Assessment of ≥50% and <50% Intracranial Stenoses by Transcranial Color-Coded Duplex Sonography

Ralf W. Baumgartner, MD; Heinrich P. Mattle, MD; Gerhard Schroth, MD

Background and Purpose—A favorable risk-benefit ratio for warfarin compared with aspirin has been reported for the prevention of major vascular events in symptomatic ≥50% intracranial stenoses. Transcranial color-coded duplex sonography (TCCS) criteria providing an accurate detection of ≥50% and <50% stenoses of the anterior, middle, and posterior cerebral arteries and basilar and vertebral arteries were evaluated retrospectively with angiography used as the standard of reference.

Methods—Prospectively collected TCCS, extracranial color-coded duplex sonography, and intra-arterial digital subtraction angiography data of 310 patients were reviewed. The patients had angiography for confirmation of symptomatic extracranial ≥70% carotid stenoses, symptomatic stenoses (peak systolic velocity higher than the corresponding mean value +2 SDs of 104 normal subjects), and occlusions of the middle cerebral or basilar artery previously assessed by ultrasound. The sonographer was not aware of angiographic findings.

Results—TCCS would have detected all 31 of ≥50% intracranial stenoses with 1 false-positive and 35 of 38 <50% stenoses with 3 false-positives. One of 69 stenoses (1%) and 280 of 2741 normal arteries (10%) were missed because of inadequate insonation windows. The corresponding peak systolic velocity cutoffs for ≥50%/<50% stenoses were ≥155/≥120 cm/s (anterior cerebral artery), ≥220/≥155 cm/s (middle cerebral artery), ≥145/≥100 cm/s (posterior cerebral artery), ≥140/≥100 cm/s (basilar artery), and ≥120/≥90 cm/s (vertebral artery).

Conclusions—TCCS may reliably assess ≥50% and <50% basal cerebral artery narrowing and prove useful for noninvasive management of patients with symptomatic intracranial stenoses. (Stroke. 1999;30:87-92.)

Key Words: anticoagulants • aspirin • stenosis • ultrasonography, transcranial

Atherosclerotic narrowing of the intracranial cerebral arteries is assumed to cause approximately 10% of ischemic strokes.1,2 Secondary stroke prevention in patients with transient ischemic attack or ischemic stroke caused by a stenosed intracranial artery has been empirical. The recently published Warfarin-Aspirin Symptomatic Intracranial Disease study, however, suggests that oral anticoagulation is more effective than aspirin for preventing major vascular events in patients with ≥50% symptomatic intracranial stenoses.3 This study used catheter angiography for the assessment of cerebral artery narrowing. Because of the risk, inconvenience, and cost associated with angiography, the primary use of a noninvasive diagnostic method such as transcranial color-coded duplex sonography (TCCS) would be preferable.

Conventional transcranial Doppler sonography is of established value for detecting stenoses of the intracranial arteries.6–14 TCCS criteria for detection and quantification of intracranial stenoses have not yet been established.

The purpose of the present study was to evaluate TCCS criteria providing the best possible diagnostic accuracy for detecting ≥50% and <50% intracranial stenoses with cerebral angiography used as the standard of reference.

Subjects and Methods

Patient Recruitment and Inclusion and Exclusion Criteria

Between November 1992 and December 1996, 310 consecutive patients (102 women, 208 men; mean ± SD age, 56 ± 16 years) with cerebral or ocular ischemic events were first examined by TCCS and extracranial color-coded duplex sonography (ECCS) and thereafter by cerebral intra-arterial digital subtraction angiography. Cerebral angiography was done for confirmation of symptomatic ≥70% carotid stenoses, symptomatic stenoses, and occlusions of the middle cerebral (MCA) or basilar (BA) arteries. Angiograms were done in symptomatic ≥70% carotid stenoses for confirmation of ultrasonic diagnosis before carotid endarterectomy,15 in MCA or BA occlusions with strokes of ≤6 hours’ duration to evaluate whether subjects were candidates for local arterial fibrinolysis,16 and with strokes of >6 hours’ duration for diagnostic purposes. TCCS, ECCS, cerebral angiographic, and the corresponding clinical, CT, or MRI findings were collected prospectively in a database.

