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CT Angiography for the Detection and Characterization of Carotid Artery Bifurcation Disease

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Background and Purpose—Computed tomographic angiography (CTA) is a relatively new and minimally invasive method of imaging intracranial and extracranial blood vessels. The main purpose of this study was to compare CTA to the current gold standard of arterial imaging, digital subtraction angiography (DSA), for the detection and quantification of carotid artery bifurcation stenosis. We also compared Doppler ultrasound (US) with these 2 techniques.

Methods—In a prospective study, 40 patients (80 carotid arteries) underwent CTA, US, and DSA. Patients chosen for inclusion were symptomatic with TIAs or stroke and had initial US screening that indicated >50% carotid stenosis on the side appropriate for the symptoms. Source axial, maximum intensity projection (MIP), and shaded-surface display (SSD) images were produced for each CTA study. The US, CTA, and DSA images were reviewed, with the degree of stenosis quantified and presence of ulcers determined; each type of imaging was reviewed by a separate investigator blinded to the results of the other 2 modalities. The results of CTA and US imaging were compared with the DSA images for degrees of carotid stenosis.

Results—CTA source axial images correlated with DSA more closely than MIP or SSD images for all degrees of stenosis. The correlation between US and DSA (0.808) was poorer than that between CTA and DSA (0.892 to 0.922). CTA performed well in the detection of mild (0% to 29%) carotid stenosis, as well as carotid occlusion, with values for sensitivity, specificity, and accuracy near 100%. In determining that a stenosis was >50% by DSA measurement, CTA was again useful, with a sensitivity, specificity, and accuracy of 89%, 91%, and 90%, respectively. While CTA was quite specific and accurate in identifying degrees of stenoses in either the 50% to 69% or the 70% to 99% ranges, in this task it was much less sensitive: 65% for 50%–69% stenosis and 73% for 70%–99% stenosis. These results did not change significantly when only the data from the most clinically relevant symptomatic arteries were analyzed. CTA was found to correlate quite well with DSA in the detection of ulcers associated with the carotid stenosis.

Conclusions—CTA was found to be an excellent examination for the detection of carotid occlusion and categorization of stenosis in either the 0%–29% or >50% ranges. However, CTA was unable to reliably distinguish between moderate (50%–69%) and severe (70%–99%) stenosis, which is an important limitation in the investigation and treatment of carotid stenosis. (*Stroke*. 2000;31:2168-2174.)

Key Words: angiography, computed tomographic ■ carotid endarterectomy ■ carotid stenosis

Computed tomographic angiography (CTA) is a relatively new and minimally invasive investigative technique consisting of an intravenous bolus injection of contrast solution followed by high-speed spiral CT scanning and computer-assisted generation of images of large to medium-sized arteries in the region scanned. In the cerebral circulation, the utility of CTA has recently been demonstrated in the detection of intracranial aneurysms^{1–5} and carotid stenosis.^{6–22} The gold standard for imaging the cerebral arteries is digital subtraction angiography (DSA), although DSA is not always a benign investigation, with total complication rates as high as 5% and permanent stroke in up to 0.5% of patients.^{23–26} There is a need for a less-invasive investigation than DSA for carotid artery disease. One well-studied tech-

nique is Doppler ultrasound (US), which poses virtually no risk to the patient. US has been reported^{27–35} to have a relatively high sensitivity compared with DSA. The main problem with US is its high interobserver and intermachine variability.^{19,31} Recent reports^{14,17,20,36} have suggested that CTA has a higher accuracy than US.

Clinical trials that have demonstrated the effectiveness of carotid endarterectomy over medical therapy in reducing stroke risk from carotid stenosis have used catheter-based angiographic determinations of carotid narrowing, so that the results of those studies^{37–41} pertain to quite precisely determined degrees of stenosis. For example, in the North American Symptomatic Carotid Endarterectomy Trial (NASCET), the greatest benefit from surgery was in the group of patients

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with stenoses in the 70%–99% range; in this group, it has been calculated³⁹ that only 8 patients needed to undergo surgery to prevent 1 stroke over a 2-year period. It was also demonstrated⁴² that severe stenosis combined with plaque ulceration was associated with an increased stroke rate when treated with medical therapy alone, indicating a greater benefit from surgery in this patient group.

