Contrast-Enhanced Transcranial Color-Coded Sonography in Acute Hemispheric Brain Infarction

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Purpose—The aim of the present study was to investigate the diagnostic potential of contrast-enhanced transcranial color-coded real-time sonography (CE-TCCS) in otherwise ultrasound-refractory acute stroke patients with an ischemia in the territory of the middle cerebral artery (MCA). Furthermore, correlations of CE-TCCS findings with clinical, angiographic, and CT results were investigated.

Methods—In 90 acute stroke patients with inadequate insonation conditions in unenhanced transcranial color-coded real-time sonography (TCCS) examinations, CE-TCCS, clinical, angiographic, and CT examinations were performed within 12 hours, 36 hours (CE-TCCS only), and 1 week after onset of clinical symptoms. A CT angiography (CTA) as reference method was available in 39 individuals. After application of a galactose-based echo-enhancing agent, the portion of conclusive ultrasound examinations of the MCA, as manifested by an MCA occlusion, decreased or increased flow velocity (FV), and symmetrical MCA FV, was evaluated. CE-TCCS findings on admission and during follow-up were correlated with infarction size as demonstrated on follow-up CT, and clinical findings were assessed by use of the European Stroke Scale.

Results—Adequate diagnosis was achieved in 74 of 90 patients (82%) by the use of echo contrast agents. MCA occlusion or reduction of MCA FV was found in 20 and 27 patients, respectively. MCA occlusion was confirmed by CTA in 17 cases. In one individual, false-positive diagnosis of MCA occlusion was made according to ultrasound criteria. In 5 patients with MCA occlusion, vessel recanalization was observed during follow-up; 15 of 27 patients with decreased flow velocities showed normalization after the third examination that was associated with a significantly better clinical outcome (P<0.0001). Furthermore, MCA occlusion or decreased FV in the first 12 hours were associated with significantly larger infarctions in the MCA territory compared with normal CE-TCCS findings (P<0.0001).

Conclusions—CE-TCCS enables adequate diagnosis in approximately 80% of acute hemispheric stroke patients with insufficient unenhanced TCCS examinations. It is a reliable diagnostic tool regarding MCA mainstem and branch occlusions. Because this method conveys useful information concerning cerebral tissue and clinical prognosis, it may be useful to identify those patients who benefit most from local or intra-arterial thrombolytic therapy. (Stroke. 1999;30:1819-1826.)

Key Words: cerebral ischemia ■ contrast media ■ diagnostic imaging ■ ultrasonography, Doppler, transcranial

Transcranial color-coded real-time sonography (TCCS) is a useful imaging modality in diagnosis and management of stroke patients allowing rapid visual identification of vascular and parenchymal pathology, thus complementing other imaging techniques such as computed tomography and MRI. However, due to absorption of 60% to 80% of the emitted ultrasound energy, the temporal bone does not allow insonation of the basal cerebral arteries in approximately 30% of patients with cerebrovascular diseases. Adequate transcranial ultrasound studies are believed to be unobtainable, particularly in older subjects and in women. A promising technique of solving this problem is provided by the use of echo contrast agents. TCCS investigations with various echo contrast agents in healthy individuals demonstrated improved visualization of intracranial vascular structures compared with unenhanced examinations. In patients with inadequate acoustic bone windows (IABW), echo-contrast-enhanced TCCS (CE-TCCS) has been shown to overcome hyperostosis of the skull in the majority of patients. Nevertheless, studies on the clinical value of CE-TCCS in stroke patients with IABW are limited. In preliminary studies it could be demonstrated that CE-TCCS may provide conclusive diagnostic information about intracranial occlusive diseases and cross-flow through the communicating arteries due to extracranial occlusions of the brain supplying vessels. The aim of the present study was to analyze the
diagnostic potential of CE-TCCS in a large group of patients with hemispheric stroke and IABW and to define the predictive value of CE-TCCS for the site and severity of the eventual tissue damage after hemispheric stroke.

