Duplex Scanning Exploration of the Ophthalmic Artery for the Detection of the Hemodynamically Significant ICA Stenosis

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Background and Purpose—The North American and the European Carotid Endarterectomy Trials demonstrated a significant benefit of surgery in preventing stroke for patients with symptomatic hemodynamically significant internal carotid artery (ICA) stenosis. Because the 3 angiographic methods of measuring carotid stenosis provide discrepant results, the indication for surgery depends on the method used for the evaluation of the angiogram. The goal of this study was to verify whether color duplex scanning of the ophthalmic artery alone might be reliable for detection of the extracranial hemodynamically significant ICA stenosis.

Methods—Three groups of patients (351 total patients) with transient ischemic attack or minor stroke referred for possible carotid endarterectomy were examined by means of color duplex scanning of the ICA, transcranial Doppler, color duplex scanning of the ophthalmic artery, and angiography of the ICA.

Results—In the first group (n = 31) the comparison of findings from each method and the direct measurement of the residual lumen of plaque removed “en bloc” showed that the findings of the ophthalmic artery color duplex scanning, subdivided into 5 categories—NP (normal positive), LP (low positive), NF (no flow), REV (reverse flow), PP (pathological positive)—were associated with the best overall agreement (96.7%). The accuracy of the various categories of the ophthalmic artery color duplex scanning signals was studied in the second group of patients (n = 200). The results pointed out that all but low positive categories were associated with high diagnostic accuracy. Finally, the results obtained in the third group (n = 120) showed that a significant increase in the specificity of the low positive signal could be obtained by processing this signal in terms of pulsatility index and of transmission of pulsatility index.

Conclusions—Our results suggest that the diagnostic capacity of color duplex scanning for the detection of ICA critical stenosis can be appropriately increased if it is performed also at the level of the ophthalmic artery and if the Doppler signals are processed on the basis of criteria we applied. (Stroke. 1999;30:821-826.)

Key Words: Doppler, duplex ■ ophthalmic artery ■ stenosis ■ ultrasonography

The North American and the European Carotid Endarterectomy Trials1,2 have demonstrated a significant benefit of surgery in preventing stroke for patients with symptomatic hemodynamically significant internal carotid artery (ICA) stenosis. The detection of the hemodynamically significant ICA stenosis has become mandatory for all researchers in the diagnosis of ICA occlusive disease.

Arteriography provides an incomplete evaluation of the ICA stenosis because it images the lumen alone and does not give any information on the vessel wall. To accurately calculate the diameter stenosis, the residual lumen and the original diameter of the artery should both be measured.3 Furthermore, because the 3 angiographic methods of measuring carotid stenosis provide discrepant results, the indication for surgery depends on the method used for the evaluation of the angiogram.4 Finally, arteriography is not suitable for screening because of the ever-present risk of a disabling stroke and systemic complications5–10 and also because of its high cost.11 Ultrasound duplex scanning has become the leading routine method for the evaluation of ICA stenosis because not only is it noninvasive but it also appears capable of detecting the flow abnormalities associated with increasing degrees of narrowing.

Dawson et al12 have clearly shown that when skillful sonographers perform ultrasound studies it is possible to proceed to carotid endarterectomy without arteriography. Duplex scanning however, may be difficult when the bifurcation is very high, when the patient’s neck is very thick, and when the carotid plaque is heavily calcified, preventing adequate insonation of the bulb.12–14 These limitations can be overcome if, as suggested by the pioneers of cerebrovascular ultrasound exploration,15–18 we perform additional studies of the collateral blood supply, which is automatically activated when the ICA narrowing becomes hemodynamically significant.19
The ophthalmic artery (OA) appears very suitable for study because of the following characteristics: (1) OA is the first branch of the ICA and therefore the nearest to the carotid bulb in which the stenosis is located; (2) according to its distribution, OA performs like a catheter that transfers straight away the values of the perfusion pressure gradient from downstream of the ICA stenosis toward the eyelids; (3) the easy insonation with color duplex scanning of the OA (OA CDS) allows us, without interference from the bony skull, to overcome the frequent limitations (5% to 19%)²⁰ of transcranial Doppler ultrasonography (TCD) in the exploration of the middle cerebral artery and of the anterior cerebral artery because of the temporal bone thickness; and (4) finally, OA is placed at the watershed between the ICA and the external carotid artery (ECA) territories, therefore it is particularly liable to ischemias for hemodynamic reasons.

