For Severe Carotid Stenosis Found on Ultrasound, Further Arterial Evaluation Is Unnecessary

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The objective of performing carotid endarterectomy (CEA) is to reduce the risk of stroke. CEA can be justified only if the stroke morbidity and mortality from operation is significantly less than with alternative methods of management. Complications associated with preoperative invasive diagnostic procedures must be counted against the risk of operation because the invasive diagnosis would likely not be performed if surgery were not contemplated.

Intra-arterial contrast angiography carries several risks including the risk of stroke and death. These risks are increased in patients with severe cerebrovascular occlusive disease as opposed to the risk in patients with indications for angiography other than carotid bifurcation disease.

The benefits of carotid endarterectomy become more compelling to the extent that morbidity and mortality related to all aspects of perioperative management can be reduced. Clinical investigation, experience, and surgeon competence have combined to bring the risk of operation close to an irreducible minimum. The opportunity to further reduce perioperative risk by eliminating the need for contrast angiography is perhaps the single best method to achieve a major risk reduction for patients selected to undergo carotid endarterectomy.

Risks of Angiography

The risk of minor stroke as a consequence of diagnostic angiography is reported to range from 1.3% to 4.5%, and the risk of major stroke from 0.6% to 1.3%. In the Asymptomatic Carotid Atherosclerosis Study (ACAS) trial, in which randomization occurred prior to angiography, all patients who were randomized to the surgical arm were required to undergo postrandomization angiography. That design provided the opportunity to assess the true audited risk of angiography as it took place in centers of excellence participating in the trial. The combined neurologic morbidity and mortality from angiography in asymptomatic patients with hemodynamically significant carotid stenosis was 1.2%. The risk of stroke morbidity and mortality from carotid endarterectomy itself was 1.52%. Therefore, had the operation been done on the basis of ultrasound alone, the risk of operation would have been cut almost in half and the comparative benefit of CEA versus medical management would have been even more compelling.

Angiography carries an even greater risk in symptomatic patients. Theodotou et al reported a 7.7% stroke morbidity and mortality in patients undergoing contrast angiography for stroke-in-evolution and a 12.5% risk in patients who had bilateral severe carotid stenosis. Perhaps the risk of angiography could be justified if the findings contributed to important clinical decisions or to surgical management, but it rarely does. Akers et al reviewed their experience with 1000 aortocranial angiograms and noted that only 6 patients were found to have significant lesions of the aortic arch trunks. Furthermore, tandem intracranial lesions in the distribution of the carotid artery, exceeding a 75% stenosis, are also rare.

Angiography of the cerebral circulation is often referred to as a "gold standard." Unfortunately, this is also a misconception. The real gold standard for carotid bifurcation disease is the explanted atherosclerotic specimen. When the results of duplex sonography and carotid angiography are compared with the explanted lesion, rather than with each other, duplex sonography is actually found to be more accurate than carotid angiography. Because carotid angiography is a 2-dimensional study of a plaque that often has eccentric configuration, it is almost inevitable that the angiogram underestimates the percent stenosis.

There has been an increasing experience with CEA on the basis of sonography alone. Reports of this experience document both safety and accuracy of the technique while avoiding the risk and expense of routine angiography.

Suffice it to say that the willingness to accept duplex ultrasound as the definitive preoperative test is based on the reliability of the ultrasound laboratory in which the test is performed. Given that the duplex ultrasound examination is both technician- and machine-dependent, the laboratory performing the test must be able to show that it has validated its testing procedures. In the United States, the Intersocietal Commission for Accreditation of Vascular Laboratories (ICAVL) has established validation criteria, and laboratories...
that are certified by ICAVL can be regarded as providing data with the highest standards of accuracy. On the basis of these arguments, I can comfortably state that, with rare exception, patients with severe carotid stenosis as documented by duplex ultrasound do not require invasive angiography prior to carotid endarterectomy.