**Subjects and Methods**

A total of 483 consecutive stroke patients, who were admitted to our department within 12 hours after the onset of clinical symptoms suggestive for an infarction in the territory of the MCA, were examined with TCCS within a period of 24 months. Ninety of them (19%) had an IABW (52 men and 38 women; mean age 72 years, range 59 to 88 years) and were included in the study. A specific inclusion criterion for this study was the inability to obtain vascular signals by means of unenhanced color and spectral Doppler sonography on the affected side. Exclusion criteria were a history of cerebrovascular diseases, demonstration of previous ischemic lesions, or acute intracranial hemorrhages in CT scans. All patients received a complete neurological evaluation, extracranial color-coded and continuous-wave Doppler, unenhanced TCCS, CE-TCCS, and CT examinations. Neurological deficits were assessed according to the European Stroke Scale (ESS). Patients with 0 to 40, 41 to 70, and 71 to 99 points were considered severely, moderately, and mildly affected, respectively. In 39 severely or moderately affected individuals, additional CT angiographic (CTA) studies were performed. Neurological and CE-TCCS examinations were repeated within 36 hours and 7 days after the onset of stroke symptoms, and a follow-up CT scan was obtained within 7 days.

**Unenhanced and CE-TCCS Examinations**

TCCS recordings were made with a phased-array ultrasound system (Ultramark 9 HDI or Ultramark 3000 HDI, ATL) equipped with a 2.25-MHz 90° sector scan. Pulse repetition frequencies ranged between 1000 and 4500 Hz, depending on optimal visualization of vascular structures. The color ultrasound gain level was set just below the level of appearance of background noise, and insonation depth in enhanced and native examinations was 12 cm. The temporal bone window was defined as absent if neither a vascular nor a parenchymal structure could be identified in conventional images. If the brain stem, the contralateral skull, or both structures could be delineated weakly, without visualization of vascular structures, the bone window was defined as insufficient. The presence of an insufficient or absent temporal bone window was stated when at least 2 experienced ultrasound investigators (T.P., S.M., T.B.) were in agreement in their opinion. Exclusion criterion for the application of the echo contrast agent was galactosemia. Patients or relatives (in aphasic individuals) gave informed consent to the application of an echo contrast agent. CE-TCCS investigations were performed after slow and continuous injection of 4-g galactose-based microbubbles in a concentration of 400 mg/mL over a period of 5 minutes (Levovist, Schering AG). If color artifacts occurred during the phase of echo contrast enhancement (“blooming”), the color gain was temporarily reduced. Technical details of transcranial B-mode sonography have been previously defined. Briefly, by use of the transtemporal approach, a B-mode image was created, depicting brain parenchyma in different shades of gray. Superimposed vascular blood flow was color coded with respect to the flow direction. With the patient in a supine position, the MCA was examined on both sides after echo contrast application (left MCA from the left side, right MCA from the right side) with the use of pulsed-wave Doppler and the velocities measured from the spectral display. The Doppler sample volume was placed within the color-flow image of the first segment of the MCA, and correction of the angle of insonation by alignment of a cursor along the direction of blood flow was performed. The angle of insonation was recorded; if insufficient artery was imaged to allow this adjustment to be made accurately, no velocity measurements were taken. Mean flow velocities (FV) in centimeters per second were measured in every insonated MCA with insonation angles <60° and in an axis vessel view of >2 cm in length. The side-to-side difference in blood FV (AI) was calculated according to a previously proposed formula,\(^{18}\)

\[
AI = \frac{(MV1 - MV2)}{(MV1 + MV2)} \times 200
\]

where MV1 and MV2 represent the mean velocity in the symptomatic and contralateral MCA. A negative AI indicates a reduction in the mean FV in the symptomatic MCA; conversely, a positive AI indicates an increase in the mean FV on the affected side. The threshold value for asymmetry was defined as ±21%.\(^{18}\) Criteria for hyperperfusion and exclusion of stenosis were increased FV over the entire course of the vessel and absence of turbulent flow in spectral Doppler examinations. Criteria for the diagnosis of a MCA occlusion were missing or discontinued color-coded signal of the MCA and lack of pulsed-wave Doppler signal; detection of the ACA, PCA, or both vessels on the affected side; and visualization of the MCA on the contralateral side. During the follow-up period, a reopening of the MCA was defined as a previously absent color-coded and pulsed-wave Doppler signal that reappeared. In all patients the affected side was examined first. After measurement of the MCA velocity, the anterior cerebral artery (ACA; A1 segment) and posterior cerebral artery (PCA; P1 segment) were tried to identify with respect to color-coded and spectral Doppler imaging. Presence of cross-flow through the posterior or anterior communicating artery to the MCA was assessed as reported previously.\(^ {19}\) Ultrasound examiners were blinded to the CT and CTA results.

