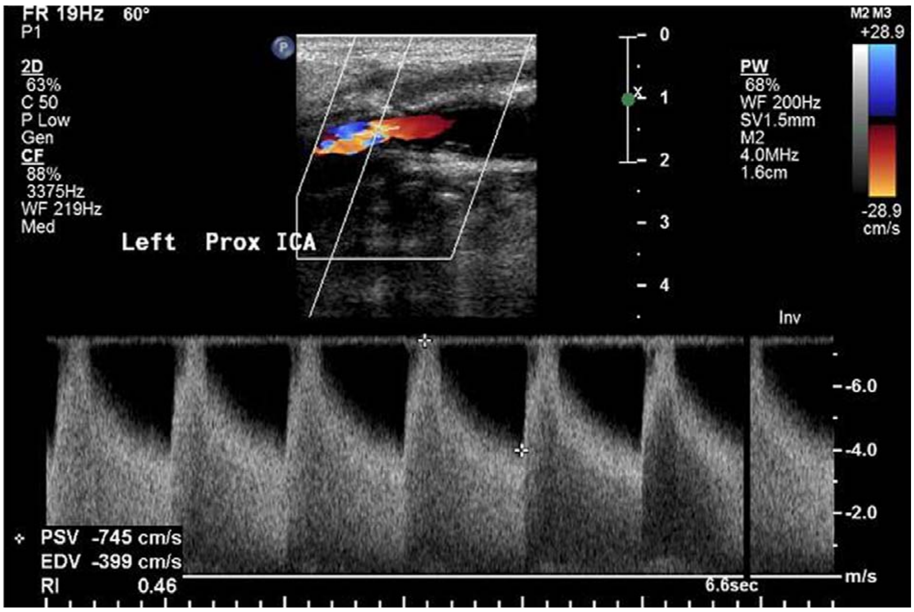

Figure 4 Duplex ultrasonography of a severe ICA stenosis. Gray-scale, color, and Doppler analysis with appropriate Doppler angle, demonstrating PSV 745 cm/s and EDV 399 cm/s, consistent with >80% ICA stenosis.

- ECA: higher resistance with increased pulsatility compared with CCA and ICA, rapid sharp systolic upstroke, and diminished diastolic flow.
- VA: low-resistance waveform with continuous forward flow throughout diastole.

Technologists are often required to scan in multiple planes to minimize 'acoustic shadowing', a common Doppler artifact due to plaque calcification. PSV and end-diastolic velocity (EDV) must be recorded throughout the CCA and ICA, including the most distal aspect of the ICA.

Lack of interrogation of the origin of the CCA may result in lack of appreciation of aortic arch disease. Although less common than bifurcation stenoses, DUS cannot visualize the distal ICA beyond the angle of the jaw, nor can DUS determine the presence of intracranial stenosis. Densely calcific carotid plaque will result in obscuration of the lumen of the ICA, thereby making direct determination of stenosis severity difficult (Figure 5).

Limitations of carotid duplex includes acoustic shadowing from calcific atherosclerotic plaque, which inhibits Doppler interrogation, false elevation in PSV with contralateral ICA occlusion, and increased PSV in tortuous vessels without stenosis.

DUS and carotid revascularization

There is extensive literature suggesting the reliability of DUS in determining patency of carotid endarterectomy over time. However, recently, carotid stents have gained United States Food and Drug Administration approval for use in patients at high risk for carotid endarterectomy with 70–99% symptomatic carotid stenosis. Although images of carotid stents are quite simple to obtain (Figure 6), reliable Doppler criteria to predict hemodynamically important in-stent restenosis are lacking. There are several aspects to the determination of in-stent restenosis on DUS which should be considered:

1) focal increase in both PSV and EDV
2) increase in the ratio of the PSV within the ICA and CCA
3) turbulence at the exit of the stenosis (post-stenotic turbulence (PST))
4) diffuse spectral broadening
5) diminished velocities beyond the stenosis, often found within the stent
6) color Doppler changes such as a decreased lumen at the site of increased velocities and/or color bruit
7) detectable change in the audible Doppler signal both at the area of stenosis and in the region of PST
8) a measurable change in the PSV, EDV, and ICA/CCA systolic velocity ratio when compared with previous examinations.

