Role of Conventional Angiography in Evaluation of Patients With Carotid Artery Stenosis Demonstrated by Doppler Ultrasound in General Practice

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Background and Purpose—Previous studies have suggested that patients with carotid stenosis who are candidates for endarterectomy can be effectively identified on the basis of carotid Doppler ultrasound alone. Before widespread acceptance of this policy, the accuracy of carotid Doppler ultrasound outside selected centers and clinical trials needs to be evaluated. We performed a 12-month prospective study to evaluate the accuracy of Doppler ultrasound in identifying patients for carotid intervention in general practice settings.

Methods—Each patient referred to our endovascular service for diagnostic angiography to evaluate for carotid stenosis was interviewed and examined by a neurologist. Subjects consisted of symptomatic patients with ≥50% stenosis and asymptomatic patients with ≥60% stenosis by Doppler ultrasound. Information pertaining to demographic and cerebrovascular risk factors and the results of the carotid Doppler ultrasound were recorded. The severity of stenosis on angiograms was measured with North American Symptomatic Carotid Endarterectomy Trial criteria by a blinded observer. The results of both studies were compared to determine the relative accuracy of ultrasound results.

Results—Of 130 patients (mean age, 69 ± 8.8 years) who met Doppler ultrasound criteria, 22 (17%) and 8 patients (6%) were found to have 30% to 49% or <30% stenosis by angiography, respectively. The positive predictive value of carotid Doppler ultrasound for identifying appropriate symptomatic candidates for carotid intervention (angiographic stenosis ≥50%) was 80%, with a false-positive value of 20%. The positive predictive value of carotid Doppler ultrasound for identifying appropriate asymptomatic candidates for carotid intervention (angiographic stenosis ≥60%) was 59%, with a false-positive value of 41%. Carotid endarterectomy or angioplasty and stent placement were undertaken subsequently in 60 (46%) of the patients. In 94 patients who underwent cerebral angiography alone, no complications were observed.

Conclusions—The present accuracy of carotid Doppler ultrasound in general practice does not justify its use as the sole basis of selecting appropriate patients for carotid intervention. Given the relatively low rate of associated morbidity with present day techniques, additional confirmatory studies such as angiography should be performed in every patient before a decision regarding intervention is made. (Stroke. 2001;32:2287-2291.)

Key Words: angiography ■ carotid endarterectomy ■ carotid stenosis ■ stroke, ischemic ■ ultrasonography, Doppler

Carotid endarterectomy has been shown to reduce the risk of stroke in patients with high-grade symptomatic internal carotid artery stenosis in both the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST).1-3 In 659 patients with 70% to 99% stenosis randomized in NASCET, the cumulative risk of any ipsilateral stroke at 2 years was 26% in medically treated patients and 9% in surgically treated patients.1 For moderate carotid stenosis (50% to 69%), the 5-year risk of any ipsilateral stroke was 15.7% with surgical treatment and 22.2% with medical treatment.2 The benefit of carotid endarterectomy has also been demonstrated for asymptomatic patients with carotid artery stenosis ≥60% in the Asymptomatic Carotid Atherosclerosis Study (ACAS).4 The aggregate risk for ipsilateral stroke, perioperative stroke, or death over a 5-year period was estimated to be 11.0% for medically treated groups and 5.1% for surgically treated groups. On the basis of these results, patients with either symptomatic stenosis ≥50% or asymptomatic stenosis ≥60% are presently considered for carotid endarterectomy.

The selection of patients for surgery has been based on conventional angiography in these trials. The cost and com-
Applications associated with conventional angiography have prompted investigators to assess noninvasive methods for selection of patients for carotid endarterectomy. Recent studies have suggested that carotid endarterectomy can be performed effectively on the basis of results of carotid Doppler ultrasound.\(^5\)\(^6\) The results of these studies are based on studies performed at a designated ultrasound laboratory in academic centers. A major proportion of carotid endarterectomy procedures, however, are performed in general practice settings.\(^10\)\(^11\) Before widespread acceptance, the effectiveness of endarterectomy without conventional angiography needs to be evaluated outside selected centers and clinical trials. Our neurosurgery service is a major referral base for treatment of patients with carotid stenosis in Buffalo, NY. Patients are referred by physicians in general practice on the basis of carotid Doppler ultrasound or MR angiography findings. It is our policy to perform cerebral angiography before making a decision regarding treatment in each patient. This provides a unique opportunity for evaluation of the accuracy of carotid Doppler ultrasound for detection of carotid stenosis and determination of its severity. We performed this prospective study to assess the appropriateness of patient selection on the basis of carotid Doppler ultrasound in general practice and the morbidity associated with present techniques used for angiography.