**Extracranial Duplex Sonography**

The color-coded duplex examinations of the extracranial brain-supplying vessels were performed with a 7.5-MHz linear scanner before the transcranial studies. For diagnosis of an occlusion or a high-grade stenosis of the internal carotid artery (ICA), criteria identical to those in previously published studies were used.\(^ {20}\)

**CT and CTA**

CT was performed with a Somatom Plus 4A Scanner (Siemens). Slice thickness (axial planes parallel to the orbitomeatal line) was 4 mm from the sella region up to the cella media. CT findings were classified on the basis of the anatomic MCA vascular territories involved: (1) normal, (2) infarction exceeding 2/3 of the MCA territory (involvement of the entire MCA territory, including structures supplied by the lenticulostriate arteries and MCA cortical branches), (3) large infarction of >1/3 but <2/3 of the MCA territory (lesion larger than 3.5 cm in the largest axis), (4) <1/3 of the MCA territory, and (5) lacunar infarction.

CTA was performed with a Somatom Plus 4A Scanner (Siemens) by use of spiral scanning mode. Scanning direction was caudocranial, beginning at the orbitomeatal line. Scanning time was 30 seconds, with 2-mm collimation at a table speed of 2 mm/s. Spiral CT acquisition began 15 to 25 seconds after the start of intravenous administration, with a 20-gauge needle, of 100 mL of a 0.623 g/mL iodinated nonionic contrast medium (Ultravist 300, Schering AG) into the antecubital vein at a rate of 3 mL/s. Reconstruction interval of the spiral raw data were 1 mm. The images obtained were sent to a Sienet MagicView 1000 workstation (Siemens) via local network. Bone structures were manually eliminated, and 3D maximum intensity projection reconstruction with 360 projections in sagittal rotation was performed. If CTA scans demonstrated an absent or interrupted signal of the MCA, occlusion was diagnosed; otherwise, the vessel was considered patent. All CT and CTA scans were evaluated by a neuroradiologist, who was blinded to CE-TCCS and clinical results.

**Results**

**Clinical Findings**

Forty-two patients were examined within 6 hours and 48 between 6 and 12 hours after the onset of symptoms. Stroke involved the left hemisphere in 53 patients; in 37 subjects the right hemisphere was affected. Eighty-one patients had a
completed stroke; symptoms disappeared within 24 hours (no CT lesions) in 8 patients and within 7 days in 1. On admission, 39 subjects were severely affected (ESS score of 0 to 40 points) and 51 were moderately or mildly affected (ESS 41 to 99). Twelve patients died between the second and the third ultrasound examinations (8 with MCA occlusion, 1 with FV reduction, and 3 symmetrical MCA FV). Seven patients with MCA occlusion and the 1 with decreased FV died due to malignant brain edema and cerebral herniation. The remaining 4 died of pulmonary infections (n=2), pulmonary embolism (n=1), or an unclear cause of death (n=1).

CE-TCCS Examinations
In 90 patients, a total of 216 (90 on admission, 70 within 24 hours, 56 within 7 days) CE-TCCS examinations were performed, and no serious adverse events were observed. In 74 patients with conclusive ultrasound examinations after echo contrast application, clinical, radiological, and ultrasound follow-up examinations were performed. Demographic data and clinical findings in this subgroup are summarized in Table 1. In 14 of 28 individuals with absent acoustic bone windows, CE-TCCS images provided adequate diagnostic information; in 60 of 62 patients with IABWs it was possible to conclusively examine the MCA on both sides after the application of the echo contrast agent. CE-TCCS examinations lasted between 4 and 10 minutes. The PCA and ACA could be successfully examined in color-coded and pulsed-wave images in 69 and 54 patients, respectively. In all 74 individuals with conclusive MCA examinations, at least 1 other intracranial artery (either the PCA or the ACA) could be assessed. Those individuals with inconclusive CE-TCCS examinations were excluded from follow-up.

