TCD, MRA and MRI in acute cerebral ischemia


Objectives – The aim of this study was to determine accuracy of transcranial Doppler ultrasound (TCD) and compare efficacy of three non-invasive tests [TCD, magnetic resonance angiography (MRA), and magnetic resonance imaging (MRI)] in patients with acute cerebral ischemia. Material and methods – This prospective study involved 30 patients. MRI, MRA, and TCD were performed within 24 h after onset of ictus. The 2nd MRI was repeated at 48–72 h and was used as the standard for the evaluation of sensitivity and specificity of MRA, TCD, and initial MRI. Results – TCD showed a sensitivity of 96% and a specificity of 33% for recognizing abnormal cerebral blood flow velocities. MRA showed a sensitivity of 46% and a specificity of 75% for assessing intracranial vascular anatomy, while initial MRI revealed a sensitivity of 84% and a specificity of 100% for evaluation of ischemic parenchymal changes. Conclusion – Our results revealed that TCD is an accurate indicator of blood flow status and correlated well with MRI, MRA abnormalities in acute stroke.

Currently, acute cerebral infarction is presumed when a patient presents with an acute neurological deficit and when other diagnostic possibilities are excluded by computed tomography (CT) or magnetic resonance imaging (MRI) and laboratory tests. However, in the first 24–48 h following stroke the CT often fails to reveal any detectable abnormality, since it is negative in 25–50% of cases (1). In addition, symptomatic infarction is less commonly visualized on CT scan on day 0 through 2, compared to day 3 (2). Other imaging tests, such as positron emission tomography or single photon emission computer tomography, are frequently neither available nor practical. Angiography during this period carries a 1.2% complication rate and may be of limited availability (3). MRI has been shown to be more sensitive in the imaging of acute stroke, up to 82% of MRI studies being abnormal on admission compared with 58% of CT scans during the first 24 h (1). Magnetic resonance angiography (MRA) is a non-invasive method of visualizing the cerebrovascular anatomy and preliminary studies of patients with cerebrovascular disease have been performed (4–6). Transcranial Doppler ultrasonography (TCD) is another non-invasive, non-ionizing and inexpensive method of assessing cerebral blood flow velocities (CBFV). The TCD technique has been used in the diagnosis of intra and extracranial disease and for the sequential monitoring of patency of cerebral arteries in stroke (7–12). MRA and TCD, or recently emerged transcranial color-coded Doppler ultrasonography permit non-invasive detection of intracranial vascular stenosis or occlusion with considerable accuracy, but each of these techniques has specific and different limitations (6–9, 13, 14). The limitations of both the methods can produce mistakes or misinterpretations in the acute period of cerebral ischemia because of possible early spontaneous revascularization, development of collateral pathways, evolution of infarction, time of scanning, etc. To our knowledge there were no comparative studies between these two conventional techniques (MRA and TCD) in the literature. This study is an attempt to evaluate the accuracy of TCD and define the efficacy of TCD, MRA and MRI in the diagnosis of vascular disease in patients presenting with acute neurological deficit.

Material and methods

Patients hospitalized at our institution, in whom an initial clinical diagnosis of possible acute stroke was made, were studied prospectively within 24 h of the event. Over the study period 171 patients were
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considered for inclusion in the protocol. One hundred and five patients (61%) were immediately excluded for different reasons, the main factor being presentation at greater than 24 h from the definable stroke onset [79 cases (74%)]. Clinical exclusion criteria were age less than 21 years, subarachnoid hemorrhage, serious concomitant disease, history of previous stroke or neurosurgery, indeterminate time of onset of stroke, and pregnancy. Radiological exclusion criteria were: significant mass effect, intra or extracranial hemorrhage, evidence of other pathology (e.g., tumor), or patient ineligibility for MR for standard reasons (e.g., cardiac pacemaker). All patients were assessed neurologically, including the application of Canadian Neurological Score, prior to imaging. Only 7 patients (7%) were missed by the referral process and 4 patients (4%) were excluded from imaging studies because of pacemakers. Among the other reasons for exclusion were primary intracerebral hemorrhage in 6 patients (6%), 4 patients (4%) were discharged before imaging was possible; and uncertain diagnosis 3 patients (3%). Of the 66 patients (39%) who were considered “clinically” suitable for inclusion, 36 (55%) could not be imaged. The principal reasons can be divided into three main areas: patient safety considerations (61%), being unable to get scanner (32%) and patient preferences (7%).