References

For Severe Carotid Stenosis Found on Ultrasound, Further Arterial Evaluation Prior to Carotid Endarterectomy Is Unnecessary: The Argument Against

Peter M. Rothwell, MD, PhD, FRCP

Carotid endarterectomy reduces the risk of stroke in certain patients with recently symptomatic carotid stenosis and to a lesser extent inpatients with severe asymptomatic stenosis. Screening of patients for inclusion in the randomized controlled trials (RCTs) was usually performed with Doppler ultrasound (DU), but conventional arterial angiography (CAA) was required prior to randomization in the RCTs in symptomatic stenosis and prior to surgery in ACAS. However, CAA is costly, time-consuming, and can cause stroke. A systematic review of prospective studies of the risks of CAA inpatients with cerebrovascular disease reported a 0.1% risk of death and a 1.0% risk of permanent neurological sequelae. More recent studies have reported lower risks in both academic centers and community hospitals, but many centers have already adopted a policy of operating on the basis of DU alone.

What Are the Advantages of Doppler Ultrasound?
The main advantage of DU over CAA is the absence of a procedural risk. However, it should be noted that most studies of the risk of CAA classified all strokes that occurred within 24 hours of CAA as procedural complications. Given that the risk of stroke shortly after presentation with symptomatic carotid stenosis and prior to endarterectomy is about 0.5% per day, the excess stroke risk due to CAA in recently symptomatic patients is probably only about 0.5%.

Has Practice With Ultrasound Alone Been Shown to Be Adequate?
In contrast to pharmaceutical products, new diagnostic or imaging strategies are not subject to regulatory control, and no standards are set for validation. Given that the available techniques of carotid imaging use completely different source data to estimate stenosis, and that there is major variation in carotid bifurcation anatomy between individuals and between the sexes, translation of measurements of stenosis from one technique to another is not straightforward. Although several hundred studies of carotid imaging have been published over the past 2 decades, the majority are undermined by poor design, inadequate sample size, and inappropriate analysis and presentation of data. However, a meta-analysis of methodologically sound studies of noninvasive carotid imaging published prior to 1995 concluded that DU could not substitute for CAA as the sole pre-endarterectomy imaging because of the frequency with which the degree of stenosis was misclassified. More recent studies have confirmed this.

Does Misclassification of the Degree of Carotid Stenosis Matter?
Benefit from endarterectomy is highly dependent on the degree of symptomatic carotid stenosis as measured on CAA. Misclassification of stenosis with DU will lead to some patients being operated on unnecessarily and others being denied appropriate surgery. This harm must be balanced against the 0.5% excess risk of stroke associated with CAA, ie, 1 additional stroke per 200 patients. For example, given the 33.8% reduction in the 8-year absolute risk of stroke with endarterectomy in patients with 90% to 99% symptomatic stenosis, for every 3 patients who are not operated on, possibly because a complete occlusion is seen with DU, 1 stroke will go unprevented. A rate of misclassification of 90% to 99% stenosis as complete occlusion of only 1.5% would therefore be sufficient to offset the risk of CAA. Similarly, given the 15.1% reduction in the 8-year risk of stroke with endarterectomy in patients with 60% to 69% symptomatic stenosis, misclassification of 10% of such patients as <50% stenosis with DU would offset the risk of CAA. In practice, misclassification rates can be much higher. A recent comparison of CAA with DU in 569 consecutive patients in "accredited" laboratories with experienced radiologists found that 28% of decisions about endarterectomy based on DU alone were inappropriate. The reliability of DU varies significantly between laboratories, and misclassification in nonaccredited laboratories is likely to be even greater.

What Other Useful Information Is Lost With Use of Doppler Ultrasound Alone?
Plaque surface ulceration on CAA indicates a particularly high risk of stroke on medical treatment, increased benefit from endarterectomy, and identifies patients at high risk of coronary vascular events. Currently available DU techniques do not provide reliable data on plaque surface morphology. In contrast, the risk of stroke on medical treatment is low in patients with poststenotic narrowing of the internal carotid artery or "near-occlusions," and this group derives little benefit from surgery. There are few data on the reliability of DU at detecting near-occlusions. Other angiographic characteristics, including the presence of distal disease and collateral circulation to the symptomatic hemisphere, also influence the risks and benefits of endarterectomy. DU may provide some of this information, but the assessments that are required are far from routine.