A recent single center study of 111 patients who underwent carotid stenting and subsequent surveillance DUS within 30 days of the procedure and then every 6 months thereafter demonstrated the importance of comparison examinations over time. The duplex criteria suggestive of > 75% stenosis included PSV > 300 cm/s, EDV > 125 cm/s, ratio of PSV of the ICA stent to the CCA > 4.0. During the mean 33-month follow-up, six stents developed duplex criteria suggestive of > 75% stenosis, all confirmed on arteriography.[15]

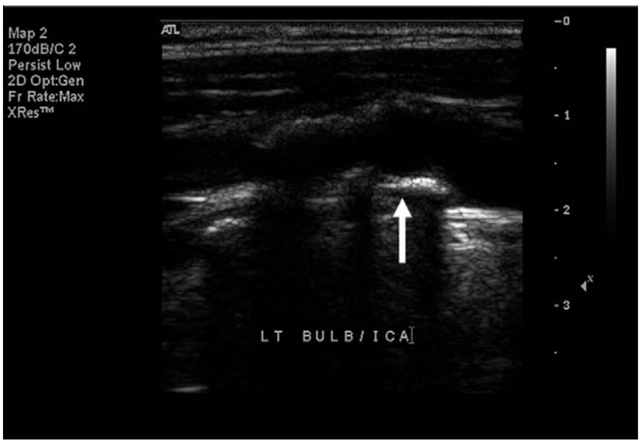

Figure 5 Gray-scale duplex ultrasonography of the ICA. There is a densely calcific atherosclerotic plaque in the ICA, causing acoustic shadowing posteriorly.

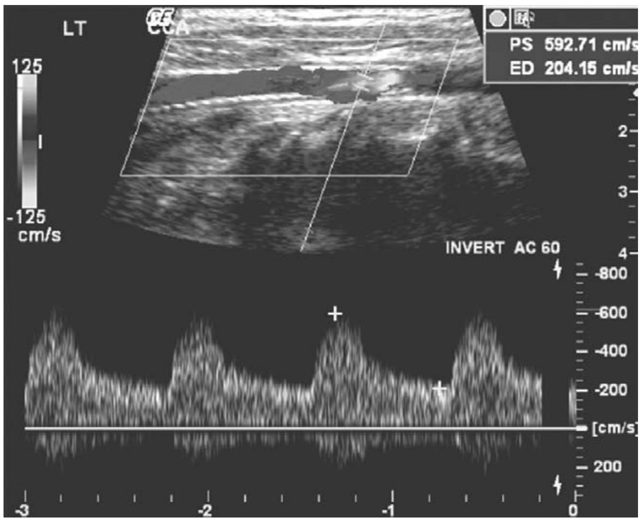

Figure 6 Gray-scale Doppler image of an ICA stent. Doppler interrogation of a proximal ICA stent, with PSV 592 cm/s and EDV 204 cm/s, consistent with severe in-stent restenosis.

MR angiography

MRA has been in development over the past 20 years as an alternative to conventional catheter arteriography. It is non-invasive and does not expose the patient to ionizing radiation or iodinated contrast. MRA can yield a 3D rendition of the entire carotid artery, and offers the possibility of additional concurrent 'one-stop' brain imaging. Disadvantages of MRA include cost, well-documented contraindications, administration of intravenous gadolinium, and certain technical limitations, as discussed below.