Criteria for inclusion in the study were cerebral hemispheric ischemia (stroke and transient ischemic attack (TIA)) suspected on clinical grounds in patients who presented within 24 h of ictus with first ever neurological deficit. We used the standard clinical criteria for acute stroke (15), the basis of which is the presentation of a new measurable neurologic deficit within the previous 24 h that persisted for at least 24 h. Such clinical criteria are estimated to be 90% sensitive (1). TIA was defined as an episode of focal neurological dysfunction in the carotid or vertebrobasilar territory lasting less than 24 h with no residual neurologic deficit (15).

Thirty patients were actually studied (mean age 65 ± 13 years, range 34–85 years, 14 women and 16 men). Our inclusion criteria were met by 26 patients with stroke and 4 patients with TIAs. None of these patients underwent thrombolytic therapy.

1) Five-mm-thick sagittal T1 localizer images were acquired with parameters of 500/20/1 (repetition time/echo time/excitations). A 24 cm field of view (FOV) was used with a matrix size of 256 × 192.

2) Oblique axial spin echo proton density and T2-weighted with parameters of 3000/30, 100/0.75 (repetition time/echo time/excitations) images were obtained with 5-mm-thick sections, no gap, a 24 cm FOV, and a 256 × 192 matrix.

3) Axial two-dimensional time of flight (TOF) MRA with parameters of 45/6.9/1/60° (repetition time/echo time/excitations/flip angle) of the carotid bifurcation were performed with a section thickness of 1.5 mm, a 20-cm FOV, 256 × 192 matrix, for a total of 32 sections. Both sources images and maximum intensity projection (MIP) renderings were acquired.

4) Axial three-dimensional TOF MRA of the circle of Willis were obtained with parameters of 40/6.9/1/20° (repetition time/echo time/excitations/flip angle), a section thickness of 0.9 mm, a 20-cm FOV, and a 256 × 192 matrix, for a total of 60 sections. Both sources images and MIP renderings were acquired.

The MRI studies were separated into two sets, initial (first 24 h) and follow-up examinations (48–72 h).

Criteria for abnormal MRI diagnosis

A completed stroke was defined clinically as persistence of a neurologic deficit for more than 24 h and the presence of a clinically appropriate spin-density T2-weighted MR evidence of stroke on Day 1 and/or 2–3. A TIA was defined as the resolution of the acute neurologic deficit by 24 h after ictus with no spin-density T2-weighted MR changes in the affected territory.

Criteria for abnormal MRA diagnosis

All neuroradiologists were blinded to the clinical information, except that the patient had a possible stroke. Three readers independently reviewed each MRA and a consensus was obtained for final analysis. Both the source and MIP images were used in the evaluation of the MR angiograms. The signal from flow in each common carotid artery, internal cerebral artery (ICA) (extracranial and intracranial), M1 segment of the middle cerebral artery (MCA) and A1 segment of the anterior cerebral artery (ACA) were graded as normal, partially occluded (reduced signal intensity; i.e. narrowed lumen of slowed flow), or occluded (absent signal).

MR technique

Patients underwent conventional MRI scanning as part of their routine investigation using a standard head coil on a 1.5 Tesla Signa scanner (General Electric Medical Systems, Milwaukee, WI). The scanning protocol used was:
TCD in acute cerebral ischemia

TCD technique

TCD examinations were performed by the same examiner without knowledge of the MRI, MRA, cerebral angiography (XRA), or clinical findings, except that the patient had a possible stroke. All TCD studies were performed using a 2 MHz pulsed ultrasound probe (Transpect, Medasonics, Fremont, CA). The signal was processed by fast-Fourier transformation spectral analysis. The intracranial vessels were insonated as previously described (16). For our analysis we used time-averaged maximum CBFV (cm/s), all further references to CBFV in this work refer to the time-averaged maximum CBFV. We used the transtemporal approach to study the MCA, ACA, terminal branch of the ICA (C1 segment) and posterior cerebral artery (PCA). The transorbital approach was used for ophthalmic artery (OA) and carotid siphon (C3 segment of the ICA) insonation. The MCA was evaluated at a depth of 40–55 mm, the ICA and ACA were usually obtained at depths of 65–70 mm, the OA was insonated between 40–50 mm and the ICA (C3 segment) at a depth of 60–65 mm. The suboccipital approach through the foramen magnum was used for vertebrobasilar system insonation. The TCD signals from both the vertebral arteries (VA) were obtained at the depth of 60–70 mm and basilar artery (BA) between 80–110 mm.