Previously, Spencer and Whisler²¹ applied duplex scanning of the OA for the detection of intracranial ICA stenosis, and Schneider et al²² used duplex scanning for the assessment of the OA for the detection of intracranial ICA stenosis, and microscopic Doppler ultrasonography (TCD) in the exploration of the middle cerebral artery and of the anterior cerebral artery territories, therefore it is particularly liable to ischemias for hemodynamic reasons.

Subjects and Methods

We studied 3 groups of patients (n=351) with transient ischemic attack or minor stroke referred for possible carotid endarterectomy, by means of ICA CDS, TCD, color duplex scanning of the OA, and arteriography. Patients with severe contralateral stenosis or intracranial artery stenosis were excluded from this study.

Our protocol included the following. Before carotid endarterectomy all patients underwent ICA CDS with an Acuson 128 XP ultrasound device with 7.0- and 5.0-MHz linear array transducers. The peak systolic velocity and the end-diastolic velocity at the level of the first part of the aortic arch. Biplanar traction technique via the femoral artery with the injection of contrast medium at the level of the first part of the aortic arch. Bipolar images were obtained for each ICA. The measurements of ICA diameter reduction were performed by the NASCET method and by visual estimation by 2 independent angiographers. All measurements were blindly assessed. Three experienced examiners (D.R., I.N., and F.B.) performed ICA CDS, TCD, and OA CDS examinations without knowledge of the degree and side of the stenosis or occlusion. Table 2 shows the criteria used for discrimination between hemodynamically and nonhemodynamically significant ICA stenosis.

Statistical analysis was performed with the Student’s (2-tailed) t test, and the results are given as mean±SD. All subjects gave informed consent to participate in the study, which was approved by the Ethics Committee of the University of Florence.

Results

In the first group of 31 patients (24 men and 7 women; mean age, 64 years; age range, 52 to 73 years) we compared the findings of ICA angiography, color duplex sonography of ICA, TCD, and (4) OA CDS versus the residual lumen of ICA,
TABLE 1. Accuracy of the 4 Diagnostic Methods Used Versus the Direct Measure of Residual ICA Lumen

<table>
<thead>
<tr>
<th>Measure</th>
<th>AGF</th>
<th>ICA CDS</th>
<th>TCD</th>
<th>OA CDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic ICA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stenosis:</td>
<td>13</td>
<td>11</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>residual lumen</td>
<td>≤1.5 mm</td>
<td>4 (FP)</td>
<td>1 (ND)</td>
<td>4 (FP)</td>
</tr>
<tr>
<td>Nonhemodynamic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA stenosis:</td>
<td>18</td>
<td>12</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>residual lumen</td>
<td>&gt;1.5 mm</td>
<td>1 (FN)</td>
<td>2 (ND)</td>
<td>1 (FN)</td>
</tr>
</tbody>
</table>

Sensitivity 91.6% 100% 91.0% 92.3%
Accuracy 74.2% 87.0% 87.0% 96.7%
Specificity 75.0% 100% 100% 100%

AGF indicates arteriography; FP, false positives; FN, false negatives; and ND, nondiagnostic tests.

TABLE 2. Criteria Used for Discrimination between Hemodynamically and Nonhemodynamically Significant ICA Stenosis

<table>
<thead>
<tr>
<th>AGF</th>
<th>ICA CDS</th>
<th>TCD</th>
<th>OA CDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic ICA stenosis: Ipsilateral ICA stenosis ≥70% Systolic velocity of the ipsilateral ICA ≥250 cm/s End-diastolic velocity ≤100 cm/s Reversal of the ipsilateral ACA flow associated with increase of velocity on the ipsilateral CCC LP: OA systolic velocity of the stenotic side at least 25% lower than that of the controlateral side, associated with a significant decrease or disappearance on the ipsilateral CCC NF: No Doppler signal was detected at the stenotic side REV: Backward flow at the stenotic side PP: When the anterograde Doppler signal disappeared during contralateral CCC and did not change during ipsilateral CCC</td>
<td></td>
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<tr>
<td>Nonhemodynamic ICA stenosis: Ipsilateral ICA stenosis &lt;70% Systolic velocity of the ipsilateral ICA &lt;250 cm/s End-diastolic velocity &lt;100 cm/s Normal direction of flow in the ipsilateral ACA associated with decrease of flow velocity on the ipsilateral CCC NP: Anterograde Doppler signal of OA with systolic velocity of 48.5±7.8 cm/s, associated with significant reduction of velocity on the ipsilateral CCC</td>
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</tbody>
</table>

LAGF indicates arteriography; ACA, anterior cerebral artery. See text for definition of ratings for OA CDS.

obtained by the whole plaque removed en bloc at the time of carotid endarterectomy.

