Hemodynamic Studies in Early Ischemic Stroke
Serial Transcranial Doppler and Magnetic Resonance Angiography Evaluation
S. Akopov, MD, PhD; G.T. Whitman, MD

Background and Purpose—After acute stroke, it is often standard practice to obtain magnetic resonance angiography (MRA) to seek evidence of a plausible stroke mechanism. However, hemodynamic patterns after acute ischemic stroke are variable and dynamic. We evaluated information obtained by serial transcranial Doppler ultrasonography (TCD) examinations within the first week after acute ischemic stroke and compared it with that obtained from a single MRA study.

Methods—Forty-seven patients (aged 61±7 years) with acute ischemic hemispheric stroke were examined. TCD was performed within 24 hours, from 24 to 48 hours, and 4 to 8 days after ictus. Norms for TCD examination were determined in an age-matched control group that included 41 subjects without cerebrovascular disease (aged 57±10 years).

Results—In 17 stroke patients, the results of initial TCD examination were normal, although TCD follow-up showed gradual deterioration of middle cerebral artery (MCA) for 1 patient with normal MRA. In 12 patients, initial TCD study and MRA showed MCA or posterior cerebral artery occlusion. Serial TCD examinations documented recanalization (6 patients), formation of a residual MCA stenosis (1 patient), or progressive deterioration of flow through a symptomatic MCA (1 patient), not evident on MRA. In 5 patients MRA was normal, but early TCD demonstrated signs of previous recanalization (transitory hyperemia, slow flow restoration). In 2 patients with MCA branch occlusion, MRA suggested occlusion but failed to document either improvement (1 patient) or deterioration (1 patient) of flow that was evident with serial TCD. In 4 patients with proximal MCA stenosis and 5 patients with internal carotid artery occlusion or stenosis, serial TCD demonstrated different patterns of collateralization and suggested dynamic collateralization patterns after stroke that were not evident on MRA.

Conclusions—Serial TCD examination may reveal dynamic changes in cerebral circulation that may be missed on a single MRA study. (Stroke. 2002;33:1274-1279.)

Key Words: occlusion ■ stenosis ■ stroke ■ ultrasonography, Doppler, transcranial

One challenge of contemporary ischemic stroke therapy is to reverse the neurological deficit by reopening intracranial vessels with thrombolytic agents. Meanwhile, the clinical course of stroke may include either spontaneous improvements or deterioration related to dynamic changes in brain perfusion. These changes are associated with spontaneous thrombolysis, reocclusion, microembolism, thrombus propagation, and/or collateralization.1-6 It would theoretically be possible to prevent or to counteract neurological deterioration or to plan conservative treatment of patients likely to improve spontaneously if the mechanisms underlying these clinical evolutions could be monitored. Digital subtraction angiography, contrast-enhanced CT angiography, and magnetic resonance angiography (MRA) are useful modalities of visualizing the cerebrovascular anatomy and evaluation of collateral circulation in acute stroke.7-9 However, in some institutions these methods may not be readily available immediately after admission of acute stroke patients. More importantly, serial examinations with these methods are difficult for patients and impractical in view of an increasing tendency toward cost containment. Accordingly, in clinical practice it is difficult to monitor dynamic changes in cerebral hemodynamics with these methods. Transcranial Doppler ultrasonography (TCD) is an alternative noninvasive, nonionizing, and inexpensive method of assessing patterns of cerebral circulation. The bedside availability, convenience to the patient, and serial or even continuous monitoring options make TCD particularly suitable and practical for emergency evaluations. Recently, TCD has been evaluated in detail and validated in the setting of acute cerebral ischemia.9-12

In the present study we evaluated the diagnostic yield of serial TCD in acute ischemic stroke in contrast to a single MRA examination. Several previous publications have compared sensitivity and specificity of TCD and MRA in acute ischemic stroke9,12,13; however, these reports focused on comparison of single MRA versus single TCD. Meanwhile,
the major advantage of TCD appears to be the possibility of convenient and inexpensive monitoring of cerebral circulation dynamics. In addition, TCD has several limitations associated with an impenetrable bony window in some patients, dependence on operator skill, and the relative difficulty of assessing the posterior circulation. It is unlikely that TCD may substitute for imaging methods such as MRA in clinical practice. In the present study we used serial TCD as an adjunct to MRA. The aim of the study was to assess additional information regarding cerebral hemodynamics that may be obtained if a single MRA is combined with serial TCD.