NASCET also demonstrated that for those patients with stenoses in the 50%–69% range, endarterectomy also lowered the overall stroke risk significantly, but the benefit was somewhat less than for the severe stenosis group: 20 patients with moderate stenoses needed to undergo endarterectomy to prevent 1 stroke over 2 years.⁴⁰ Patients with less than 50% stenosis did not benefit from surgery in NASCET.

For patients with asymptomatic carotid stenosis, only those with >60% stenosis by angiographic measurement benefited from prophylactic endarterectomy in the Asymptomatic Carotid Atherosclerosis Study (ACAS). The benefit was relatively modest, with 83 patients requiring endarterectomy to prevent 1 stroke over 2 years, and with major strokes not being reduced by surgery.^{41,43}

It is apparent that the precise degree of carotid artery stenosis and some aspects of plaque morphology are associated with differences in stroke risk and natural history, as well as response to surgery, and this may have important management implications, such as the relative appropriateness of surgery.^{44,45} In this study we wished primarily to determine how accurately CTA could distinguish between clinically important degrees of carotid artery stenosis. As US is frequently used for the diagnosis of carotid stenosis, we wished to also compare US with CTA and DSA.

Subjects and Methods

Eligible patients were symptomatic with either transient or permanent ischemic neurological deficits who had undergone color-coded Doppler US indicating >50% carotid stenosis (based on written reports). The US examinations were performed at several different laboratories and were not standardized, this method representing the actual clinical situation presented to clinicians in our region. Patients who gave their informed consent to participate in the study then underwent CTA and DSA, the 2 exams performed within 1 month of each other. Ethical approval for this study was granted from the institution, and informed consent for participation was obtained from each patient.

CTA was performed with a GE CTi helical scanner (General Electric). A 20-gauge intravenous catheter was placed in an antecubital vein and 120 mL of nonionic contrast (Omnipaque 300, Nycomed) was infused at 3 mL/s after an initial injection delay. Three-millimeter helical cuts were made starting from the C6 vertebral body to the skull base. The pitch was 1.5, with 120 kV and 200 to 320 mA. Scanning began once a Hounsfield unit (HU) of 40 was detected by a cursor in the common carotid artery at the C6 level. The 3-mm axial source images were then reconstructed to 1-mm axial cuts. The reconstructed images were sent to a computer workstation (GE), where generation of 3-D maximum intensity projection (MIP) and shaded-surface display (SSD) images was performed. Generation of MIP images was performed with manual editing to exclude all structures except the common, internal, and external carotid arteries in each axial slice. Mural calcification was removed by manual editing on each axial slice. SSD images were produced by using a threshold level of 100 to 300 HU, depending on the degree of luminal contrast. Hard copy images were made rotating the MIP and SSD images every 30 degrees for a total of 360 degrees.

TABLE 1. Correlation Between CTA and US With DSA

	<i>r</i> *
CTA	
Axial	0.922
MIP	0.892
SSD	0.917
US	0.808

**r*=Spearman correlation coefficient; *P*=0.01.

The total time to produce the 1 mm reconstructed source axial, MIP, and SSD images was 20 to 25 minutes per artery.

DSA exams were performed using the transfemoral Seldinger technique. Common carotid arteries were selectively catheterized, and lateral, anteroposterior, and lateral oblique images were produced.