**Subjects and Methods**

**Patients**

A neurologist (A.I.Q.) evaluated each patient with presumptive carotid stenosis who was referred to the neurosurgery service between January 1 and December 31, 1999, for surgical or endovascular treatment of carotid stenosis. Subjects consisted of patients with symptomatic carotid stenosis \(\geq 50\%\) or asymptomatic carotid stenosis \(\geq 60\%\) by either Doppler ultrasound or MR angiography. The following information was collected for each patient by a personal interview: age and sex; hypertension, diabetes mellitus, hypercholesterolemia (defined as serum cholesterol \(\geq 200\) mg/dL or use of antilipemic medications), current or previous smoking, coronary artery disease, and renal insufficiency. Also recorded was the time interval between Doppler ultrasound and cerebral angiography when available (available in 72\% of the patients). Further information was supplemented from review of records sent by referring physicians. The use of antihypertensive, antilipemic, antiplatelet, and cardiac medication was also recorded. Each patient’s clinical symptoms were noted and used to evaluate whether internal carotid artery stenosis was symptomatic or asymptomatic. Each patient was evaluated immediately after the procedure by a neurologist or neurosurgeon and subsequently monitored in the hospital for 6 hours after the procedure. Each patient was evaluated in the neurosurgery outpatient clinic after 2 to 4 weeks for postprocedure disposition. Any complications during angiography or before discharge were also recorded. The final treatment outcome, carotid endarterectomy or angioplasty with stent placement, was also recorded.

**Evaluation of Angiograms**

Angiograms were obtained by a transfemoral approach on imaging systems manufactured by Toshiba or Philips. Almost all catheterizations were performed with the use of a hydrophilic 4F or 5F Simmons/Sidewinder 2 catheter (Terumo Corporation). Three vessels were catheterized in each patient: common carotid arteries bilaterally and left subclavian artery. In selected patients, right subclavian artery catheterization and/or aortograms were also performed. Digital subtraction angiographic images were collected for each patient. Ipsilateral diagnostic images of the extracranial carotid arteries were obtained. An investigator blinded to the clinical and Doppler ultrasound data measured the stenosis in the internal carotid artery using fine calipers. Measurements were performed on the angiographic view that demonstrated the maximum severity of stenosis. The diameters of the stenosis and of the distal internal carotid artery were measured. The degree of stenosis was calculated according to the NASCET method, i.e., \(1 - \text{diameter of stenosis/distant internal carotid artery diameter}\).\(^1\)\(^2\) In patients with bilateral carotid stenosis, angiographic measurements were performed on either the symptomatic carotid stenosis or the artery with more severe stenosis as demonstrated by Doppler ultrasound (in asymptomatic patients). Images of the contralateral carotid artery (whenever available) were collected for the other subgroup analysis. In patients with near occlusion where distal contrast column was possibly attenuated (2 patients), no adjustments were made to compensate for possible artifactual reduction in distal reference vessel. Fifteen angiograms were graded again in a blinded fashion by the same investigator and another investigator to estimate the intraobserver and interobserver variability. Good intraobserver agreement (Pearson’s correlation coefficient of 0.89) and interobserver agreement (Pearson’s correlation coefficient of 0.86) were observed.