The 31 plaques consisted of short portions of the common carotid artery and of the ECA with the diseased segment of the ICA, which always included the point of maximum lumen encroachment. They were promptly placed in 10% formalin

method gave appropriate answers in 17 cases and nonappropriate answers in 1 (sensitivity, 91.0%). In 3 cases the test was nondiagnostic because the temporal windows were closed. The overall agreement between the gold standard and TCD was 87.0%.

Finally, the OA CDS signals in the first group of plaques gave appropriate answers in 12 cases (in 6 the signal was REV, in 1 it was NF, in 1 it was PP, and in 1 it was LP) and nonappropriate answers in 0 (specificity, 100%), whereas in the second group of plaques the OA CDS gave appropriate answers in 18 (in these cases the signals were NP) and nonappropriate answers in 1 (LP signal; sensitivity, 92.3%). The overall agreement between this method and the gold standard was 96.7%.

In a second group of 200 patients (148 men and 52 women; mean age, 68.4 years; 397 ICAs), we verified, on the basis of the results obtained in the first group, the accuracy of each of the 5 categories of the OA signals versus its screening capacity between the hemodynamically and nonhemodynamically significant ICA stenoses. The results obtained in this second group of patients are shown in Figure 2. In this group, 285 ICAs showed a nonhemodynamically significant stenosis, 51 a hemodynamically significant stenosis, and 61 an ICA occlusion.

The NP signal was in any case associated with a nonhemodynamically significant ICA stenosis. The NF signal was constantly associated with hemodynamically significant ICA occlusive disease: 13 ICAs with 80% to 99% luminal narrowing and 16 ICAs with occlusion of the lumen. The REV signal was constantly associated with hemodynamically significant ICA occlusive disease: 18 ICAs with 80% to 99% stenosis of the lumen and 19 ICAs with occlusion of the lumen. The PP signal was constantly associated with hemodynamically significant ICA occlusive disease: 10 ICAs with 80% to 99% stenosis and 10 ICAs with occlusion of the lumen.

The LP Doppler signal was associated with 90 ICAs with <60% nonhemodynamically significant stenosis, 30 ICAs with 60% to 79% nonhemodynamically significant ICA stenosis, 10 ICAs with 80% to 99% hemodynamically significant ICA stenosis, and 16 ICAs with occlusion of the lumen.

Finally we examined a third group of 120 patients (63 men, 57 women; mean age, 69.1 years; age range, 56 to 80 years; 240 ICAs), who showed LP signal at 1 eye. Toward the aim of increasing the specificity of LP signal, we processed this parameter in terms of the pulsatility index (PI)^26: (PI = systolic velocity − diastolic velocity/mean velocity). We also calculated the transmission of the PI (TPI)^27: (TPI = PI of the stenotic side/PI of nonstenotic side × 100) between the 2 OAs. Because the reproducibility of PI, as automatically provided by our device, was low, we measured straight away on the display the value of the systolic and diastolic velocities. Then we traced the envelope of each OA CDS signal and received automatically the values of PI. In 5 patients without ICA occlusive disease, we tested the maximum and the mean reproducibilities of PI (5.9% and 4.7%, respectively) and of TPI (6.1% and 4.2%, respectively). We classified the signal as NP if the TPI value was >90% and LP if this value was <80%, whereas the TPI values ranged between 80% and 90% and were classified “uncertain values.” On the basis of arteriography, ICA CDS, and TCD, the ICAs were classified into 3 subgroups: (1) patients with nonhemodynamically significant stenosis (n = 55 with <60% stenosis and n = 25 with 60% to 79% ICA stenosis); (2) n = 15 patients with 80% to 99% ICA stenosis; and (3) n = 25 patients with occlusion. The OA PI value was 1.29 ± 0.54 ipsilateral to an ICA with hemodynamically significant occlusive disease, whereas it was 1.62 ± 0.37 in the presence of noncritical ICA stenosis (P < 0.01). The average length for a complete measurement of TPI in each patient was 8.1 ± 2.5 minutes.

In the first subgroup, the values of TPI ranged between 89% and 107%, mean ± SD 96.9% ± 5.1 (<60% ICA steno-
sis), and between 87% and 106%, mean±SD 96.1±5.9 (60% to 79% ICA stenosis). In the second subgroup, the value of TPI ranged from 48% to 84%, mean±SD 68.2±9.8 (80% to 99% ICA stenosis), and in the third subgroup 43% to 88%, mean±SD 69.8±12.9 (occlusion of ICA). The difference between the mean value of TPI of the ICAs of the first 2 subgroups (96.6±5.3) and that of the other 2 subgroups (69.2±11.7) was statistically significant (P<0.01). Figure 3 also shows that in 7 cases the TPI values dropped in the “uncertain area”: 2 cases of the first subgroup, 2 of the second, and 3 of the third subgroup; therefore there were 2 cases of false-positive results and 5 cases of false-negative results.