The US, CTA (axial, MIP, SSD), and DSA images were reviewed by 3 separate investigators (each modality reviewed by a single reviewer) blinded to the results of the other 2 imaging modalities. The degree of stenosis was categorized into one of the following categories: 0%–29%, 30%–49%, 50%–69%, 70%–99%, and 100%. The CTA and DSA images were measured using calipers and a finely calibrated ruler and the point of maximal stenosis was compared with the normal distal internal carotid diameter (beyond the bifurcation) for degree of stenosis calculation. Ulcers were defined to be present if there was a luminal cleft in the plaque of >2 mm in depth.

Statistical analysis was performed by using Spearman correlation coefficient to assess overall agreement. Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and accuracy were used to compare each test to DSA. Statistical significance was calculated using Fisher's exact test and χ^2 tests.

Results

A total of 40 patients (80 arteries) were studied. There were 24 men (aged 44 to 83 years) and 16 women (aged 52 to 78 years). Seven source axial, 4 MIP, and 9 SSD images were not included in the data (up to 11% of CTA images were uninterpretable) because they were of poor quality due to motion artifact or poor contrast density. Agreement was best between axial images and DSA (84%) and worst between US and DSA (49%). All of the image types, but especially US, tended to overestimate the degree of stenosis compared with DSA.

The overall correlation between CTA, US, and DSA was good. CTA correlated with DSA more than US did, and the CTA axial images correlated better than the other 2 types of CTA images, MIP and SSD (Table 1).

The data were analyzed for carotid occlusion and for different ranges of stenosis. For the identification of carotid occlusion, there was a trend for CTA axial images to be the most accurate (Table 2), and again the axial images were superior, with the MIP and SSD images comparable to US (Figure 1; *P*=0.33). For identification of occlusion, sensitivity was 100%, specificity 98%, and accuracy 99% for CTA axial images. The predictive values and likelihood ratios were all excellent for the axial images.

Table 2 displays the results of CTA and US in detecting stenoses in the 50%–99% range. The axial source images were again the superior modality, with a sensitivity and specificity of 89% and 91%, respectively, and an accuracy of 90%. CTA MIP and SSD images were slightly less accurate than the axial images but better than US alone. For this degree

TABLE 2. Comparison of CTA and US With DSA for Various Degrees of Carotid Stenosis

Degree of Stenosis	Sensitivity	Specificity	PPV	NPV	+LR	-LR	Accuracy	<i>P</i>
Occlusion								
CTA								
Axial	1.00	0.98	0.93	1.00	50	0.00	0.99	<0.001
MIP	0.69	0.98	0.9	0.94	34.5	0.32	0.93	<0.001
SSD	0.75	0.98	0.9	0.95	37.5	0.26	0.94	<0.001
US	0.70	0.96	0.78	0.94	17.5	0.30	0.92	<0.001
>50%								
CTA								
Axial	0.89	0.91	0.86	0.93	9.9	0.12	0.9	<0.001
MIP	0.90	0.82	0.78	0.93	5.00	0.12	0.86	<0.001
SSD	0.85	0.86	0.75	0.90	6.1	0.17	0.86	<0.001
US	0.95	0.60	0.78	0.88	2.4	0.08	0.81	<0.001
70%–99%								
CTA								
Axial	0.73	0.92	0.62	0.95	9.1	0.29	0.89	<0.001
MIP	0.77	0.84	0.5	0.95	4.8	0.27	0.83	<0.001
SSD	0.67	0.86	0.5	0.93	4.8	0.38	0.83	<0.001
US	0.82	0.71	0.38	0.95	2.8	0.25	0.73	0.002
50%–69%								
CTA								
Axial	0.65	0.91	0.69	0.89	7.2	0.38	0.85	<0.001
MIP	0.61	0.88	0.69	0.88	5.1	0.44	0.84	<0.001
SSD	0.60	0.93	0.69	0.89	8.6	0.43	0.86	<0.001
US	0.35	0.87	0.5	0.78	2.7	0.75	0.73	0.07

PPV and NPV indicate positive and negative predictive values, respectively; positive and negative likelihood ratios are noted as +LR and -LR, respectively. Probability values were calculated with Fisher's exact test (2-tailed).

of stenosis, US was quite sensitive (95%) but was not specific (60%). Again, the predictive values and likelihood ratios were superior for the axial images.

