Benefit of Echoccontrast-Enhanced Transcranial Color-Coded Duplex Ultrasound in the Assessment of Intracranial Collateral Pathways

Dirk W. Droste, MD; Rasmus Jürgens; Sepp Weber, MD; Ralf Tietje; E. Bernd Ringelstein, MD

Background and Purpose—Although clinically important, proper assessment of intracranial arterial collateral pathways by transcranial color-coded duplex sonography (TCCD) in patients with internal carotid artery (ICA) high-grade stenosis or occlusion is occasionally made difficult by an insufficient temporal bone window, an unfavorable insonation angle, or low flow velocity or volume. In these cases, echocontrast could be helpful to increase the diagnostic confidence or to make the diagnosis at all.

Methods—We investigated 50 temporal windows of 44 patients with ipsilateral high-grade (≥70%) ICA stenosis or occlusion and insufficient native transtemporal insonation conditions before and after the application of the echo enhancer Levovist with an infusion pump.

Results—Compared with the precontrast scans, echocounter allowed for more segments to be evaluated by pulsed Doppler sonography (P<0.0001) and for longer lumen segments to be displayed on color mode (P<0.0001). Also, collateral flow via the anterior and posterior communicating artery could be demonstrated in 25 and 32 scans, respectively, compared with only 1 demonstration of each collateral pathway before the application of contrast medium (both P<0.0001). Similarly, with the help of contrast medium, flow velocity in the middle cerebral artery could be measured in 45 cases compared with only 26 cases before contrast was applied (P<0.0001).

Conclusions—in patients with poor precontrast visualization of intracranial arteries, echocontrast-enhanced TCCD is very helpful in the assessment of intracranial collateral pathways recruited downstream to ICA stenoses and occlusions.

Key Words: carotid artery diseases ■ contrast media ■ ultrasonography, Doppler, duplex

Transcranial color-coded duplex sonography (TCCD) is a noninvasive, highly accurate procedure to detect stenoses, occlusions, and pathological collateral flow conditions in the large intracranial arteries.1–5 The refined spatial resolution and the appearance of color-coded flow signals help to adequately place the Doppler sample volume in the different arterial segments of interest.

In patients with extracranial high-grade stenoses and occlusions, this technique is capable of demonstrating collateral blood flow within the circle of Willis and its branches to identify patients at low versus high hemodynamic risk.6–13 By doing this, TCCD adds further details to the quantification and prognostic evaluation of extracranial carotid artery disease.14 Occasionally, TCCD is made difficult by an insufficient temporal bone window, by an unfavorable insonation angle, by low flow volume or low flow velocity in single arterial segments, or by a combination of these factors. Echocounter agents able to survive pulmonary and capillary transit have recently been developed to improve the echogenicity of the flowing blood and to overcome these restrictions.

Leovist (Schering AG) is the most widely used echocounter agent in neurosonology. After preparation, Leovist is a suspension of air-filled microbubbles with a palmitic acid layer adherent to galactose microgranules. The median diameter of these microbubbles is 3 μm. Presently, attempts are made to prolong the echocounter agent’s diagnostic time window by its continuous intravenous infusion.

In the present study we describe and quantify the benefit of echocounter enhancement in assessing the collateral supply downstream to an internal carotid artery (ICA) high-grade stenosis or occlusion in patients with poor precontrast insonation conditions. A new type of application was used, namely, continuous infusion by means of a pump.

Subjects and Methods

In the study period of 4 months, a total of 637 patients were investigated in our neurosonological laboratory. Of these, 133 patients (71% men, 29% women) had extracranial carotid artery occlusion or high-grade stenosis. All patients received a continuous-wave Doppler investigation of their neck arteries, as well as of the supratrochlear arteries, including compression tests of the facial and
the superficial temporal artery. Furthermore, they underwent TCCD of the large basal arteries. The carotid arteries and the extracranial part of the vertebral arteries (V2 segment) were also investigated by extracranial color-coded duplex sonography. For extracranial continuous-wave Doppler and intracranial pulsed-wave Doppler, we used the Multidop X (DWL) with 4-, 8-, and 2-MHz probes, respectively. Extracranial and intracranial color-coded duplex sonography were performed with the Sonos 2500 system (Hewlett Packard) using a 7.5-MHz linear probe and a 2.0-MHz sector probe. In the 44 patients selected for transtemporal echo enhancement, either (1) the maximal systolic and end-diastolic flow velocity in the middle cerebral artery (MCA) main stem, or (2) the presence or absence of collateral flow via the posterior communicating artery (ACoA and PCoA, respectively) could not be assessed. Six patients had bilateral disease and required 2 echocontrast investigations. Thus, we investigated a total of 50 temporal windows in these 44 patients with ipsilateral high-grade (>70%) ICA stenosis or occlusion. Four patients had intracranial high-grade ICA stenosis. Sixteen arteries were occluded and the remaining 30 arteries showed extracranial stenosis. There were 13 women and 31 men, aged from 35 to 85 years (mean 63 years). There were 8 smokers and 10 diabetics. Twenty-three individuals were hypertensive, and 17 suffered from hyperlipidemia. Twenty-seven patients had suffered a stroke, 4 patients a transient ischemic attack, 2 transient monocular blindness, and 1 optic nerve ischemia on the side of the carotid artery under investigation. The time span from the ischemic event to the investigation varied from hours to 11 years.