Criteria for abnormal TCD diagnosis

The diagnosis of intracranial artery stenosis was made according to typical TCD findings: significantly increased CBFV in the basal cerebral arteries to levels above those seen in normal subjects, turbulent flow immediately distal to stenosis, and low-frequency noise (17). An MCA, ICA and ACA stenosis were considered if CBFV was 80 cm/s (18-21); ICA siphon stenosis if CBFV was 65 cm/s (17); BA and VA stenosis was considered if CBFV was 60 cm/s (22). A side-to-side difference greater than 30% was also considered abnormal (23, 24).

The absence of blood flow via OA and ICA at the level of the carotid siphon was taken to indicate an occlusion of the ipsilateral ICA and absence of collateralization through the external common carotid artery (25). Abnormal TCD data in the basal cerebral arteries were manifested by an unobtainable blood flow (8), by moderate CBFV decrease characterized by asymmetrical CBFV (with CBFV asymmetry more than 21%) (26), or by major CBFV decrease with a significantly reduced CBFV (lower than 30 cm/s) (27). The identification of ipsilateral PCA or ACA signals, often with increased CBFV as a consequence of collateral flow via the leptomeningeal anastomoses, was helpful in confirming that the temporal “window” was adequate and implied true absence of MCA CBFV (19, 28). Additionally, failure to detect MCA CBFV by contralateral insonation through a patent temporal “window” served as a confirmation of MCA occlusion (8, 9).

Temporal bone “windows” were considered unavailable when there were no detectable acoustic signals bilaterally.

Embolic signals were identified according to their previously defined features: short-duration (lasting 0.01-0.1 s), unidirectional, high-intensity signals visible in the Doppler spectrum, occurring randomly within the cardiac cycle, accompanied by a characteristic “chirping” or “clicking” sound, and without any possible source of artifact at the same time (29).

Carotid compression was not performed in these acute patients.

Nine patients were investigated by XRA. Common carotid and vertebral arteries injections were made with imaging in two projections.

Comparison between TCD and MRA findings

We judged TCD, MRI, and MRA data as “clinically appropriate”, if there were positive findings in a vascular distribution that corresponded with the initial history and physical examination. Physical findings were required to be consistent with the localization of clinical symptoms. For diagnostic discrimination of tests, the presence of clinically appropriate ischemic parenchymal changes seen on the 2nd MRI study was used as the standard and radiological confirmation of infarction. The evaluation of sensitivity and specificity of TCD, MRA and MRI for detection of cerebral ischemia during first 24 h after ictus were made with this standard.

Data for TCD and MRA performance time were compared using non-paired student t-test. The level of significance was set at \( P \leq 0.05 \). Results are indicated as mean ± standard deviation.

All neuroradiological studies, including TCD, are available 24 h a day at the Johns Hopkins Hospital. The study was approved by the Institutional Review Board of the Johns Hopkins Medical Institutions and informed consent was given by all patients included (or relatives if patients were not able to communicate).
Table 1. Comparison of findings in patients with acute cerebral ischemia examined during first 24 h with MRI, MRA and TCD

<table>
<thead>
<tr>
<th>Methods</th>
<th>Lesion in correct area</th>
<th>Lesion in wrong area</th>
<th>No lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>True positive (clinically appropriate)</td>
<td>False positive (clinically not appropriate)</td>
<td>False negative (clinically not appropriate)</td>
</tr>
<tr>
<td>MRI</td>
<td>22</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>MRA</td>
<td>12</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>TCD</td>
<td>25</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>XRA</td>
<td>7</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

**Results**

Based only on the clinical features of the initial neurologists’ examinations there were 22 patients with anterior circulation deficit, and 8 patients with posterior circulation deficit. The mean time to first scan was 18±6 h (range 9–24 h) for MRI and 19±5 h (range 6–24 h) for TCD. The mean-time interval between performing MRA and TCD was 10±7 h (range 3–13 h). In 22 patients MRA was performed first and the mean time-interval for the MRA and TCD was 9±4 h (range 3–13 h). In 8 patients TCD was performed first and the mean time-interval between TCD and MRA was 8±3 h (range 3–12 h). There was no difference for TCD first and MRA second vs MRA first and TCD second time-intervals ($P < 0.05$).

In 30 patients with acute clinical symptomatic presentation of neurological deficit, initial MRI in 22 cases (73%) showed acute parenchymal changes compatible with the clinical findings, while follow-up MRI study revealed clinically appropriate MRI lesions in 26 (87%) patients. The remaining 4 patients had TIAs. During the first 24 h clinically appropriate MRA and TCD abnormalities were seen in 12 cases (40%) and in 25 cases (84%), respectively (Table 1). TCD showed a sensitivity of 96% and a specificity of 33% for the assessment of intracranial hemodynamics, while MRA demonstrated a sensitivity of 46% and a specificity of 75% for assessing cerebral vessels. For TCD and MRA positive predictive values were 89% and 92%, and negative predictive values were 100% and 17%, respectively. The initial MRI revealed sensitivity of 84% and specificity of 100%, positive predictive value of 100% and negative predictive value of 50%. As an illustrative case, TCD recordings (Fig. 1), MRI (Fig. 2), MRA (Fig. 3), and XRA (Fig. 4) of a patient with MCA stroke are shown.