Techniques

The techniques commonly used for carotid MRA are time-of-flight imaging (TOF-MRA), which can be done either with 2D or 3D acquisition, and gadolinium contrast enhanced angiography (CE-MRA). TOF-MRA relies on the movement of magnetized blood through the volume being imaged, and thus is susceptible to degradation by phenomena such as turbulence and slow flow, which disrupt smooth linear flow of blood through the vessel lumen. 3D TOF (which includes multiple overlapping thin slab acquisition or 'MOTSA') provides better spatial resolution than 2D TOF, but takes longer, with greater likelihood of patient movement during the exam. CE-MRA is less dependent on blood flow for vascular contrast, and provides better visualization of the arterial lumen (Figure 7). CE-MRA tends to overestimate the degree of stenosis when compared with DSA, but the rate of misclassification appears to be low enough to outweigh the risks of DSA (up to 1% risk of stroke at some centers and in some trials).[16,17] Moreover, DSA itself may underestimate the degree of carotid stenosis compared with rotational angiography, suggesting that underestimation by DSA, rather than overestimation by MRA, is at least in part responsible for the discrepancy between MRA and DSA.[18] The sensitivity and specificity of MRA for the detection of significant (≥ 70%) carotid stenosis can be difficult to compare between various magnetic resonance imaging (MRI) pulse sequences due to differences in the precise hardware and scanning parameters used in clinical trials. In several studies which examined MRA as a screening tool for severe stenosis, using DSA as a gold standard, CE-MRA showed sensitivity of 87–95% and specificity of 46–88%; 3D TOF-MRA showed sensitivity of 86–94% and specificity of 73–100%; and 2D TOF-MRA showed sensitivity of 84–94% and specificity of 94–97%[18–23] (Table 3). Recently developed 3D gradient echo CE-MRA sequences, which use k-space segmentation and temporal interpolation of k-space views, such as TRICKS (time-resolved imaging of

Figure 7 MRA of the carotid arteries. (A) 2D TOF-MRA showing complete signal dropout of the extra and intra-cranial ICA (arrow); CTA or catheter arteriography is required to distinguish 'string sign' (hairline residual lumen) from true total occlusion. (B) Gadolinium contrast-enhanced MRA of normal arch and carotid arteries. (C) Gadolinium contrast-enhanced MRA showing severe stenosis of the ICA origin (arrow). There is a possible ulcerated plaque just distal to the stenotic segment (arrowheads).

Table 3 Sensitivity and specificity of MRA

Method	Detection of ≥70% stenosis (DSA gold standard)		Reference
	Sensitivity	Specificity	
CE-MRA	87–95%	46–88%	U-King-Im[20] Johnston[21] Nederkoorn[22]
2D TOF-MRA	84–94%	94–97%	DeMarco[19] Scarabino[23]
3D TOF-MRA	86–94%	73–100%	Anzalone[18] Nederkoorn[22] Scarabino[23]

contrast kinetics), allow imaging to be done in a fraction of the time required for conventional CE-MRA, and also permit time-resolved images showing distinct arterial and venous phases.[24]

Pitfalls, artifacts, and limitations

In all MR imaging, patient motion (including swallowing and vessel pulsation) can degrade image quality. TOF-MRA, because it is dependent on the flow of freshly magnetized blood into the volume being imaged, is highly susceptible to conditions that disrupt laminar flow. In vessels with significant stenosis, flow is often turbulent rather than laminar distal to severe stenoses, resulting in signal loss due to intravoxel dephasing, as well as the admixture of magnetized and demagnetized blood in a single voxel. This phenomenon is called 'signal dropout' (see Figure 8A). Although the presence of signal dropout roughly corresponds to severe stenosis according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria,[25] this relationship is inconstant, and varies with such scan parameters as echo time (TE). Moreover, signal dropout occurs both with true complete occlusion and with slow flow distal to a severe stenosis ('hairline lumen'), so that TOF-MRA is unreliable for distinguishing these two conditions. Another artifact that decreases the accuracy of TOF-MRA is 'in plane' flow-related signal dropout, which occurs with tortuous vessels that are not perpendicular to the imaging plane. Because of these flow-dependent artifacts, TOF-MRA cannot be used for reliable monitoring of fine increments of stenosis progression.

Because CE-MRA – like DSA – relies primarily on the presence of endovascular contrast rather than on blood flow for lumenal measurement, it is significantly less sensitive than TOF-MRA to flow artifacts, though intravoxel dephasing can still reduce accuracy.[26,27] CE-MRA has been shown to overestimate the degree of carotid stenosis for reasons that may be intrinsic to the technique,[16] although the rate of misclassification of stenosis is low.[17] CE-MRA may also be inaccurate in the presence of metallic surgical clips which introduce susceptibility artifacts,[28] although this occurs with TOF imaging as well.