The presenting ischemic ocular or cerebral deficits were classified as amaurosis fugax (monocular blindness lasting ≥24 hours), retinal infarct (monocular blindness lasting >24 hours), transient ischemic attack (focal neurological deficit lasting ≥24 hours), or stroke (focal neurological deficit lasting >24 hours). Two hundred one patients had ischemic strokes, 78 had transient ischemic attacks, 21 had amaurosis fugax, and 10 had retinal infarcts. The median interval

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between ultrasonic studies and the onset of stroke was 31 days (range, 2 to 126 days), and that between ultrasonic studies and cerebral angiography was 2 days (range, 0 to 6 days).

Patients were excluded from the study if the indication for cerebral angiography was for a tumor, aneurysm, vasospasm, arteriovenous fistula, sinovenous thrombosis, or a diagnostic workup of intracranial hemorrhage and vascular malformation.

**ECCS Studies**

The extracranial cerebral arteries were examined with an Acuson 128 XP/10 equipped with a 5.0/7.0-MHz linear scan. Ultrasonographic evaluation of arterial stenoses and occlusions was performed according to previously published criteria.15,16

**TCCS Studies**

The intracranial cerebral arteries were studied with an Acuson 128 XP/10 equipped with a 2.0/2.5-MHz 90° sector scan with the same Doppler energy output and method of examination as described previously.19 In brief, the MCA, anterior (ACA), precommunicating (P1), and postcommunicating (P2) posterior (PCA) cerebral arteries were insonated through the temporal window with the patient in a supine position, whereas the BA and intracranial vertebral (VA) arteries were investigated through the foramen magnum with the patient in a sitting position. Each large cerebral artery was investigated by spectral Doppler sonography with the color-coded Doppler signal used as a “road map” for the presence of stenoses, occlusions, and cross-flow through the circle of Willis (see below). Flow direction (antegrade or reversed) and peak systolic (PSV) and end-diastolic (PDV) velocities were noted for every insonated artery. In case of suspicion of an intracranial stenosis (see below), the presence of low-frequency, high-intensity Doppler signals was also evaluated. Angle correction was performed when the Doppler sample volume was located within a straight vessel segment ≥20 mm in length.20

The sonographer was aware of extracranial ultrasonographic findings but was blinded to the results of cerebral angiography.

An intracranial stenosis (Figures 1 and 2) was diagnosed during prospective data collection when spectral Doppler sonography showed both a focal increase of PSV and/or PDV that was higher than the mean value +2 SDs for the corresponding cerebral artery of 104 normal subjects reported previously and low-frequency, high-intensity Doppler signals. ACA velocity is often increased in the presence of cross-flow through the anterior communicating artery22 and in high-grade stenosis or occlusion11,12 of the ipsilateral MCA. A high-grade stenosis of the MCA was diagnosed with the use of the velocity cutoffs established by Röther et al.13 P1 PCA velocity is enhanced in case of collateral flow through the posterior communicating artery to the carotid artery.5,22,24 Consequently, no ACA and P1 PCA stenoses were diagnosed when TCCS findings suggested the presence of cross-flow through the anterior communicating artery and posterior communicating artery, respectively, and no ACA stenosis was diagnosed when TCCS findings suggested the presence of high-grade stenosis or occlusion of the ipsilateral MCA.

An intracranial occlusion was diagnosed when the Doppler signal of the corresponding cerebral artery was lacking and other ipsilateral basal cerebral arteries were identified.23,25 For diagnosis of occlusions of the intracranial VA or BA, the criteria established by von Büdingen and Staudacher26 also had to be fulfilled. Cross-flow through the circle of Willis was assessed as reported recently.27