An AI below –21% in the initial CE-TCCS examination could be shown in 27 cases; in 20 patients an occlusion of the MCA was diagnosed; and 3 individuals had an increased AI. The mean angles of insonation for the symptomatic and unaffected MCAs were 14° and 16°, respectively. Eight patients had an occlusion or a stenosis of >70% of the ICA on the affected side; cross-flow was detectable through the anterior communicating artery in 5 of the individuals and the posterior communicating artery in 1. Of the 27 cases with decreased MCA FV in the first examination, 12 exhibited normalization at day 2 and another 3 at day 7. In no case did the AI become abnormal in the second and third examination following an acute normal value. In 20 patients MCA occlusion was diagnosed because no color-coded or pulsed-wave Doppler signals could be depicted from the MCA despite adequate visualization of the ACA, PCA, or both vessels. Five subjects underwent vessel recanalization within 36 hours or 7 days. Eight individuals in the subgroup of patients with MCA occlusion died. Additional ICA occlusion could be demonstrated in 4 individuals with MCA occlusion or decreased FV, and in 2 individuals without asymmetry of the MCA FV the ICA was occluded.

Correlation of CT, CTA, and CE-TCCS Findings
Table 2
All patients with an infarction exceeding 2/3 of the MCA territory had an occluded MCA or decreased FV on the initial CE-TCCS examination. Large infarctions encompassing 1/3 to >2/3 of the MCA territory were associated in all but 2 individuals with an MCA occlusion or decreased MCA FV (Figure 1), whereas only 8 of 30 individuals with persistent neurological deficit and small infarctions of <1/3 of the MCA territory, lacunes, or no CT lesions exhibited decreased FV. This difference was statistically significant (P<0.005, χ² test for independence). In territorial MCA infarctions (<1/3, 1/3 to 2/3, and >2/3 of the MCA territory), the size of the ischemic lesions significantly correlated with the presence of

| TABLE 2. CT and Initial CE-TCCS Findings in 74 Stroke Patients |
|-----------------|-------|-------------------|-------------------|-------------------|
|                 | No CT Lesion | Lacunar inf | MCA Inf <1/3 | MCA Inf 1/3–2/3 |
| Normal FV       | 4*     | 9                 | 10 (1 ICAO)    | 1 (1 ICAO)       |
| Increased FV    | 0      | 0                 | 2               | 1                 |
| Decreased FV    | 3†     | 0                 | 8               | 10 (2 ICAO)      |
| Occlusion       | 0      | 0                 | 5               | 15 (2 ICAO)      |

ICAO indicates occlusion or high-grade stenosis of internal carotid artery; inf, infarction.
*One patient had a deficit lasting <24 h.
†All 3 patients had transient deficits lasting <24 h.
decreased FV or MCA occlusion at the initial examination ($P<0.0001$, $\chi^2$ test for independence). Sixteen of 27 of the patients with decreased MCA FV exhibited a large or complete infarction in the territory of the MCA in follow-up CT scans; 8 of these had an infarction encompassing <1/3 of the MCA territory. All 3 individuals with decreased FV and without CT lesions had transient neurological deficit, and FV returned to normal values in all those subjects on the second examination. All subjects with MCA occlusion (n=20) in CE-TCCS images had either an infarction exceeding 1/3 of the MCA territory or a complete MCA infarction. Twenty-three of 24 patients with symmetrical MCA exhibited lacunar infarctions (n=9), small infarctions of <1/3 of the MCA territory (n=10), or no infarctions (n=4).

In 39 severely or moderately affected patients with conclusive CE-TCCS examinations, CTA was performed. In 17 individuals the MCA was occluded, and in 22 cases the vessel was patent. This result could be confirmed in all cases by CE-TCCS examinations (Figure 2), except 1 patient in whom MCA occlusion was misdiagnosed. In this individual the PCA was clearly detectable after application of the echo contrast agent, whereas anterior parts of the circle of Willis were not. For further analysis, this patient was included in the subgroup of ultrasound-refractory patients after echo contrast application. In 4 of the individuals with MCA recanalization shown in CE-TCCS examinations, CTA was repeated. The diagnosis of vessel reperfusion was confirmed in all cases.