MRA and stents

With stenting of the carotid arteries becoming widespread, there is a great need for an accurate method of follow-up imaging to assess potential complications such as neointimal hyperplasia, thrombosis, and violation of stent integrity, as well as to evaluate for re-stenosis. Ultrasound is the most common modality used for this purpose, and is considered superior to MRA (Figure 8). One study of MRA in the presence of the Wallstent showed impaired evaluation of the stent lumen by metallic-related artifacts.[29] The inaccuracy was greatest in the days

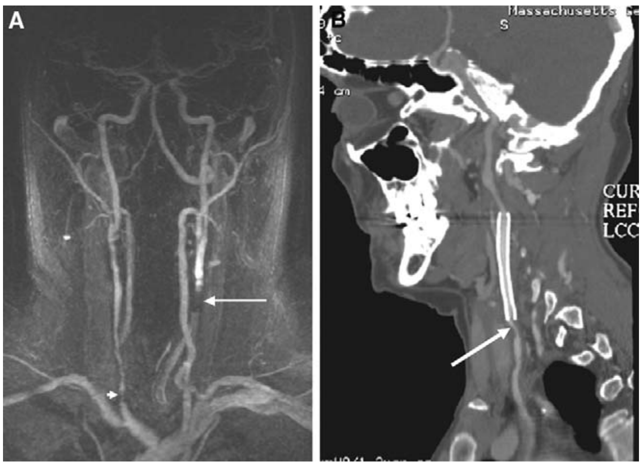

Figure 8 Evaluation of an ICA stent (see Figure 6). (A) MRA of the patient in Figure 6 showing signal dropout in the region of the stent (arrow) due to metallic artifact; CTA or DSA is required for evaluation. There is also evidence of severe, contralateral proximal common carotid artery narrowing (small arrow). (B) CTA of the same patient demonstrates a patent stent lumen but with severe stenoses at the proximal stent margin (arrow).

following stent implantation, but even many months after the procedure, when the effects of stent-related artifacts was lessened, MRA could not be used to accurately assess re-stenosis.

CT angiography

Although CTA exposes a patient to ionizing radiation and iodinated contrast, it has several advantages over DUS and MRA for carotid imaging. First of all, CTA has better overall spatial resolution than MRA, with smaller pixels providing more accurate and exquisitely detailed vascular anatomy (Figure 9). A recent meta-analysis of the diagnostic accuracy of CTA for the assessment of carotid stenosis reviewed 28 studies which compared CTA with DSA.[30] CTA was found to be highly accurate for diagnosing the degree of carotid occlusion, with an overall sensitivity of 97% and specificity of 99%. For severe stenoses (70–99% range), CTA was found to be reliable, with sensitivity of 85% and specificity of 93%. Measurement of residual lumen diameter by CTA compares favorably to DSA, MRA, and ultrasonography.[9,31–34]

CTA is less susceptible to artifacts than MRA because – like DSA – it is a digital subtraction technique that relies on intralumenal contrast rather than signal changes attributable to alterations in blood flow. Also, because it is a faster scan, degradation by patient motion is less common. Another advantage of CTA is that it provides information about surrounding anatomy, such as osseous structures, that is useful in surgical planning.[35] In addition, CT is a technology that is far more widely available than MRI, and hence can reach more patients. CTA has significantly higher sensitivity and specificity, and is used routinely as a first-line diagnostic test at our institution in the emergency department evaluation of suspected acute neurovascular disease, to 'rule in' such entities as dissection, pseudo-occlusion, ICA thrombosis, pseudoaneurysm, and blunt or direct traumatic cervical blood vessel injury (Figure 10).

Severe ICA disease

Severe ICA origin stenosis on MRA can result in complete signal dropout despite the presence of a hairline residual lumen, hence the term 'pseudo-occlusion'. This appearance can be attributed to low post-stenotic pulse pressure, collapse of the vessel wall, and extremely slow and turbulent flow.[36,37] Distinguishing between pseudo-occlusion and true complete occlusion may have important prognostic implications for some patients, and may be important in the selection between surgical and medical treatment.[38,39] Because CT has high spatial resolution and is unaffected by slow flow, CTA is the most appropriate non-invasive method, short of DSA, for differentiating these two entities (Figure 11). One study showed accuracy of at least 85% in distinguishing between occlusion and hairline lumen using CTA,[40] despite the fact that scanning was performed on an older, single detector row helical scanner. A delayed CTA scan immediately following the arterial phase bolus administration is often helpful for the detection of hairline lumen when pseudo-occlusion is indeterminate secondary to very slow flow in the presence of a critical focal proximal ICA stenosis.