Is the Combination of Doppler Ultrasound With Other Noninvasive Techniques Adequate?
Given the major shortcomings of DU alone in selection of patients for endarterectomy, the combination of DU with other noninvasive methods of imaging, usually magnetic resonance angiography (MRA), has been studied. The rate of inappropriate decisions in comparison with CAA is reduced to <10% in patients in whom the results of DU and MRA are concordant. MRA provides useful information about tandem lesions and distal disease, but contrast-enhanced MRA does not appear to offer any additional benefit. CAA is still required in the 25% of patients in whom DU and MRA do not produce concordant results.

Conclusions
Even very low rates of misclassification of symptomatic patients as appropriate or inappropriate for surgery, by DU or other noninvasive methods of imaging used in isolation, will nullify any gain that is obtained by avoiding the risk of CAA. Although CAA is far from ideal, the accurate determination of degree of stenosis and demonstration of other clinically useful information mean that it remains the "gold standard" imaging method for selection of symptomatic patients for endarterectomy, provided that it can be performed without significant delay to surgery. Whether the very small benefits of endarterectomy for asymptomatic stenosis justify the use of CAA is less certain. Further studies of the combination of DU and MRA are required.

References
The crux of the question addressed by our protagonists is whether the benefits of carotid angiography (CAA) outweigh the potential risks of the procedure compared with the noninvasive but less precise use of carotid Doppler ultrasound (DU) and lack of information about the intracranial circulation. The interpretation of the existing data can be, in part, philosophical: as Rothwell outlined, the net increase in risk for angiography is about 1 stroke for every 200 cases studied. Does this outweigh the benefits of intracranial vascular imaging provided by CAA? The downside of DU as the sole investigation prior to endarterectomy is the possibility that inappropriate surgery is undertaken due to a spurious result, failure to detect tandem lesions or intracranial aneurysms.

One of us (S.M.D.) is swayed by the arguments that the decisions for endarterectomy are based on NASCET angiographic criteria for stenosis, that tandem lesions and incidental intracranial aneurysms are not uncommon and may influence clinical management decisions. Intracranial disease is even more important in Asian patients, where it is the predominant type of cerebral atherosclerosis. Patients with intracranial disease have a worse prognosis and arguably medical therapy may need to be more intensive. At our institution, CAA is routinely performed before surgery and DU is used only as a screening test. However, CAA is becoming replaced by magnetic resonance angiography (MRA) and computed tomographic angiography (CTA), and its main role is likely to be restricted to patients requiring endovascular interventions such as angioplasty and stenting. In most cases, a combination of DU and high-resolution MRA would provide sufficient information about the surgical extracranial plaque and relevant intracranial arterial pathology.

The other (G.A.D.) is less convinced. The risk of 1 stroke for every 200 cases is clinically meaningful and may be significantly greater, as highlighted by Moore. For example, aspirin is routinely given after acute ischemic stroke to save approximately 1 stroke for every 100 treated. It would seem illogical to be employing a procedure with almost the same magnitude of risk as the benefit accrued for a standard therapy. Further, the risk of surgery is not increased by the presence of tandem intracranial stenotic lesions (NASCET) nor small intracranial aneurysms, and the benefits are not dissimilar. Our practice is to perform CEA based on ultrasound evidence alone but with the caveat that DU results from other institutions are cross-checked with a repeat study from our own laboratory.

Where to from here? Imaging technology and interventional strategies are evolving so rapidly that this argument is likely to recede into the pages of history over the next decade. Again, science advances, patients benefit!

**References**


_**Key Words:** carotid endarterectomy † carotid stenosis † magnetic resonance angiography † ultrasonography, Doppler, transcranial_
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