**Correlation of Follow-Up CE-TCCS Examinations and Clinical Findings (Tables 3 and 4)**

Twenty-seven of 30 patients with conclusive CE-TCCS examinations and ESS scores between 1 and 40 on admission had a decreased MCA FV on the affected side or had an MCA occlusion. Only 3 patients with ESS scores of >70 had a decreased MCA FV; an MCA occlusion was not found in this subgroup. Moderately affected individuals with an ESS score between 41 and 70 had an MCA occlusion in 3 of 22 examinations, a reduction in MCA FV in 2, and symmetrical MCA FV in 17 of 22 conclusive CE-TCCS examinations. Severity of neurological deficits was significantly associated with the presence of MCA occlusion or decreased FV ($P<0.0001$, $\chi^2$ test for independence).

The ESS score of only 1 patient with a recanalization of the MCA improved clearly after 1 week; 2 individuals with MCA recanalization and 6 patients without recanalization died within the first week. In contrast, patients with normalization
individuals with normalization of FV had an ESS score between 41 and 99, whereas 11 of 14 patients with permanent FV diminution at this time point were clinically severely affected. This relationship becomes even more pronounced at the third examination. All patients with symmetrical MCA FV were only mildly or moderately affected, whereas those patients with decreased FV had ESS scores between 0 and 40. At both time points this difference was significant ($P<0.0005$ after 36 hours, $P<0.0001$ within 1 week; Fisher exact test).

**Discussion**

Various studies have shown that CE-TCCS has a promising diagnostic potential in patients with IABW. It has been demonstrated\textsuperscript{10–12} that the use of intravenously administered echo contrast agents enables visualization of major parts of the circle of Willis in otherwise ultrasound-refractory patients. However, only 4 pilot studies that include 15 to 32 patients about the diagnostic value of CE-TCCS in acute hemispheric stroke patients have previously been published.\textsuperscript{13–16} In addition to relatively small numbers of study patients, further limitations of these studies exist: prolonged time intervals between onset of symptoms and ultrasound examinations, highly selected populations, missing correlation with clinical findings and results of imaging techniques, missing angiographic reference methods, and lack of follow-up examinations (see Table 5). The purpose of the present study was to evaluate the diagnostic potential of CE-TCCS in a large population of ultrasound-refractory acute stroke patients and to assess the predictive value of CE-TCCS for clinical outcome and infarction size. Our data show that CE-TCCS may overcome an IABW in approximately 80% of the examinations in patients with hemispheric stroke that affects the territory of the MCA. Particularly in individuals with weak depiction of parenchymal structures such as the midbrain, but without visualization of intracranial vessels, the application of echo contrast agents was promising, with a diagnostically relevant success rate of 96%, whereas the absence of any parenchymal structure was an unfavorable predictor (50%) for a diagnostic benefit. In comparison, Baumgartner et al\textsuperscript{15} found positive and negative predictive values for the midbrain of 100\% and 61\%, respectively; other CE-TCCS studies have not analyzed this point systematically.

We agree with Görtl er et al\textsuperscript{14} that TCCS images may be partially obscured by asymmetrical temporal bones. In older patients, anterior parts of the circle of Willis in particular cannot be insonated in TCCS images, whereas the PCA is easily detectable. In our study a patent MCA was misdiagnosed as an MCA occlusion in 1 individual with “asymmetrical” IABW. Although accurate diagnosis of MCA occlusion was possible in all other individuals with only 1 other detectable intracranial artery after echo contrast application, our misdiagnosis in 1 individual supports the need for assessment of both other major intracranial arteries (the PCA and ACA) to increase the diagnostic reliability of MCA occlusion in TCCS images.