Pitfalls and limitations

There are several limitations of CTA for the evaluation of ICA stenosis. Heavy, circumferential calcification of the ICA can cause beam hardening artifact

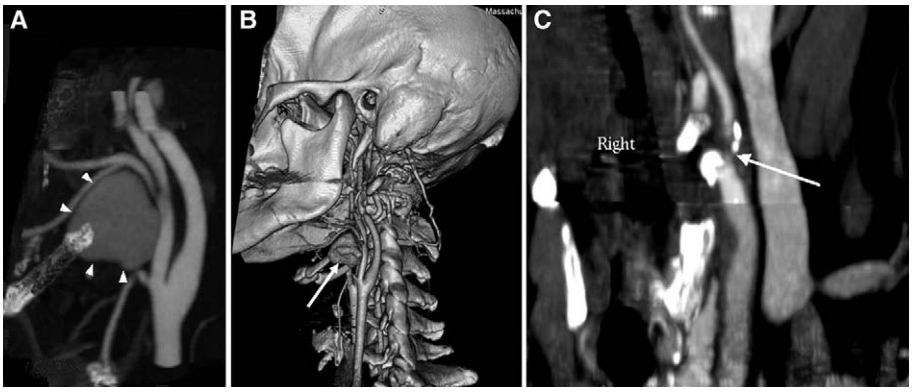

Figure 9 CT angiography of normal and abnormal carotid arteries. (A) Thick-slab maximum intensity projection (MIP) reformatted image from a CT angiogram shows a normal ICA. An ECA pseudoaneurysm (arrowheads) is incidentally noted. (B) CT angiogram from the same patient reconstructed as a 3D surface-shaded display, showing the relationship of the vessels to the surrounding osseous structures (arrow). (C) Thick-slab MIP reformatted image from a CT angiogram shows severe calcified stenosis of the right ICA just distal to the bifurcation (arrow). There is marked narrowing of the entire extra-cranial ICA distal to the stenosis ('string sign').