For stenoses in the 70%–99% range, the results of CTA and US are shown in Table 2. Again, there was a trend for axial images to be the most accurate CTA images, with a sensitivity of 73%, specificity of 92%, and accuracy of 89% ($P=0.11$). MIP and SSD images (Figure 2) were more accurate than US alone ($P=0.15$). The positive predictive values were poor for all modalities, which indicates a relatively high false-positive rate. The positive likelihood ratio was marginal for axial images (+LR should be >10), indicating a high ratio of true-positive to false-positive results. The negative likelihood ratio was poor for all modalities (-LR should be <0.20), indicating a relatively high ratio of false-negative to true-negative results.

In the moderate, 50%–69% stenosis range, there was little difference between the 3 CTA image types (Table 2). Although CTA images were quite specific (88% to 93%) and accurate (84% to 86%), their sensitivities were poor (60% to 65%). All CTA images were again more accurate than US alone ($P=0.057$). The US images had only a sensitivity of 35% for detecting stenoses in this range. All modalities had a poor

positive predictive value indicating a relatively high false-positive rate. The likelihood ratios were poor for all modalities, which indicates a low ratio of true-positive to false-positive results and a high ratio of false-negative to true-negative results.

Because clinicians are usually most concerned with the symptomatic carotid artery, we also analyzed the results from this side alone (40 arteries). The results did not change significantly from the combined results presented above.

US and CTA were also compared for the determination of mild stenosis (0%–29%). For this range of stenosis, CTA was again better than US; of the CTA image types, the SSD images were best, with a sensitivity, specificity, and accuracy of 93%, 98%, and 96%, respectively. The CTA axial images results were close to these. US was insensitive (57%) but specific (93%) for this degree of stenosis. The predictive values and likelihood ratios were best for SSD and axial images.

The incidence of distal cerebrovascular lesions (so-called tandem lesions) was also evaluated. No aneurysms or AVMs were uncovered during the DSA examinations in this series of patients, although 2 intracranial occlusions were noted. There were 11 carotid siphon stenoses detected by DSA, and all were mild ($<30%$ luminal reduction). These siphon stenoses