**Discussion**

Our results point out that the duplex scanning approach of the OA appears very suitable for the assessment of hemodynamically significant ICA occlusive disease. The comparison of the gold standard and the findings obtained by the other methods of ICA examination has shown that the ones delivered by OA CDS were associated with the overall best agreement: OA CDS, 96.7%; ICA CDS, 87.0%; TCD, 87.0%; and arteriography, 74.2% (Table 1).

Figure 2 shows that not all of the 5 categories of the OA CDS signals have shown the same degree of reliability. NP, NF, REV, and PP parameters showed a very high degree of specificity (100%). The NP parameter was constantly associated with nonhemodynamically significant ICA stenosis, whereas NF and REV signals were, in any case, associated with hemodynamically significant ICA occlusive disease. However, these 2 parameters were not able to discriminate between hemodynamically significant stenosis and occlusion of the ICA: NF and REV signals were found in 13 and 18 patients, respectively, with hemodynamically significant ICA stenosis and in 16 and 19 patients with ICA occlusion. These results are in keeping with those obtained by others.20

The PP OA CDS signal, for which the incidence rate has been equal to 5% of all ICAs studied and which can be easily discriminated by NP and LP signals on the basis of the ipsilateral and contralateral CCCs, was found in 10 patients with hemodynamically significant ICA stenosis and in 10 patients with ICA occlusion. Therefore, this signal also appeared very reliable for the screening of hemodynamically ICA occlusive disease, but it did not discriminate between ICA stenosis and ICA occlusion. LP signal, on the other hand, has shown a very low specificity (18%). This parameter was associated with hemodynamically nonsignificant ICA stenosis in 90 patients and with hemodynamically significant ICA stenosis or occlusion in 26 patients. The very low accuracy of the LP OA CDS signal may be related to the following: (1) the abnormal origin of OA from the middle meningeal artery (branch of ECA) whose frequency ranges between 2% and 5%;28 (2) the tortuous pathway of the OA, associated with eye movement, makes the angle between the ultrasound beam and the artery lumen variable; (3) the absolute value of the velocity measurement is more liable to be wrong primarily when its value is low. These limitations may be reliably overcome if we process the LP signal in terms of PI, which, as the result of a ratio, is less dependent on the ultrasound beam angle of insonation. The results shown in Figure 3 point out that the LP OA CDS signal when processed in terms of PI and TPI can properly discriminate between hemodynamically nonsignificant and significant ICA stenosis. The >90% TPI value (the value with the highest sensitivity) was in all cases associated with hemodynamically nonsignificant ICA stenosis or occlusion. Finally, the TPI values ranged between 80% and 90% and appeared as “uncertain values.” Because the ICA occlusion cannot be subjected to carotid endarterectomy, the most clinically relevant diagnostic problem concerns the discrimination between hemodynamically
and nonhemodynamically significant ICA stenosis. The results shown in Figure 3 point out that if we set the cutoff point at the TPI value of 90% all the hemodynamically significant ICA stenoses are discriminated, and a few (only 2 ICAs in our group of patients) hemodynamically nonsignificant ICA stenoses may be diagnosed as “false-positives.” However, because for the subgroup of transient ischemic attack patients with severe ICA stenosis the average annual risk of stroke in nonoperated patients was 14% per year and the periprocedural risk of any stroke or death was 5.8% (and functional deficit persisting beyond 90 days and death was 2.1%), we believe it is better to use a cutoff point that provides the best sensitivity rather than the best specificity.

In conclusion, our results confirm the statement that the exploration of the collateral blood supply in an arterial territory can be a reliable way to ascertain the hemodynamic meaning of the artery stenosis present in that territory. Also, if the advent of duplex ultrasound modality has unfortunately made the periorbital Doppler sonography a procedure that is not routinely performed at present for the extracranial ICA exploration, that approach still is the most cost-effective Doppler approach for the detection of the extracranial critical stenosis of this artery. Our results suggest that according to the periorbital Doppler principle if the Duplex ICA examination is performed also at the level of the OA, and if the obtained signals are assessed on the basis of the criteria we applied, its diagnostic capacity in the detection of the critical stenosis and its cost-effectiveness both can be appropriately increased.

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References
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