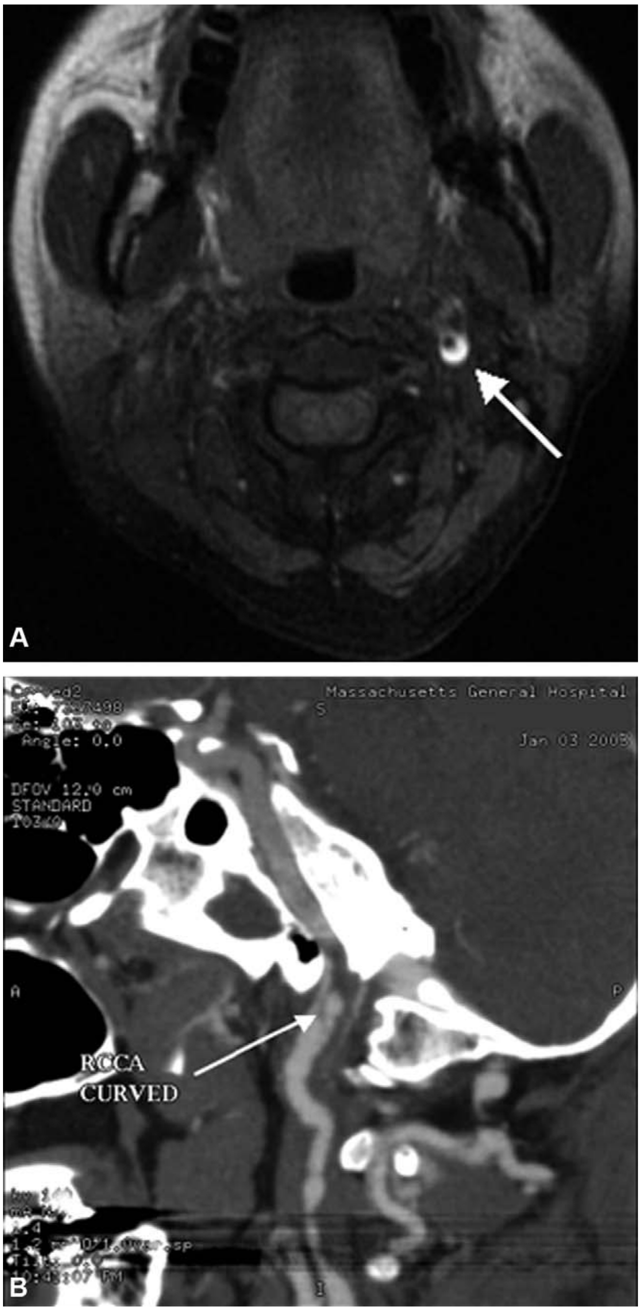

Figure 10 ICA dissection. (A) Axial T1 weighted fat-suppressed MR image just proximal to the skull base shows a crescentic hyperintense signal in the wall of the left extracranial ICA (arrow), consistent with subacute hemorrhage (extracellular met-hemoglobin) in the false lumen from carotid dissection. This is a specific but not sensitive finding. (B) An MIP reformatted CTA image shows a dissection flap (arrow) with severe narrowing at the cervical-petrous ICA junction.

which can result in overestimation of stenosis.[41] This may represent an advantage to CE-MRA, where dense calcification does not cause image degradation to the same extent as that seen with CTA. Also, differences in window width and center level display settings during digital review, as well as differences in contrast density from one examination to another, can produce apparent differences in the reported lumen size.[41–43] An important pitfall to avoid when evaluating for pseudo-occlusion is that the ascending pharyngeal artery can mimic a hairline ICA lumen, when in fact the ICA is occluded. To avoid this pitfall, the reviewing physician must follow the course of the distal ICA into the petrous carotid canal at the skull base, confirming that the vessel is indeed an ICA and not an ECA branch.[40]

In addition to the interpretation pitfalls of CTA noted above, it also must be noted that there are well-established risks associated with the use of iodinated CT contrast agents, as well as radiation exposure to such potentially radiosensitive tissues as the lenses and thyroid gland. For these reasons, CTA is not typically suggested as a first-line screening examination for asymptomatic or outpatient cohorts, but rather as a ‘problem-solving’ tool when the results of screening US and MRA are discordant, or when tandem lesions or other confounding factors that may influence surgery are suspected.

Plaque characterization

While the degree of carotid stenosis is the most widely accepted predictor of stroke risk, other imaging features are becoming recognized as significant factors. Plaque ulceration has long been thought to play a major role in the etiology of stroke from ICA disease.[44] Both ultrasound and CTA have shown some efficacy in detecting plaque ulceration.[45] However, neovascularization and inflammatory changes in the plaque are thought to accompany the processes which lead to plaque rupture, and – for a given degree of stenosis – may serve to further stratify acute stroke risk.[46,47] A recent study based on this reasoning has shown that enhancement of the vasa vasorum adjacent to severe carotid plaque during arterial phase CTA suggests a higher likelihood of symptomatic disease (TIA or stroke).[48]

Conclusions

Given the frequency of carotid artery stenosis in the US population, safe, accurate and reliable imaging is critical. Initial imaging is with high-quality DUS. If abnormal, MRA or CTA may be helpful in providing comprehensive anatomic information to aid in planning therapeutic strategies. All imaging modalities have limitations, and physicians must appreciate the skill and experience of the operators and interpreters in their respective centers.

Figure 11 MRA signal dropout in the presence of a hairline lumen. (A) This gadolinium MRA shows complete signal dropout of the extra-cranial ICA (arrow). It is not possible to distinguish occlusion from severe stenosis based on this finding. (B) An MIP of the CTA from the same patient demonstrates the presence of a narrowed but patent ICA lumen (arrow) distal to the severe bifurcation stenosis.

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