The individual patient clinical and non-invasive tests results are summarized in Table 2. Abnormal TCD data were strongly associated with proximal MCA and ICA occlusions, vertebrobasilar vascular stenosis/occlusion and related with MRI/MRA findings. TCD examinations detected emboli in 3 cases (10%) (Table 2). The 1st MRI study was insensitive in 2 cases with anterior (Table 2, cases 8, 12) and in 2 cases with posterior circulation stroke (Table 2, cases 11, 23), but TCD detected CBFVs abnormalities in 3 of them (Table 2, cases 8, 11, 23). In 26 patients with stroke 54% of the MRA studies were normal. The remaining 46% demonstrated a clinically appropriate stenotic or occlusive vascular lesion.

It is apparent from our results (Table 2) that the MRA findings in 14 patients with acute stroke were normal. TCD examination was more sensitive compared to the MRA and revealed clinically appropriate CBFVs abnormalities in 13 of them (8 – anterior circulation, 5 – posterior circulation). In 1 case (case 12) TCD detected abnormalities that were not clinically relevant. It is important to note that in these 14 cases, initial MRI was abnormal in 11 cases.

The most significant Doppler findings of the MCA included no detection of flow in the artery or very low CBFV due to insufficient collateralization when occlusion of the carotid siphon or the MCA at its origin was shown by XRA (Table 2, cases 3, 4, 8, 9). Case 17 (Table 2) demonstrated normal MRA, XRA, and TCD, but during TCD examination there was passage of emboli. Similarly, in 2 other cases (cases 15, 20) it was possible to detect emboli with TCD. The other techniques are not dynamic and therefore are insensitive to emboli detection. In 2 cases (Table 2, cases 24 and 26) XRA showed focal narrowing of both the MCAs (M1, M2 segment), ACAs (A1 segment), and PCAs (P1 segment). Both cases were diagnosed as vasculitis by XRA. In case 24 the MRA showed BA thinning, while case 26 was evaluated as normal on MRA. TCD examinations revealed elevated CBFVs which reflects the focal narrowing of the intracranial vessels in these cases and therefore was also consistent with the diagnosis of vasculitis.

In 9 patients who underwent cerebral angiography, XRA revealed clinical appropriate MCA occlusion or stenosis (3/3), ICA occlusion (3/3), and posterior circulation vascular stenosis/occlusion (1/9). In 2 cases XRA were normal. Abnormal CBFV correlated with the results of XRA. TCD correctly detected MCA occlusion/stenosis (3/3), all ICA occlusions (3/3), and posterior circulation obstruction (2/2). In the 1 case with normal angiogram (Table 2, case 17), the TCD demonstrate emboli. In a second case with a normal XRA (Table 2, case 25), the TCD investigation revealed clinically appropriate significantly decreased CBFVs through both the VAs. MRA correctly detected all ICA occlusions (3/3), but failed to detect low MCA CBFV (2/3), and crossflow...
Fig. 1. TCD data obtained at 10:30 a.m. (1 h after onset of the left hemiparesis following cervical laminectomy for spinal canal stenosis). TCD study suggested significantly decreased CBFVs in the right MCA (M1 segment) (A), right OA (B), and right carotid siphon (C) in comparison with opposite vessels (left MCA (M1 segment) (D), left OA (E), and left carotid siphon (F)).

Discussion

In general, routine radiologic studies of acute stroke are limited to CT of the head to confirm or rule out the presence of hemorrhage. Because CT findings are negative in 25–50% of cases during the first 24–48 h after stroke (1, 2), not only is a definite diagnosis of infarction often not made by means of CT in the acute phase, but the underlying vascular mechanism is rarely delineated.

MRI has significant advantages over CT, including better gray/white matter differentiation and con-
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Fig. 2. T₂-weighted MR image (A) obtained approximately 3 h after CVA at 12:23 p.m. shows no signal abnormalities. T₂-weighted MR image (B) obtained approximately 48 h after CVA shows (arrow) slight hyperintensity in the anterior limb of the right internal capsule. (Published with permission: Barker PB, Gillard JH, van Zijl PCM et al. Acute Stroke: Evaluation with Serial Proton MR Spectroscopic Imaging. Radiology 1994: 192: 723-32.)