**Angiographic Studies**

Selective intra-arterial digital subtraction angiography (Philips Diagnost Arc A) was performed by a femoral artery approach in both ICAs in all patients, in both VAs in 261 patients, and in 1 VA in 49 patients. The injected volume of contrast medium was 5 to 8 mL Ultravist 300 (Iopromidum, Schering AG). Standard anteroposterior and lateral views (512×512 matrix; since December 1993, 1024×1024 matrix) of the extracranial and intracranial circulation were obtained routinely. The angiograms were reviewed retrospectively and independently at separate reading sessions by 2 of the authors (H.P.M., G.S.), who were not aware of ultrasound findings. Extracranial carotid stenosis was measured by the North American Symptomatic Carotid Endarterectomy Trial technique.18 For the assessment of intracranial stenosis, the vessel being evaluated was measured at its point of maximal narrowing and compared with the angiographically normal section of the vessel adjacent to the stenosis to determine the degree of stenosis (normal lumen diameter – residual lumen/normal lumen diameter). Finally, each intracranial artery was graded separately as follows: no stenosis, stenosis <50%, stenosis 50–79%, stenosis ≥80%, occlusion.
Statistical Analysis
Differences of cerebral artery velocities in patients without, with <50%, and with ≥50% intracranial stenoses at angiography were compared by nonparametric ANOVA (Mann-Whitney U test). The same statistical test was used to compare intrastenotic MCA velocities and the degree of intracranial stenosis at angiography in patients with and without additional 70% to 100% obstructions of the ipsilateral extracranial carotid arteries. The nonparametric Spearman rank correlation coefficient was used to assess consistency of interpretation of cerebral angiograms between both observers. Two-sided probability value of <0.05 was considered significant.

Results
Angiography showed intracranially 69 stenoses (31 ≥50%, 38 <50%) in 51 patients (16%) and 20 occlusions in 18 patients (6%). Thirty-nine patients had 1, 8 patients had 2, 2 patients had 3, and another 2 patients had 4 stenoses. Ten stenoses were located in the ACA, 29 in the MCA, 15 in the PCA, 7 in the BA, and 8 in the VA. Sixteen patients had 1 occlusion, and 2 patients had 2 occlusions. One occlusion was located in the ACA, 8 were located in the MCA, 2 in the distal P2 PCA, 3 in the BA, and 6 in the VA.

TCCS identified 2461 of 2741 intracranial arteries (90%) examined by cerebral angiography. In detail, TCCS identified 515 of 620 ACAs (83%), 563 of 620 MCAs (91%), 557 of 620 PCAs (90%), 291 of 310 BAs (94%), and 535 of 571 VAs (94%).

According to the criteria shown in Tables 1 and 2, TCCS would have detected 66 of 69 stenoses (96%) with 4 false-positives; 1 narrowed ACA was missed because of an inadequate temporal bone window. In addition, 18 of 20 occlusions (90%) were identified by ultrasound.

PSVs in arteries with ≥50%, with <50%, and without stenoses are reported in Table 3. PDVs are not reported.

| TABLE 1. Ultrasonic Detection of ≥50% Intracranial Stenoses (n=31) With Angiography as Standard of Reference |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| PSV Cutoff, cm/s | Sensitivity, % | Specificity, % | Positive Predictive Value, % | Negative Predictive Value, % |
| ACA ≥155       | 100            | 100            | 100                           | 100                           |
| MCA ≥220       | 100            | 100            | 100                           | 100                           |
| PCA ≥145       | 100            | 100            | 100                           | 91                            |
| BA ≥140        | 100            | 100            | 100                           | 100                           |
| VA ≥120        | 100            | 100            | 100                           | 100                           |
| Angiography No. Mean ± SD Degree (Range) |
| 4              | 60 ± 8 (52–71) |
| 11             | 67 ± 11 (50–80) |
| 10             | 63 ± 7 (50–72) |
| 3              | 67 ± 14 (53–85) |
| 3              | 69 ± 14 (55–84) |
because they were not found to be as sensitive and accurate as the PSV values for the assessment of stenoses.

### Ultrasonic Detection of ≥50% Stenoses

When we use the PSV cutoff values given in Table 1 as diagnostic criteria, TCCS would have detected all 31 stenoses with 1 false-negative PCA stenosis. The false-positive PCA stenosis was mistaken 4 days before angiography and showed a PSV of 154 cm/s; no angle correction was done. Reexamination 1 day after angiography showed a PSV of 128 cm/s.

### Ultrasonic Detection of <50% Stenoses

Using the PSV cutoff values reported in Table 2 as diagnostic criteria, TCCS would have detected all 31 stenoses (99%) additional 70% to 100% carotid obstructions (98%, $p<0.0001$). The Spearman rank correlation coefficient between both readers of angiograms was statistically significant for differentiating between no stenoses, stenoses <50%, stenoses ≥50%, and occlusions ($r=0.93$, $P<0.0001$).

#### Discussion

With the use of the diagnostic criteria elaborated in this study, TCCS would have detected all ≥50% intracranial stenoses with 1 false-positive and 92% of <50% intracranial stenoses with 3 false-positives. In addition, 90% of intracranial occlusions were identified by ultrasound.