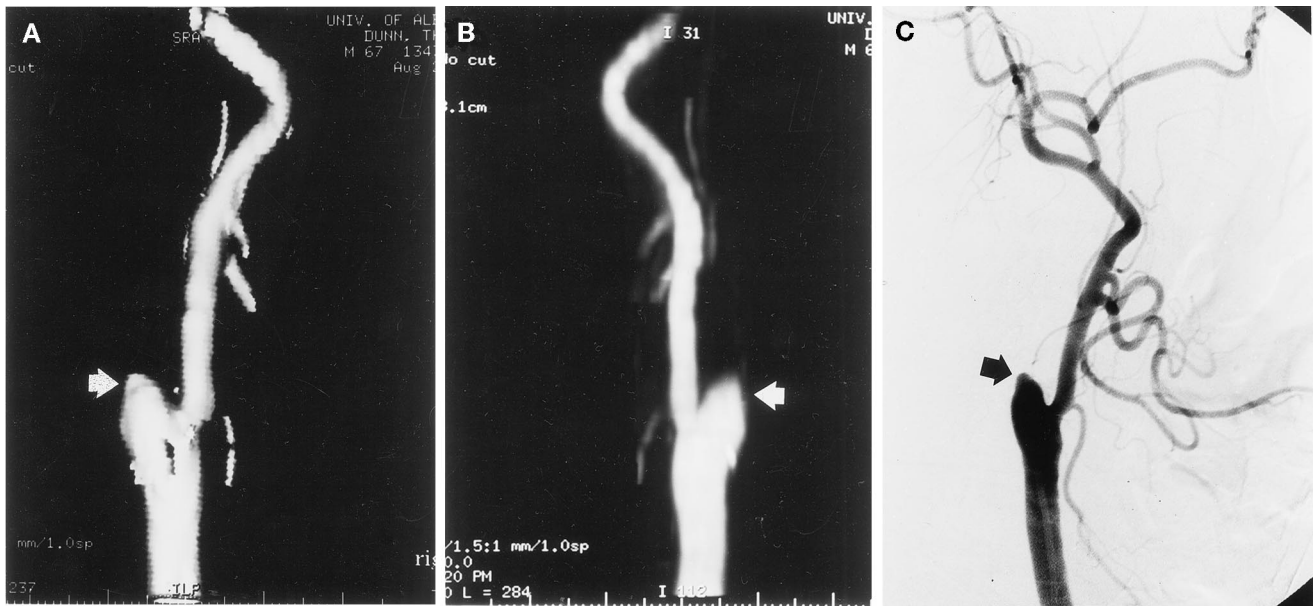


Figure 1. Occlusion of internal carotid artery (arrow) shown on CTA SSD (A), MIP (B), and DSA (C).

cannot be reliably visualized on CTA, because the carotid artery is obscured by the skull base.

Thirty percent of the bifurcations had so much calcification of the carotid arteries that it was not possible to assess the degree of stenosis on MIP or SSD images without manually removing the calcification during the processing of the images at the computer workstation. This heavy calcification resulted in increased processing time (approximately an additional 10 minutes per artery) and difficulty distinguishing the true residual lumen. The presence of ulcers was also assessed. DSA detected 9 ulcers, and CTA clearly depicted 7 of these (Figure 3).

There were no significant complications as a result of the CTA exams. After the DSA examinations there were no

reported incidences of major complications (stroke, arterial dissection), although there were several instances of mild groin hematomas.

Discussion

Doppler US has been compared with DSA for the detection and quantification of carotid stenosis in a number of studies.^{19,27–30,32–35,44,46} One study²⁸ reported a sensitivity and specificity of 96% and 95%, respectively, for detecting stenoses >50%. This same study also reported a sensitivity and specificity of 50% and 95%, respectively, for occlusion. That study, however, did not use color-flow Doppler (CFD), as is now currently used. CFD has been shown to be more accurate than conventional Doppler and is also superior in