Contrast resolution of all parenchymal structures, decreased bone-induced artifacts, ability to perform multiplanar imaging, and the lack of radiation. However, findings on conventional MRI are generally either normal or nonspecific during the early stages of ischemia (1, 30). Mohr et al. (31) revealed that neither conventional non-contrast-enhanced CT and T₁- nor T₂-weighted MRI is

Fig. 3. 3D TOF (A) and 2D TOF (B) MR angiograms at 12:58 p.m. shows complete occlusion or high-grade stenosis of the right ICA. (Published with permission: Gillard JH, Oliverio PJ, Barker PB, Oppenheimer SM, Bryan RN. MR Angiography in Acute Cerebral Ischemia of the Anterior Circulation: A Preliminary Report. AJNR 1997: 18: 343-50.)
superior in the very early (first 4 h) detection of infarction. In another study only 54% of lesions imaged in the first 24 h were associated with vascular abnormalities (32). Of the 20 patients who were scanned within 6 h of stroke onset, T₁-weighted MRI revealed abnormalities in only 1 (33). Although, the sensitivity of MRI for early ischemia is not static, but dynamic, as is the progression of the disease, usually after 24–48 h the abnormality becomes obvious (34). In our study all 26 patients with stroke at 48–72 h had clinically appropriate ischemic changes on MRI (Table 2). The results of experimental study of Knight et al. (35) suggest that T₁-weighted and T₂-weighted MRI methods are most effective more than 24 h after stroke. Hence, there is a possibility that in a substantial number of cases conventional MR imaging could fail to demonstrate or fully delineate the extent of ischemic brain regions, particularly in the acute phase (first 24 h). Also, MRI alone is insufficient for the comprehensive evaluation of cerebrovascular disease because it does not allow the direct visualization of cerebral vasculature.

MRA evaluation of stroke
Recent advances in MRA now allow non-invasive imaging of vascular occlusion related to stroke. MRA is completely non-invasive and relies on detecting moving blood to create contrast, indirectly showing the contours of the vessel wall. The anatomy of the major cerebral vessels usually involved in stroke result in two MRA techniques being of greatest interest. These are 2D TOF MRA for assessing the common carotid bifurcations and proximal internal carotid arteries and 3D TOF for cerebral arteries.

MRA can demonstrate large vessel occlusion at the cervical level. MRA has a sensitivity of 92%, specificity of 74%, and negative predictive value of 96% for 70% to 90% carotid artery bifurcation stenosis, with high interobserver agreement (36). MRA of the carotid bifurcation is accurate, comparing favorably with conventional XRA (4–6) more so than color duplex sonography. Warach et al. (37) performed MRI in 34 patients imaged at 2 to 48 h after stroke onset, in 24 patients with T₂ abnormality, 16 (67%) had MRA evidence of a major vessel occlusion. Recently, Gillard et al. (38) reported that only 13/30 (43%) patients had MRA evidence of partial or complete major vascular occlusion of the anterior circulation vessels during first 24 h after onset of their neurologic deficit. Retrospective review of the clinical records and imaging studies of 78 consecutive patients with acute (<48 h, n=50) and subacute infarctions (n=28, 3- to 14-day) revealed that the distribution of stenotic or occlusive vascular lesions correlated with the location of infarction in 93% (6). However, the discrepancy between percent of abnormal MRA findings (46%) in our study and
### Table 2. Summary of individual clinical and laboratory results. Cases 1–26 are patients with stroke, 27–30 are patients with TIA