Adequate Doppler signals were obtained in 68 of 69 angiographically proven intracranial stenoses (99%). This finding is probably incidental because the detection rate for the different cerebral arteries was 83% to 94%, which is in accord with previous TCCS studies reporting rates of 80% to 98%. Recent studies using echo contrast agents provided conclusive TCCS examinations in 67% to 72% of patients with ischemic cerebrovascular disease and ultrasound-refractory temporal windows, suggesting that the evaluation of intracranial arteries may become possible in most patients with ischemic stroke.

### Tables

#### Table 2. Ultrasonic Detection of <50% Intracranial Stenoses (n=38) With Angiography as Standard of Reference

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA*</td>
<td>≥120</td>
<td>100</td>
<td>99</td>
<td>73</td>
</tr>
<tr>
<td>MCA</td>
<td>≥155</td>
<td>94</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>PCA</td>
<td>≥100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>BA</td>
<td>≥100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>VA</td>
<td>≥90</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*One stenosed anterior cerebral artery was missed because of an inadequate temporal bone window.

#### Table 3. PSVs in Intracranial Arteries With ≥50% Stenoses, <50% Stenoses, and No Stenoses at Angiography

<table>
<thead>
<tr>
<th>Degree of Stenosis at Angiography</th>
<th>PSV Cutoff, cm/s</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive Predictive Value, %</th>
<th>Negative Predictive Value, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA</td>
<td>189±34 (155–227)</td>
<td>128±15 (109–145)</td>
<td>81±18 (33–135)</td>
<td>&lt;0.05</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MCA</td>
<td>301±49 (221–400)</td>
<td>176±24 (141–217)</td>
<td>100±20 (58–151)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCA</td>
<td>199±17 (176–228)</td>
<td>127±17 (112–154)</td>
<td>63±12 (36–100)</td>
<td>&lt;0.01</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BA</td>
<td>194±46 (144–248)</td>
<td>119±17 (109–139)</td>
<td>64±16 (28–100)</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>VA</td>
<td>191±66 (123–256)</td>
<td>100±4 (84–104)</td>
<td>47±14 (20–89)</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are mean±SD PSV (range).
The low number of false-negative intracranial stenoses found in this study may be related to the angiographically proven absence of branch occlusions in the territory of the narrowed arteries. Multiple MCA branch occlusions are associated with decreased velocities in the MCA main stem and in our experience may cause normal intrastenotic velocities and false-negative TCCS findings in case of MCA main stem narrowing. The principal reason for the absence of intracranial branch occlusions was that most TCCS investigations were performed in the chronic phase of cerebral infarction, when branch occlusions were already recanalized. Another explanation for the low number of false-negative stenoses is that the color Doppler signal was used as a road map to visualize both the vascular anatomy and focal areas with increased flow velocities. Thus, the sonographer was able to investigate all vessel segments by spectral Doppler sonography and to estimate whether the placement of the angle indicator was adequate (Figure 1) or not (Figure 2). When a stenosis was located in a curved segment and prevented the use of angle correction, the position of the ultrasound probe was changed to obtain the smallest insonation angle possible. It is important to note that intrastenotic velocity increase may persist for a few centimeters (“jet”) and surpass the anatomic extent of narrowing. The jet is likely to increase the probability of detecting a stenosis and may lead to a more favorable angle of insonation in curved vessels. Nevertheless, TCCS missed 2 <50% stenoses located in MCAs with downward convex courses at angiography. This suggests that the absence of angle correction resulted in the failure to detect both MCA stenoses and that stenoses located in curved intracranial arteries may represent a diagnostic pitfall of TCCS.

Interestingly, no intracranial stenosis would have been missed in patients with additional ≥70% stenoses of the ipsilateral extracranial carotid artery. As expected, intrastenotic MCA velocities were lower in patients with compared with those without additional ≥70% ipsilateral carotid stenoses (P<0.05). This finding may also have resulted from the trend of patients with additional ≥70% carotid stenoses to have a lower average degree of MCA stenosis at angiography.