Both the native and echocontrast-enhanced investigations were continuously recorded onto video tapes for offline analysis. Diagnostically relevant pictures were also printed out in black and white or color. One 4-g vial of the echo enhancer Levovist (11 mL suspension) was applied in a concentration of 400 mg/mL using an infusion pump with a continuous infusion rate of 2.5 mL/min. The precontrast investigations were carried out with a low pulse repetition frequency on color mode, thus allowing for slow flow velocities or flow in arterial segments with a bad insonation angle to be displayed. In this setting, aliasing occurred and the direction information was lost on color mode. In the enhanced investigation, the pulse repetition frequency could usually be increased due to the stronger signal. Immediately after the investigation, the presence or absence of a diagnostic benefit of the investigation was recorded in written form. Tapes were subjected to an offline analysis that included the recording of the following 16 parameters during both the precontrast and postcontrast conditions: the length of the visible color-coded blood flow column of (1) the MCA main stem, (2) the A1 segment of the ipsilateral anterior cerebral artery (ACA), (3) the A1 segment of the contralateral ACA, (4) the ipsilateral PCoA, (5) the P1 segment of the ipsilateral posterior cerebral artery (PCA), (6) the P2 segment of the ipsilateral PCA, (7) the length of the P1 segment of the contralateral PCA; (8 to 14) the ability to obtain a pulsed-wave Doppler spectrum in the above arterial segments and (15) in the ACoA, and (16) the number of MCA-branches identifiable as color-coded signals. The length of the ACoA was not assessed, because it cannot unequivocally be discriminated from the ACAs on color mode. On Doppler spectral mode, however, it can be pinpointed due to a frequent change in velocity and to its median location.

Intra-arterial digital subtraction angiographies were available for 13 ICAs investigated selectively, including images of the intracranial anterior (n=13) and posterior (n=11) circulation. In 5 further cases only the extracranial arteries were displayed on the angiograms. The nonparametric Wilcoxon matched-pairs signed rank test was performed to test the effect of echocontrast enhancement on each of the 16 parameters under investigation.

Results

In all the arteries of interest, there was a diagnostic benefit by the use of contrast. The Table summarizes the patients’ precontrast and postcontrast TCCD findings.

<table>
<thead>
<tr>
<th>Color-Coded Doppler Signals and Visualization of Pulsed-Wave Doppler Spectra Before and After Contrast Application</th>
<th>Before Contrast</th>
<th>After Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artery length on color mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral MCA</td>
<td>7.8±8.9 mm</td>
<td>23.5±9.0 mm</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>0.9±2.5 mm</td>
<td>7.8±3.7 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA (P1)</td>
<td>1.0±2.3 mm</td>
<td>7.6±3.3 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA (P2)</td>
<td>6.4±8.7 mm</td>
<td>23.5±9.1 mm</td>
</tr>
<tr>
<td>Ipsilateral PCoA</td>
<td>0.1±0.5 mm</td>
<td>4.6±3.6 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA</td>
<td>0.9±3.4 mm</td>
<td>6.7±0.3 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA</td>
<td>0.6±0.2 mm</td>
<td>6.3±3.4 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA</td>
<td>0.9±9.9 mm</td>
<td>7.3±10.8 mm</td>
</tr>
<tr>
<td>Ipsilateral PCA</td>
<td>0.4±0.20</td>
<td>1.28±0.88</td>
</tr>
<tr>
<td>on color mode, n</td>
<td>(0; 0–1)</td>
<td>(1; 0–3)</td>
</tr>
<tr>
<td>Possibility of obtaining a Doppler spectrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral MCA</td>
<td>52±50%</td>
<td>90±30%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>14±35%</td>
<td>86±35%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>8±27%</td>
<td>76±43%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>2±14%</td>
<td>50±51%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>18±39%</td>
<td>86±35%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>44±50%</td>
<td>92±27%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>2±14%</td>
<td>64±48%</td>
</tr>
<tr>
<td>Ipsilateral ACA</td>
<td>8±27%</td>
<td>82±39%</td>
</tr>
</tbody>
</table>

Values are mean±SD (median; range).

All the probability values for the single precontrast and postcontrast comparisons were P<0.0001.

There were 25 demonstrations of collateral flow via the ACoA and 32 of collateral flow via the PCoA. In 19 investigations, both pathways were patent. In 45 cases, flow velocity in the MCA could be measured after contrast compared with only 26 cases before contrast was applied (P<0.0001).