**Statistical Analysis**

All values are provided as either frequency with percentage or mean with SD. The positive predictive value of Doppler ultrasound was estimated by the ratio of number of patients with stenosis demonstrated by both Doppler ultrasound and angiography to number of all patients with stenosis demonstrated by Doppler ultrasound. The false-positive value of Doppler ultrasound was estimated by the ratio of number of patients with stenosis demonstrated by Doppler ultrasound but not demonstrated by angiography to number of all patients with stenosis demonstrated by Doppler ultrasound. In asymptomatic patients, the values were calculated for detection of angiographically demonstrated stenosis \(\geq 60\%\). In symptomatic patients, the values were calculated for detection of angiographically demonstrated stenosis \(\geq 50\%\). A separate analysis was performed to calculate the true and false-positive rate for symptomatic patients with stenosis \(70\%\) to \(99\%\) by carotid Doppler ultrasound. A second analysis was performed to determine the false-negative rate of Doppler ultrasound by comparing the results of angiographic and Doppler ultrasound for measurement of stenosis \(\geq 60\%\) asymptomatic in the internal carotid artery contralateral to the stenotic lesion, whenever available. The false-negative value of Doppler ultrasound was estimated by the ratio of number of patients with angiographically demonstrated stenosis not demonstrated by Doppler ultrasound to number of all patients with angiographically demonstrated stenosis.

The Doppler ultrasound studies were performed at 20 different laboratories. Since the quality of the Doppler ultrasound laboratories may influence the accuracy of the results, we performed a subset analysis of the studies performed at our hospital’s ultrasound laboratory (accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories) to determine the rate of false-positive Doppler ultrasound–demonstrated carotid stenosis in an accredited laboratory and how it compares with other laboratories.

**Results**

A total of 133 patients underwent cerebral angiography from January 1999 through December 1999 for evaluation of carotid stenosis. Of those 133, 2 were referred on the basis of MR angiography and 1 on the basis of nonselective aortogram and were not included in the study. Of the 130 patients with carotid stenosis by Doppler ultrasound, 64 were clinically symptomatic and 66 were considered asymptomatic. The mean interval between Doppler ultrasound and cerebral angiogram was 98\(\pm\)111 days. Table 1 demonstrates the demographic and clinical characteristics of the patients. A high frequency of hypertension, hyperlipidemia, and coronary artery disease was observed in these patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>69 ± 8.8</td>
</tr>
<tr>
<td>Sex (men)</td>
<td>77 (59%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>97 (75%)</td>
</tr>
<tr>
<td>Use of antihypertensive medication</td>
<td>83 (64%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>45 (35%)</td>
</tr>
<tr>
<td>Use of hypoglycemic medication</td>
<td>43 (33%)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>35 (27%)</td>
</tr>
<tr>
<td>Previous smoking</td>
<td>66 (51%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>79 (61%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>12 (9%)</td>
</tr>
<tr>
<td>Ischemic symptoms referable to affected carotid artery</td>
<td>64 (49%)</td>
</tr>
</tbody>
</table>

Of 130 patients who met Doppler ultrasound criteria, 22 (17%) and 8 (6%) were found to have 30% to 49% or <30% stenosis, respectively. Table 2 demonstrates the correlation between stenosis measured by carotid Doppler ultrasound and angiographically measured stenosis. The proportion of stenosis <50% by angiography was highest in patients with Doppler ultrasound stenosis of 50% to 69%. However, a significant proportion of patients with Doppler ultrasound stenosis of 70% to 99% also had <50% stenosis by angiography. The positive predictive value of carotid Doppler ultrasound for identifying appropriate symptomatic candidates for carotid intervention (angiographic stenosis ≥50%) was 80%, with a false-positive value of 20%. The positive predictive value of carotid Doppler ultrasound for identifying appropriate asymptomatic candidates for carotid intervention (angiographic stenosis ≥60%) was 59%, with a false-positive value of 41%. In symptomatic patients with ultrasound-demonstrated 70% to 99% stenosis, a true positive rate of 39% and a false-positive rate of 61% were observed.

The results of Doppler ultrasound and cerebral angiography were compared in the 83 patients in whom measurements were available on the side contralateral to the side of stenosis. The sensitivity and specificity of Doppler ultrasound to detect ≥60% asymptomatic carotid stenosis were 100% and 60%, respectively. There were no false-negative results. None of the 18 patients with contralateral stenoses ≥60% by angiographic measurements missed detection by Doppler ultrasound. The false-positive rate for detection of internal carotid artery stenosis (≥50% symptomatic or ≥60% asymptomatic) at our accredited ultrasound laboratory was 20% (8 of 41 patients). The rate was lower than that of the other 19 laboratories from which patients were referred (20% versus 41%; P = 0.03).