There were 1 false-positive ≥50% P2 PCA stenosis and 3 false-positive <50% ACA stenoses in this series. Inadequately high insonation angles may result in the measurement of high flow velocities and false-positive stenoses. No angle correction was performed in ACA stenoses (Figure 2) and the false-positive PCA stenosis because the angle corrector was only used when color Doppler imaging suggested the presence of straight vessel segments ≥20 mm in length. Thus, inadequately high insonation angles were probably not the cause of the false-positive stenoses. TCCS may misdiagnose intracranial stenoses in conditions with increased cerebral blood flow, such as cross-flow through the circle of Willis, leptomeningeal anastomoses supplied by the ACA in the presence of high-grade stenosis or occlusion of the MCA, and arteriovenous malformation. No ACA stenosis was diagnosed when ultrasonic findings indicated the presence of collateral flow through the anterior communicating artery or high-grade stenosis or occlusion of the ipsilateral MCA. Patients with angiographic signs of arteriovenous malformation were excluded. Thus, increased blood flow is a very unlikely explanation for the false-positive stenoses. Symmetrical ACAs are associated with higher velocities in the larger vessel. This might be the cause in 1 false-positive <50% ACA stenosis since the contralateral ACA was hypoplastic and showed slow velocities. Intracranial vasospasm, vasculitis, and thromboembolism may change the degree of luminal narrowing over time. Patients with cerebral vasospasm and vasculitis were excluded. However, recanalization is the most likely cause of the false-positive PCA stenosis because the follow-up TCCS examination performed 1 day after cerebral angiography indicated the regression to a <50% stenosis.

Cerebral angiography was used as the standard of reference in the present study. Nevertheless, this technique may have some limitations. Biplanar assessment of intracranial stenoses is mostly not obtainable, and reliable measurement of intrastenotic diameter is often difficult because of the small vessel size. Conversely, velocities measured by ultrasound are inversely proportional to the diameter squared of the insonated vessel. TCCS may thus be more sensitive for detection of <50% intracranial stenoses by principles of mathematics over angiography that measures diameter only. However, there are no data available to prove this hypothesis. This or interindividual differences in arterial diameter may be the cause of the other 2 false-positive <50% ACA stenoses.

It is remarkable that no intracranial stenosis was misdiagnosed as occlusion. Conversely, ultrasound missed 2 occlusions located in the distal P2 PCA, probably because the adjacent superior cerebellar artery was misinterpreted as PCA. Because of the low number of cerebral artery occlusions observed in this study, the diagnostic accuracy for ultrasonic assessment was not calculated.

As expected, the prevalences for intracranial stenoses and occlusions were higher than those found in previous investigations. Difference in patient selection is the most likely cause since cerebral angiography was only performed when ultrasound suggested the presence of extracranial or intracranial occlusive vascular disease.

The Warfarin-Aspirin Symptomatic Intracranial Disease study reported a favorable risk-benefit ratio for warfarin compared with aspirin for the prevention of major vascular events in patients with symptomatic 50% to 99% intracranial stenoses. The present results indicate that TCCS may provide a reliable and noninvasive assessment of such patients and supply the information needed to initiate adequate medical treatment. Intracranial stenoses may regress by recanalization of thromboembolic material. A recent study has shown good reproducibility for TCCS velocity measurements. Thus, repetitive TCCS examinations in patients with symptomatic ≥50% stenoses may detect the regression to <50% (R.W. Baumgartner, unpublished data, 1994) and prevent the inappropriate long-term use of anticoagulation and its well-known adverse effects. Because the diagnostic accuracy for TCCS diagnosis of intracranial ≥50% stenoses is unlikely to be 100% in clinical practice, some patients might erroneously receive warfarin instead of aspirin and vice versa. Consequently, in case of
TCCS findings, which are close to the cutoff PSV values for \( \geq 50\% \) stenoses, angiographic evaluation may be taken into consideration.

The main limitation of TCCS was the difficulty in differentiating between patients with normal and \(<50\%\) stenosed arteries. To our knowledge, there is no study suggesting that both groups of patients should have different treatments. Thus, we assume that this limitation is not relevant. Another drawback of TCCS is the temporal bony window, which prevents the reliable detection of stenoses located in branches of the basal cerebral arteries, such as the insular segment of the MCA or the pericallosal artery.

In conclusion, we have elaborated TCCS criteria for detecting \( \geq 50\% \) and \(<50\%\) intracranial stenoses. The criteria require prospective testing in an angiography-correlated study because they may prove useful for noninvasive assessment and long-term management of patients with symptomatic intracranial stenoses.

References

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