In the patients also investigated by intra-arterial angiography, the ultrasound diagnosis of presence or absence of collateral flow was confirmed (7 ACoAs, 9 PCoAs).
The investigations did not cause any side effects. The Figure demonstrates the TCCD findings of an illustrative case through the left temporal window of a patient with ICA occlusion before and after contrast application. Before contrast was applied, the MCA, both A1 segments, and part of the PCA could be visualized only with a low pulse repetition frequency (so-called slow-flow setting). After contrast application, the pulse repetition frequency could be raised, and the whole ipsilateral circle of Willis could be visualized, including the collateral supply via both communicating arteries.

**Discussion**

Our study shows the benefit of echocontrast-enhanced TCCD investigations in patients with a poor temporal skull window or in cases presenting an unfavorable insonation angle of single arteries. The latter applies particularly to the PCoAs and to first-order MCA branches (M2 segments). In clinical terms, this benefit refers to the increase of diagnostic confidence or to the ability to make the diagnosis at all.

By means of native TCCD scans, ie, scans without echocontrast enhancement, a Doppler spectrum of the ipsilateral MCA or of the P2 segment of the ipsilateral PCA could be obtained in only about half of the patients. The other arterial segments could be recorded in only 8% to 18% of the cases of the cohort. After the administration of contrast, however, a spectral Doppler signal could be obtained in 76% to 92% of the investigations and the ACoA and PCoA could be recorded in 50% and 64% of the investigations, respectively. A significantly higher number of arteries and longer arterial segments could be visualized on color mode with the use of contrast medium. The results of the present study are in accord with the recent literature. In a native TCCD study with a patient cohort comparable to ours except for adequate temporal bone windows in their study, Baumgartner et al found an ACoA to be present angiographically in 63% and a PCoA in 42%. Sensitivity of unenhanced TCCD in their study was 100% for the ACoA and 64% for the PCoA. The sensitivity of echocontrast-enhanced TCCD of 100% for the detection of both collateral pathways in comparison to the angiographic findings underlines the benefit of this diagnostic procedure. This is particularly true for the PCoA, which in most cases shows a large, unfavorable insonation angle (see the Figure). The authors are aware of the overestimation of collateral pathways during intra-arterial angiography because of the pressure used to inject the contrast agent.

Demonstration or lack of collateral flow in the circle of Willis in patients with ICA stenosis and the velocity and pulsatility of the Doppler flow spectrum in the ipsilateral MCA are parameters for proper classification of the ICA stenosis (see below) and help in estimation of the hemodynamic risk in the dependent hemisphere. TCCD allows the continuous visualization of the color-coded blood flow column in several arteries at the same time and thus facilitates spatial orientation and correct placement of the Doppler sample volume in the large basal arteries. Compression tests of the carotid artery to show flow increase, flow decrease, or flow reversal in order to indirectly demonstrate collateral supply bear a low though avoidable risk of embolization. The visualization of the communicating arteries with TCCD renders these tests unnecessary.

The presence of collateral flow indicates that an ICA stenosis is high grade. In contrast, the absence of collateral flow in a given ICA stenosis otherwise classified as high grade in combination with a marked side-to-side difference in the MCA spectral Doppler signals identifies a patient as being at an increased hemodynamic risk to develop ischemic ophthalmopathy and cerebral borderzone infarctions. When undergoing carotid endarterectomy, these patients are particularly vulnerable during carotid artery cross-clamping. The knowledge of this situation may lead to the use of a shunt...
during carotid endarterectomy and to special attention by the anesthesiologist to avoid drops in blood pressure during any surgical intervention. In acute stroke patients with normal or low blood pressure, the therapeutic raising of blood pressure must be considered in these cases with poor collateral supply in order to avoid stroke progression or further hemodynamic infarction. A recent SPECT study suggests that these patients are also at an increased risk of developing a so-called “malignant MCA infarction.”17 In these particular patients, close-meshed clinical and CT follow-ups are mandatory so as not to miss the time for life-saving decompressive hemicraniectomy.18,19

Echocontrast-related side effects were rare, and if present at all, were transient and minor.20 MRI, MR angiography, CT angiography, or intra-arterial angiography are potentially more harmful. In a review of 8 prospective studies, 1% arteriography-related disabling strokes and 0.06% deaths in a total of 2227 cerebral arteriographies were described.21 MRI, MR angiography, CT angiography, and intra-arterial angiography are expensive and not yet generally available. Ultrasound is a reliable, cheap, and easily repeatable bedside procedure. These are further arguments for the use of diagnostic ultrasound supported, if necessary, by echocontrast enhancement.

In summary, echocontrast agents are helpful in the assessment of suspected and definite intracranial collateral supply distally to ICA stenoses and occlusions in patients with poor precontrast investigational conditions.

Acknowledgments

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References

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