In our study 63\% of stroke patients had an MCA occlusion or decreased FV in the MCA. According to an angiographically controlled TCD study,\textsuperscript{21} a decreased FV in the MCA mainstem is a typical ultrasonic finding in patients with an
MCA occlusion distal to the origin of the temporal branches (>3 branches involved), whereas this pathological Doppler pattern was only rarely demonstrable in individuals with a more peripheral MCA branch occlusion. The pattern of different CE-TCCS findings in our study is comparable to those in the studies of Görülf et al14 and Nabavi et al13 (50% occlusions or decreased FV), whereas Baumgartner et al15 found MCA occlusions or reduced FV in the MCA on the affected side in none of their patients. In unenhanced TCCS and TCD studies in patients with adequate insonation conditions that were performed within 24 hours after onset of stroke symptoms, decreased FV or no flow were found in 43% to 63%5,6,18,22 of stroke patients. According to previously published studies,5,22 increased FV in the symptomatic MCA most likely indicates early recanalization. This could be demonstrated in 4% of our patients without spectral Doppler abnormalities suggesting MCA stenosis. CE-TCCS diagnosis of an MCA occlusion or a patent MCA mainstem was highly reliable compared with CTA. This result confirms those of 2 previously published studies on intracranial occlusive diseases that reported close correlations between TCCS and angiographic studies such as MRA and CTA.16

The present study is the first contrast-enhanced sonography study with follow-up examinations in unselected stroke patients. In total, 36% of the patients with MCA occlusion or MCA branch occlusion underwent vessel recanalization or normalization of flow velocities, respectively, within 1 week. In 1 CE-TCCS study that included only severely affected individuals, 11 MCA occlusions were diagnosed and 4 of them showed vessel recanalization within 1 week.16 From angiographic and other native TCD and TCCS studies, it is known that recanalization of an MCA occlusion occurs in 44% to 80%5,7,22 of those cases. Few data exist on the course of asymmetrical FV due to MCA branch occlusions in acute stroke patients. In a native TCD study, 67% of decreased FV became normal within 48 hours.22 This result is comparable to our study, which demonstrates normalization of FV in 46% of the patients after 36 hours and 60% of the patients within 7 days.

In our study decreased or absent flow velocities in the symptomatic MCA were associated with the extent of ultimate tissue damage demonstrated with CT. This finding confirms a previously published unenhanced TCD study18 that demonstrated the predictive value of TCD concerning cerebral tissue prognosis following hemispheric ischemia. Comparable to native TCCS and TCD studies,5,22 increased FV in the symptomatic MCA (suggesting early recanalization of the MCA) was associated with small structural lesions in CT. Furthermore, the present study demonstrates for the first time in transcranial sonography a relationship between normalization of asymmetrical flow velocities and the clinical status of the patients. The fact that this relationship was not

### TABLE 3. Clinical and CE-TCCS Follow-Up Examinations in 20 Patients With MCA Occlusion

<table>
<thead>
<tr>
<th>ESS score at corresponding time point</th>
<th>Acute CE-TCCS</th>
<th>CE-TCCS Within 36 h</th>
<th>CE-TCCS Within 7 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occlusion</td>
<td>Recanalization</td>
<td>Occlusion</td>
</tr>
<tr>
<td>0–40</td>
<td>17</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>41–70</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>71–99</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>20 (0)</td>
<td>15 (6)*</td>
<td>6</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate deaths in subgroup before next CE-TCCS examination. Sym indicates symmetrical and Dec decreased flow velocities (FV).

*One patient was lost to follow-up.
†Two patients underwent recanalization compared with the second examination.

### TABLE 4. Clinical and CE-TCCS Follow-Up Examinations in Patients With Decreased MCA Flow Velocities

<table>
<thead>
<tr>
<th>ESS Score</th>
<th>Acute CE-TCCS</th>
<th>CE-TCCS Within 36 h</th>
<th>CE-TCCS Within 7 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dec FV</td>
<td>Dec FV</td>
<td>Symm FV</td>
</tr>
<tr>
<td>0–40</td>
<td>10</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>41–70</td>
<td>14</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>71–99</td>
<td>3</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>14</td>
<td>12</td>
</tr>
</tbody>
</table>

Sym indicates symmetrical and Dec decreased flow volumes (FV).
*One patient died after the second CE-TCCS examination.
†One patient with an initial decrease of the MCA FV developed MCA occlusion as demonstrated in the third CE-TCCS examination, for other abbreviations see table 3.
TABLE 5. Comparison Between Different CE-TCCS Studies in Stroke Patients