<table>
<thead>
<tr>
<th>Patient</th>
<th>Affected vascular territory*</th>
<th>TCD</th>
<th>1st MRI</th>
<th>2nd MRI</th>
<th>MRA</th>
<th>XRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L hemiplegia</td>
<td>R ACA</td>
<td>↓ R MCA, ↓ R ACA, ↓ R ICA</td>
<td>Al</td>
<td>Al</td>
<td>R ACA occl.</td>
</tr>
<tr>
<td>2</td>
<td>R facial numb. + up. extr. weakness</td>
<td>L MCA/PCA</td>
<td>No L OA, No L ICA</td>
<td>Al</td>
<td>Al</td>
<td>L MCA, L ICA occl.</td>
</tr>
<tr>
<td>3</td>
<td>L hemiplegia</td>
<td>R MCA</td>
<td>No R MCA</td>
<td>Al</td>
<td>Al</td>
<td>R MCA occl.</td>
</tr>
<tr>
<td>4</td>
<td>Aphasia</td>
<td>R + L ICA</td>
<td>No L MCA</td>
<td>Al</td>
<td>Al</td>
<td>R + L ICA occl.</td>
</tr>
<tr>
<td>5</td>
<td>Aphasia</td>
<td>L ICA + L MCA</td>
<td>No L OA, No L ICA</td>
<td>Al</td>
<td>Al</td>
<td>L ICA occl.</td>
</tr>
<tr>
<td>6</td>
<td>R hemiparesis</td>
<td>L MCA</td>
<td>↓ ICA</td>
<td>Al</td>
<td>Al</td>
<td>L MCA occl.</td>
</tr>
<tr>
<td>7</td>
<td>R hemiparesis</td>
<td>L ICA + L MCA</td>
<td>No L OA, No L ICA</td>
<td>Al</td>
<td>Al</td>
<td>L ICA + L MCA occl.</td>
</tr>
<tr>
<td>8</td>
<td>L hemiplegia</td>
<td>R ICA + R MCA</td>
<td>↓ R MCA, ↓ R ICA</td>
<td>↑ N</td>
<td>↑ N</td>
<td>R ICA occl.</td>
</tr>
<tr>
<td>9</td>
<td>L hemiplegia</td>
<td>R ICA + R MCA</td>
<td>↓ R MCA</td>
<td>Al</td>
<td>Al</td>
<td>R ICA occl.</td>
</tr>
<tr>
<td>10</td>
<td>Aphasia</td>
<td>L MCA</td>
<td>↓ R + L MCA</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>11</td>
<td>R hemiparesis</td>
<td>L ICA</td>
<td>↓ R + L VAs</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>12</td>
<td>L hemiplegia</td>
<td>R MCA</td>
<td>↓ L BA + L VA</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>13</td>
<td>L facial + L up. &amp; lower extr. weakness</td>
<td>R MCA</td>
<td>↓ R + L VAs</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>14</td>
<td>R side weakness</td>
<td>L MCA</td>
<td>↓ L ICA (C3, C4)</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>15</td>
<td>Aphasia</td>
<td>L MCA</td>
<td>Emb: L ICA (C3)</td>
<td>Al</td>
<td>Al</td>
<td>L MCA attenuation</td>
</tr>
<tr>
<td>16</td>
<td>Aphasia</td>
<td>L MCA</td>
<td>↓ L ICA, R + L VAs,</td>
<td>BA</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>17</td>
<td>Aphasia</td>
<td>L MCA</td>
<td>↓ L ICA (C1)</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>18</td>
<td>R side weakness</td>
<td>L MCA</td>
<td>↓ L ICA, R ICA</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>19</td>
<td>L hand weakness</td>
<td>L lacuna</td>
<td>R MCA stenosis</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>20</td>
<td>L hemiparesis</td>
<td>Pontine, No R MCA,</td>
<td>↓ BA, VAs</td>
<td>Emb: L ACA, BA</td>
<td>Al</td>
<td>Al</td>
</tr>
<tr>
<td>21</td>
<td>L arm numbness</td>
<td>Pontine</td>
<td>↓ R MCA</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>22</td>
<td>L hemiparesis</td>
<td>R pontine</td>
<td>↓ L OA, R + L VAs</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>23</td>
<td>L ataxia</td>
<td>L PCA</td>
<td>↓ L VA, ↓ R ICA</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>24</td>
<td>L side weakness</td>
<td>VB</td>
<td>L MCA stenosis, ↓ L ICA</td>
<td>Al</td>
<td>Al</td>
<td>BA thinning, Focal narrowing ACAs, MCAs, PCAs</td>
</tr>
<tr>
<td>25</td>
<td>Unstable gait, vertigo</td>
<td>VB</td>
<td>↓ L R + L VAs</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>26</td>
<td>L side weakness</td>
<td>R MCA</td>
<td>R MCA, R ACA,</td>
<td>Al</td>
<td>Al</td>
<td>↑ N</td>
</tr>
<tr>
<td>27</td>
<td>R facial numbness, dizziness</td>
<td>R PCA</td>
<td>↓ R + L VAs</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>28</td>
<td>Aphasia</td>
<td>L MCA</td>
<td>L MCA stenosis</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>29</td>
<td>R arm weakness, dizziness</td>
<td>L MCA</td>
<td>↓ L VA</td>
<td>↑ N</td>
<td>↑ N</td>
<td>↑ N</td>
</tr>
<tr>
<td>30</td>
<td>L hand + arm weakness</td>
<td>R MCA</td>
<td>↓ L MCA, ↓ L ICA</td>
<td>↑ N</td>
<td>↑ N</td>
<td>L ICA irregularity</td>
</tr>
</tbody>
</table>

N: normal; No: absence of blood flow; Al: acute infarction; ↑: clinically not appropriate; R: Right; L: Left; ↓: moderate CBFV decrease; ↓↓: major CBFV decrease; MCA: middle cerebral artery; ICA: internal cerebral artery; ACA: anterior cerebral artery; OA: ophthalmic artery; VA: vertebral artery; BA: basilar artery; PCA: posterior cerebral artery; PICA: posterior inferior cerebellar artery; VB: vertebrobasilar system

* Defined by clinical examination.
that of (82%) (6) is difficult to explain. This may be because our mean time for the first MRI scan was 18 h, while Johnson and his co-workers (6) obtained the first MRI scan within 48 h after stroke.