Carotid endarterectomy or angioplasty and stent placement were undertaken subsequently in 60 (46%) of the patients. In 36 of the 42 patients, carotid angioplasty and stent placement were performed in the same session. In 94 patients who underwent cerebral angiography alone, no complications were observed. In 36 patients who underwent angiography followed by carotid angioplasty and stent placement, 11 vascular or neurological complications were observed. These included pseudoaneurysm of right external iliac artery, laceration of right femoral artery requiring surgical repair, and dissection of internal carotid artery requiring anticoagulation. Five patients had transient ischemic attacks in the perioperative period after angioplasty and stent placement. Three patients developed bradycardia and/or asystole during balloon inflation. All complications were directly related to use of larger catheters and delivery devices used for the angioplasty and stent placement. No major ischemic stroke or death was observed in any of the patients in this study.

**Discussion**

We observed a relatively high proportion of nonsignificant carotid stenosis in patients who were referred on the basis of carotid Doppler ultrasound. The proportion of nonsignificant stenosis was highest in patients with 50% to 69% stenosis by carotid Doppler ultrasound. Almost half of all patients referred on the basis of 50% to 69% stenosis by Doppler ultrasound did not have significant stenosis. However, a significant proportion (22%) of patients with 70% to 99% stenosis also had nonsignificant stenosis. Surgical or endovascular treatment was eventually provided to 46% of the patients. A low complication rate was observed for cerebral angiography in our settings. Our study points out the alarming inaccuracy of carotid Doppler ultrasound in identifying patients with carotid stenosis in general practice settings.

Presently, there is a strong argument in the literature for proceeding to carotid endarterectomy on the basis of carotid Doppler ultrasound. 7–9 This argument is based on the relative accuracy of Doppler ultrasound in previous studies. 5,6,12–15 Dawson et al 5 prospectively studied 103 patients with 111 carotid stenoses with duplex scanning and conventional angiography. Carotid duplex studies were performed at vascular laboratories at 2 institutions. The investigators found that carotid duplex provided accurate information in 93% of the patients. In 7 patients carotid duplex scanning was

**TABLE 2. Correlation Between Stenosis Demonstrated by Carotid Doppler Ultrasound and Angiography**

<table>
<thead>
<tr>
<th>Doppler Ultrasound–Measured Stenosis</th>
<th>Angiographically Measured Stenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>3 (27%)</td>
<td>11</td>
</tr>
<tr>
<td>30–49%</td>
<td>4 (36%)</td>
<td></td>
</tr>
<tr>
<td>50–69%</td>
<td>3 (27%)</td>
<td></td>
</tr>
<tr>
<td>70–99%</td>
<td>1 (9%)</td>
<td></td>
</tr>
<tr>
<td>&gt;100%</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>130</td>
</tr>
</tbody>
</table>

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inconclusive. Five of the 103 patients developed complications related to angiography. These included significant arrhythmias in 2 patients, groin hematoma in 1, and purulent infection of the femoral access site. Erdoes et al.6 prospectively evaluated 103 consecutive patients with carotid occlusive disease using color-flow duplex imaging and cerebral angiography. Duplex imaging was performed at ultrasound laboratories accredited by the Intersocietal Commission for Accreditation of Vascular Laboratories. A total of 29% of the patients were considered to require cerebral angiography after review of duplex studies for further confirmation of stenosis. In the remaining 73 patients, cerebral angiography added information to alter management in only 1 patient. Both studies concluded that treatment decisions could be made without angiography in the majority of patients with carotid stenosis.

Two factors need to be considered before the role of angiography can be defined in clinical practice: (1) the accuracy of carotid Doppler ultrasound in settings where patients are referred on the basis of ultrasound studies performed at different laboratories and (2) the complication rate associated with diagnostic angiography with present techniques. Our study points out the high proportion of inaccurate Doppler ultrasound results seen in patients with carotid stenosis. The inaccuracy was predominantly reflected as overestimation of the severity of stenosis. Since the benefit of carotid intervention varies depending on the severity of stenosis, the overestimation has implications in clinical decision making.