<table>
<thead>
<tr>
<th></th>
<th>Goertler et al 14</th>
<th>Postert et al 16</th>
<th>Nabavi et al 15</th>
<th>Baumgartner et al 16</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>23</td>
<td>20</td>
<td>15 (anterior circulation)</td>
<td>32</td>
<td>90</td>
</tr>
<tr>
<td>Time interval between stroke and CE-TCCS</td>
<td>5 h</td>
<td>12 h</td>
<td>48 h</td>
<td>NI</td>
<td>12 h</td>
</tr>
<tr>
<td>Mode of Levovist application</td>
<td>4 g, 300 mg/mL, bolus</td>
<td>4 g, 400 mg/mL, bolus/continuous/5 min</td>
<td>4 g, 400 mg/mL, bolus/continuous</td>
<td>4 g, 200–400 mg/mL, bolus</td>
<td>4 g, 400 mg/mL, continuous</td>
</tr>
<tr>
<td>Conclusive CE-TCCS exam</td>
<td>20/23 (in 7 patients native exam conclusive)</td>
<td>22/22</td>
<td>13/15</td>
<td>21/32</td>
<td>74/90</td>
</tr>
<tr>
<td>Angiographic method (no. of patients)</td>
<td>None</td>
<td>CTA/DSA/MRA (20)</td>
<td>MRA (4)</td>
<td>DSA (6)</td>
<td>CTA (39)</td>
</tr>
<tr>
<td>CE-TCCS and clinical findings</td>
<td>Improvement in patients with stenoses or normal examination on admission</td>
<td>6 patients with occlusion had severe outcome or died</td>
<td>NI</td>
<td>NI</td>
<td>0 and BO associated with severe deficit, recanal. of BO = clinical improvement</td>
</tr>
<tr>
<td>CE-TCCS and CT findings</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
<td>O and BO correlated with large infarction</td>
</tr>
<tr>
<td>CE-TCCS follow-up</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Normalization of O or BO in 20 of 47 patients (1 week)</td>
<td></td>
</tr>
</tbody>
</table>

*O indicates occlusion of the mainstem of the MCA; BO, branch occlusion resulting in decreased flow velocity in the MCA; ER, increased flow velocities most likely due to early recanalization; N, normal symmetrical flow velocities; and NI, not indicated.
†Only patients with severe neurological deficit suggestive for MCA occlusion were included.

demonstrable for those individuals with recanalized MCAs is most likely attributed to the facts that the number of recanalized MCA occlusions was relatively small and that the exact time point of recanalization remained unknown due to the time interval of at least 12 hours between 2 examinations. Furthermore, early collateral blood supply by leptomeningeal anastomoses has a crucial importance in this specific vascular syndrome and can be diagnosed only indirectly by assessment of increased flow velocities of the ACA and PCA. Nevertheless, because a preliminary study in 2 patients has shown that transcranial sonography may represent a reliable tool with which to monitor successful treatment during application of thrombolytic agents in MCA occlusion, further transcranial sonography studies selecting closer time intervals between CE-TCCS examinations may give more precise informations about the time point of MCA recanalizations. In this regard CE-TCCS may provide superior data compared with angiography, which is not suitable for repeated examination of stroke patients in the acute phase. The main limitation of CE-TCCS in individuals with IABW is the missing information about parenchymal structures. For this reason, it is not possible to detect hemorrhagic transformation or midline shift due to space-occupying infarctions by means of gray scale images, as has been reported for patients with adequate insonation conditions. Taking into account that an IABW is found in approximately 30% of stroke patients, the use of echo contrast agents reduces the rate of ultrasound-refractory patients to 5% to 10%. Comparable to native TCD and TCCS studies, this method may predict the severity of the clinical outcome and extent of the hemispheric brain infarction and correlates with angiographic methods. Considering reliability and “bedside” applicability, this technique is well suited as an adequate diagnostic tool in the acute phase and for the monitoring of stroke patients, which may reduce the need and frequency for other neurovascular imaging techniques. CE-TCCS examinations may help to triage patients for intravenous or intraarterial thrombolysis.

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