Certain limitations exist with the use of MRA. 2D TOF MRA does overestimate the degree of stenosis and one must be careful not to over-diagnose complete vessel occlusion (34). 3D TOF requires longer imaging times and cooperation of patients (14). Among technical limitations for MRA are: turbulent dephasing or very slow flow within a patent vessel causing signal loss (39); exposure of spins to multiple radiofrequency pulses (39); saturation effects at the margins of the volume or slab; limitation of spatial resolution; under-estimation of vessel dimensions; patient motion significantly impairs image, etc. (6).

TCD evaluation of stroke

TCD is a technique to define CBVF within the vessels at the skull base. TCD allows quantitative non-invasive evaluation of the cerebral hemodynamic consequences of cerebrovascular disease (CVD). Because blood flow through an artery is the product of mean velocity and cross-sectional area, TCD ultrasound does not directly measure cerebral blood flow (CBF). However, with the assumption that vessel diameter does not change, the CBVF is directly proportional to flow, and so a CBVF change accurately detects any change in CBF and could be informative about blood flow in the stroke region. Conversely the CBVF determined by means of TCD is a very sensitive indirect measure of the diameter change secondary due to the CVD, because a 20% change in diameter, which is barely detectable by angiogram, leads to a 50% change in CBVF under conditions of constant flow (40). TCD evaluation of the circle of Willis arterial CBVFVs is ideally suited for the detection of the acute occlusion of the carotid or vertebral arteries, because a proximal obstruction will be detected as an immediate attenuation of CBVF in more distal segments. Interobserver variability studies have revealed coefficients of variation from 10.2% for anterior circulation and to 17.5% for vertebrobasilar (VB) system, and intraobserver coefficient of variation of 7.5% (41). It is well established that specificity and sensitivity of TCD vary from one segment to another. MCA occlusion was detected with specificity exceeding 98%, while ICA proximal and distal stenosis were detected with specificity of 88% and 97%, respectively (19). Eighty-five patients with a complete stroke and 48 patients with TIAs were studied by both TCD and XRA to determine TCD accuracy for detection of stenosis or occlusion lesions. The authors reported 86% sensitivity, 100% specificity for the occlusion in the carotid siphon, 91% sensitivity and 99% specificity for the occlusion of the M1 segment of the MCA (18). For a given patient, the side-to-side difference of CBVFVs can serve as the most sensitive and reliable criterion for the presence, or absence of blood flow abnormalities (19). In 535 patients without any neurological deficit Mattle et al. (24) revealed side-to-side difference equal to 4.2 cm/s for ICA, 5.9 cm/s for MCA, and 12 cm/s for ACA. Thirty-four percent of our patients had anterior circulation CBVFVs asymmetries that was the basis for abnormal TCD diagnosis. Of 32 patients with VB angiographic occlusive disease, 24 TCD studies correlated well, resulting in a sensitivity of 75% and specificity of 86% (42).

Our study suggests that in the first 24 h after acute stroke TCD sensitivity was 96%, while specificity of TCD in detecting low CBVF due to the obstruction of the intracranial vessels or extracranial disease is about 33%. This is lower than the figures reported by Camerlingo et al. (43), who found a specificity for TCD of about 92%. However, the former authors considered only patients with an MCA stroke during first 6 h after onset and they used as a standard – arteriography. In our study we have only 17 (65%) patients with presumed involvement of the MCA territories and as the gold standard we used an MRI, which is not a real gold standard for defining vascular lesions. Also, we report an average 19 ± 5 h period of temporal resolution in comparison with 6 h, so some degree of recanalization due to the natural history of stroke could have occurred. In selected (from our population) patients with only MCA affected territory we found a specificity of 100% and a sensitivity of 93%, that correlate well with Ley-Pozo et al. (19) and Camerlingo et al. (43) data. Among the reasons that can contribute to a low specificity, is a collateralization (anterior-to-anterior, posterior-to-anterior or vice versa). Anzola et al. (44) reported excellent correlation between TCD and MRA in assessing the hemodynamic contribution of the anterior part of the circle of Willis in patients with fixed lesions of the extra- and intracranial ICAs. In contrast, the contribution of the posterior communicating artery is difficult to evaluate with either techniques. Additionally, in cases of MCA stenosis TCD has been shown to be superior to MRA in demonstrating the patency of the vessel (44).