Previous studies have reported a neurological complication rate of 0.5% to 4%, arterial puncture site complication rate of approximately 5%, and contrast-induced renal dysfunction in 1% to 5% of patients undergoing angiography.5 The overall risk of thromboembolic-related complications occurring either during the procedure or within 24 hours thereafter ranges from 1.0% to 2.6%. Permanent neurological deficits occur in 0.1% to 0.5% of cases.5 Dion and coworkers13 assessed the delayed risk between 24 and 72 hours after the procedure. Ischemic complications occurred in 1.8% of cases; one third of the resultant deficits were permanent. Earnest et al.16 differentiated the thromboembolic risks according to different indications for diagnostic angiographic evaluation: cerebrovascular disease carried a 4.2% risk (0.6% permanent), followed by subarachnoid hemorrhage or aneurysm with 3.8% risk (0% permanent). Patients older than 60 years and those with cerebrovascular disease, especially transient ischemic attacks and recent or evolving stroke, have a substantially higher risk of new or worsened neurological symptoms after angiography.15-18 Theodotou et al.18 found a 4.5% risk in patients with transient ischemic attacks, which increased to 7.7% in patients with evolving stroke. We observed that the complication rate associated with diagnostic angiography using new hydrophilic catheters was very low. Similarly, with the use of new iso-osmolar contrast agents, no clinically evident nephrotoxicity was observed even in patients with renal insufficiency.

An issue related to the interpretation of our results is whether the results are representative of carotid Doppler ultrasound performed at other institutions. Our patients are referred predominantly from private practice settings. The patients are referred for consideration for endovascular or surgical treatment of carotid stenosis. Diagnostic angiography is performed for all patients referred for treatment at our center and not only for patients in whom Doppler ultrasound is considered inadequate. Given that patients were referred from multiple sources, the possibility that patients with nondiagnostic Doppler ultrasound results were more likely to be referred to our service cannot be completely excluded. A subset analysis of 41 patients who underwent Doppler ultrasound study at the laboratory in our hospital revealed a false-positive rate of 20% (8 of 41 with carotid stenosis by Doppler ultrasound). This high rate was observed despite the fact that the laboratory is accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories, and stenosis is quantified by both duplex imaging and velocity measurements with the use of color duplex ultrasound equipment. The accuracy of carotid Doppler ultrasound was higher in our laboratory than in 19 other laboratories (combined false-positive rate of 41%). However, our report suggests that an inappropriate surgical intervention can result in 1 of every 5 patients, even with studies performed in the best ultrasound laboratories. The Doppler ultrasound demonstrated more severe stenosis than measured on subsequent angiography. The mean interval between Doppler ultrasound and cerebral angiography was approximately 3 months. Any progression of disease in that interval could potentially reduce the difference between severity of stenosis measured by Doppler ultrasound and cerebral angiography. Therefore, the overestimation of the severity of stenosis by Doppler ultrasound could be undermined by progression of disease. Carotid revascularization was undertaken in 60 of the 130 patients referred to our service on the basis of clinical status and angiographic results. No definite comments can be made regarding the adequacy of patient exclusion on the basis of our results in the absence of long-term follow-up information.

Given the differences in referral base, time interval between ultrasound and cerebral angiography, and quality of Doppler ultrasound studies, the results from this study may not be generalizable to all institutions. Furthermore, our endovascular practice represents a large-volume service. The service volume influences the complication rate, as seen in other procedures.19,20 The low complication rate associated with cerebral angiography may not be observed at other institutions. Therefore, the most appropriate application of these results is in high-volume settings similar to ours.

Our results suggest that a high proportion of patients referred on the basis of carotid Doppler ultrasound do not have significant stenosis that may benefit from carotid intervention. Given the present low procedure-related morbidity and high degree of accuracy in centers with documented low morbidity, cerebral angiography may be considered in each patient before a decision is made regarding carotid intervention.

References


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