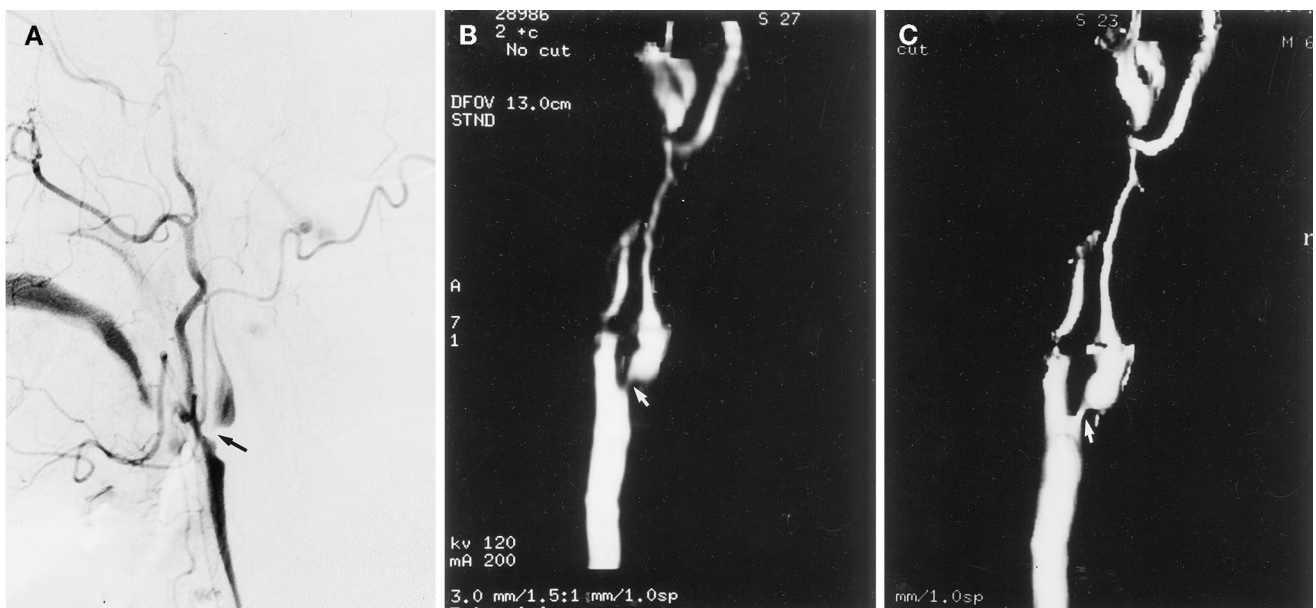


Figure 2. Severe carotid stenosis (arrow) shown on DSA (A), MIP (B), and SSD (C) images.



Figure 3. Severe carotid stenosis with ulcer (arrow) shown on DSA (A), MIP (B), and SSD (C) images.

depiction of plaque morphology, such as ulceration.³⁴ Steinke et al³⁴ demonstrated accuracy for CFD in the 91%–96% range, with the lowest accuracy for stenoses in the 40%–60% range. A more recent study³⁵ of 38 arteries reported a 100% sensitivity for >50% and 70%–99% stenosis, but poor specificity (17% and 64% for the 2 stenosis ranges, respectively). The study also showed poor sensitivity (63%) but good specificity (90%) for 50%–69% stenosis. The data from our study is in agreement with these results.

In a study similar to ours with nonstandardized US, Srinivasan et al³³ also reported results close to our own. Their sensitivity and specificity for >50% stenoses were 90% and 76%, respectively. For occlusion and for severe and moderate stenoses, the sensitivities and specificities were 92% and 99%, 71% and 91%, and 69% and 80%, respectively.

Several studies^{27,29,30,32,43} have compared US to DSA for severe 70%–99% stenoses alone. Sensitivity and specificity values range from 81% to 94% and 83% to 98%, respectively, and accuracy from 86% to 95%. Faught et al²⁹ report a sensitivity, specificity, and accuracy of 92%, 97%, and 97%, respectively, for 50%–69% stenosis. Our own results are poorer than these, possible because our exams were nonstandardized. Previous reports^{19,31} have documented interobserver and intermachine variability in carotid stenosis measurement. US results may be more comparable to DSA in labs that have verified the accuracy of their machine and parameters with DSA.

In the late 1980s it was reported that the carotid artery bifurcation could be visualized with contrast-infused CT scanning.⁴⁷ Since then, using true spiral CT technology, several studies^{6,7,11–13,16,21} have reported good overall agreement between CTA with DSA for the detection of carotid artery disease. Schwartz et al¹⁸ reported on the first large series of 40 arteries. With SSD for stenosis calculation, their data revealed perfect agreement between CTA and DSA for occlusion and for moderate and severe stenosis. More recent studies^{8,9,14,15,20,36} have also demonstrated near-perfect sensi-

tivity and accuracy for occlusion and 80% to 95% sensitivities for severe (70%–99%) stenosis, but detection of moderate stenosis by CTA was less sensitive (50%–90%).

Sameshima et al¹⁷ have reported the largest series to date (128 arteries), comparing CTA MIP images with DSA. They found an overall correlation of 0.987. They had perfect agreement for complete occlusions, and the sensitivity, specificity, and accuracy were 93%, 100%, and 98%, respectively, for 70%–99% stenoses. They found, as we did, a poorer accuracy of CTA in detecting moderate degrees of stenosis.