The time-difference in our study between TCD and MRA is modest but may change the sensitivity of early TCD, or MRA study if recanalization occurred between MRA and TCD completion.
Although spontaneous recanalization of thrombosed extra- and intracranial vessels is known to occur, the timing of spontaneous recanalization of an occluded intracerebral artery is unknown. Only a few investigators have studied with angiography the frequency with which recanalization happens in the first 24 h after stroke onset, and even fewer have reported findings in the first 6 h (11) or less (45). In 80 patients, who underwent angiography during first 24 h after stroke onset, arterial patency was detected in 19 (24%) patients (46). Partial or complete recanalization of the MCA (M1 and M2 segment) at 7.5 h after symptom onset was observed angiographically in 2/14 (14%) placebo received patients in PROACT study (47). To the best of our knowledge this is the only study which angiographically documented recanalization of a previously occluded MCA. However, in this study one cannot exclude the potential effect of saline infusion because an infusion microcatheter was placed into the clot and could cause a mechanical disruption of the thrombus, and contribution of the heparin therapy received by patients. Serial TCD studies shows that early recanalization (at 24 h) occur in 15% and late recanalization (at 48 h) in 11% of patients with first-ever ischemic hemispheric stroke (48). This cumulative experience suggest spontaneous recanalization frequency between 14% and 24% could occur during first 24 h after onset of cerebral ischemia. However, our considerations are based on estimation and we do not know what really happened subsequently after symptom onset. Only a serial assessment of arterial status, with angiography or Doppler ultrasonography, is likely to provide further insights into the true rate of recanalization during acute stroke.

Timing of MRA and TCD investigations could influence the findings. For example, if there was a long delay between performance of the two tests, significant recanalization might have occurred during the interval. In this study, 22 patients underwent MRA followed by TCD (mean delay 9±4 h) and 8 patients underwent TCD followed by MRA (mean delay 8±3 h). Within this short period of time significant recanalization is unlikely to have occurred (47, 48). The fact that this cannot be entirely excluded is however a limitation of the study. Ideally, MRI/MRA/TCD comparisons should be made in studies performed within 2–4 h of each other to limit discrepancies caused by the natural history of thrombosis. While there have been no large studies of acute stroke with MRA and TCD, it is likely that both these techniques will become part of the initial study of acute stroke in addition to MRI, which evaluates parenchymal changes.

In the majority of the cases we found decreased CBFV in the territory of the MCAs, BAs, VAs, OAs, ICAs, or ACAs, which correlated with clinical findings. This fact together with data from other authors (26, 27) confirms the potential importance of TCD during acute stroke which may have practical importance for emergency medical or surgical revascularization. Several TCD limitations should be noted – it is good for large vessel occlusion, but smaller, more distally located vessel occlusions will be missed. Also, the TCD technique is quite subjective and dependent upon the capabilities of the person performing the test. Among the limitations of this study is the fact that we used three different non-invasive methods to investigate the effect of acute stroke on the brain. The MRI could delineate early signs of brain infarction, MRA helps to visualize the lesions of the vessels, and TCD defines cerebral hemodynamic changes after the stroke. Combination of these techniques could greatly increase the ability to specify the pathophysiology of acute stroke.

Diffusion-weighted (DW) MRI has been recently introduced for the acute evaluation of focal brain ischemia (49–51). Preliminary studies in acute human stroke have demonstrated that ischemic regions are identifiable before T1 increases occur (50). Sorensen et al. (51) demonstrated that acute focal ischemia of the brain can be depicted earlier with multisectonal DW and hemodynamically weighted MRI than with conventional MRI or CT. However, there are theoretical and practical concerns for DW MRI (52), among them quantitation of the absolute diffusion constants (53), and rapid changes in physiological variables (breathing, brain pulsation).

The lack of correlation between initial clinical presentation and imaging findings further justifies obtaining appropriate studies to define information about cerebrovascular hemodynamics and vessels. Rapid, repeatable measurements of cerebral hemodynamics may offer new insight into the process of acute stroke and provide guidance for and monitoring of therapeutic interventions. Non-invasive identification of major cerebrovascular lesions in the acute stroke with MRA and quantitative measurements of the CBFV with TCD could be a powerful tool for use in selecting patients for different therapies to facilitate recanalization.

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