Aside from the study reported here, only 1 other group¹⁰ has compared axial, MIP, and SSD images in their ability to detect carotid stenosis. Their results were quite similar to ours, with axial images having the highest correlation with DSA ($r=0.935$). Their data also demonstrated excellent accuracy for occlusion and severe stenosis, with poorer CTA detection of moderate stenosis.

Our data support axial images as the most accurate CTA image. Although the 3-D CTA images are more visually appealing and provide a sense of the location and length of the carotid plaque and the location and orientation of calcifications, they are less reliable in stenosis calculation. CTA also appears to be more accurate than nonstandardized US in the quantification of all degrees of stenosis.

If we had used 70%–99% stenosis as the only definite indication for endarterectomy in our series of 40 patients, depending solely on CTA imaging could have resulted in 3 (8%) patients wrongfully denied surgery and 5 (13%) patients having surgery with stenoses <70%. Our detection rates for 70%–99% stenosis are slightly poorer than those previously reported (sensitivity of 67% to 77% versus 80% to 95%), which may reflect the relative difficulty and inaccuracy of precise measurements on CTA axial and MIP images compared with DSA. US would result in more errors, with 3 patients (9%) wrongfully denied surgery and 15 patients (47%) undergoing less-certain surgery for stenoses <70%.

CTA was found in our study to be a good test for detection of carotid occlusion and of stenoses >50%. Whether the latter determination is itself sufficient to make a decision with respect to surgery is uncertain. Stenoses $\geq 70\%$ that have caused symptoms are the most clearly appropriate lesions for surgery. More moderate stenoses that cause symptoms in the 50%–69% range benefit less and have a response to surgery that appears to depend on additional factors, such as sex, coexistent illnesses (including diabetes mellitus), clinical presentation (TIA versus minor stroke), and the presence or absence of intracranial stenoses undetectable on CTA.^{40,48} Surgery is ineffective for asymptomatic stenoses <60% but has a possible role for more severe stenoses,⁴¹ with a number of studies suggesting that the natural history risk and therefore role for prophylactic surgery is greater for increasing degrees of asymptomatic stenosis.^{39,43,49–51} A strong argument can therefore be made for highly accurate and precise stenosis measurement, such as that obtained by DSA, before making a recommendation regarding carotid endarterectomy.

In addition to providing a precise measurement of carotid stenosis, cerebral angiography also demonstrates the cervical height of the carotid bifurcation in the neck; the length and morphology of the atherosclerotic plaque; the presence of intraluminal thrombus or additional vascular abnormalities, including distal stenosis; and the completeness of the circle of Willis as well as intracranial flow patterns. However rarely significant variations are detected, knowledge of these when present can be quite important to surgical planning and in some circumstances can even lower treatment risk.⁵² For example, the presence of intraluminal thrombus has been reported to correlate with a high risk of embolic stroke⁴² as well as a high risk of intraoperative stroke,^{53,54} which has led some authors⁵⁵ to recommend anticoagulant therapy alone. It has been reported that patients without collateral flow (patent anterior communicating complex and ipsilateral posterior communicating artery) demonstrated on preoperative angiography require shunting as defined and dictated by EEG changes.⁵⁶ Related to this, using intraoperative somatosensory evoked potentials, Wain et al⁵⁷ reported that 25% of patients without cross-flow via the anterior communicating artery on angiography required shunting. Knowledge of collateral flow and the presence of intraluminal thrombus, therefore, may influence some aspects of surgical management.

In conclusion, without standardization of US units we found US to be relatively inaccurate in the quantification of carotid stenosis. CTA was superior to US, and the source axial CTA images were more accurate than the 3-D reconstructed images. Although CTA was accurate in detection of carotid occlusion and stenoses >50%, it did not accurately discriminate degrees of stenoses in the 50%–99% range. Weighing the advantage of being a more minimal and less costly procedure versus the disadvantage of less accuracy and overall information, we do not believe that CTA in its present form is an adequate replacement for DSA in the investigation of carotid stenosis.

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