Subjects and Methods
We examined 52 nonconsecutive patients with acute, focal, cerebral deficits in whom the initial clinical diagnosis was stroke. Inclusion criteria were as follows: (1) admission within 24 hours after symptom onset; (2) complete TCD examination available immediately after admission; (3) absence of hemorrhage on initial and repeated CT; (4) no induced thrombosis; and (5) absence of severe systemic disease (cancer, myocardial infarction, severe renal insufficiency, or congestive heart failure). Five patients were excluded because of absence of a temporal acoustic window. Forty-seven patients (25 women, 22 men) were included. Mean age was 61 ± 7 years. Diagnosis of hemispheric ischemic stroke was established by clinical examination and results of imaging studies. By stroke mechanisms, patients were characterized as having large-vessel disease (14 cases), embolism (9 cases), small-artery disease (13 patients), and undetermined stroke (11 cases). All patients were treated with antiplatelet medications or intravenous heparin infusion and received intravenous fluid infusion. Three patients died from stroke within the study period.

Initial TCD examination was performed within 24 hours after symptom onset. The second TCD examination was performed within the next 24 to 48 hours, and the third examination was performed 4 to 8 days after ictus. For 6 patients, 2 TCD examinations were performed within this period. MRA was performed together with the first TCD examination for 7 patients. For all others, MRA was performed within this period. MRA was performed within 24 to 72 hours after the ictus and close to the second TCD examination for 7 patients. For all others, MRA was performed together with the second TCD examination 4 to 8 days after ictus. Extracranial and intracranial MRAs were performed with the use of a 1.5-T superconducting magnet (Picker). The following sequences were obtained: 2-dimensional time of flight MRA through the neck and 3-dimensional time of flight MRA through the circle of Willis.

Neuroradiologists who were blinded to the clinical information, except that the patient had a possible stroke, interpreted MRA examinations. TCD was performed by the authors without knowledge of MRA results. The final analysis was performed retrospectively beyond the study period.

Results
The Table shows mean flow velocities in major intracerebral arteries in a control population. We observed no statistically significant age-related differences in flow velocities among subjects aged 40 to 80 years, although there was a trend toward lower flow velocities with increasing age in MCA (Figure 1A) and other basal arteries (not shown). There was no significant difference in flow velocities between men and women (Figure 1B). Analysis of AI for intracerebral arteries demonstrated that upper limits of the CIs (5% of the distribution of the right tail) are equal to 22% for MCA, 30% for

### Table 1. Mean Blood Velocities in Cerebral Arteries in 41 Asymptomatic Subjects

<table>
<thead>
<tr>
<th>Artery</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td>55.49±11.03</td>
<td>54.73±10.44</td>
</tr>
<tr>
<td>ACA</td>
<td>47.20±9.75</td>
<td>47.56±9.29</td>
</tr>
<tr>
<td>PCA</td>
<td>41.22±8.82</td>
<td>40.76±8.41</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>42.27±8.57</td>
<td>42.27±8.57</td>
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</tbody>
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**Figure 1.** Mean flow velocities in relation to age and sex in subjects without cerebrovascular disease. A, Distribution of mean flow velocities in MCA in relation to age. B, Average of mean flow velocities in MCA, ACA, and PCA in men (closed bars; n=28) and women (open bars; n=13).
AC, and 32% for PCA. These data were used as threshold values for the assessment of asymmetry between homologous arteries in analysis of hemodynamic patterns in patients with stroke.

The hemodynamic course in acute ischemic stroke was remarkably variable. We were able to distinguish the following subtypes of flow patterns in symptomatic intracranial arteries, on the basis of initial TCD (within 24 hours after ictus).

Patients With Normal Initial Results of TCD Examination
The first group included 17 patients in whom the initial TCD showed normal flow velocities in intracerebral arteries without significant asymmetries between them.

Follow-up TCD showed stable flow patterns in 16 of 17 patients (94.1%) of this group. In 1 patient, we observed development of an asymmetry of MCA flow consistent with decreasing flow in the MCA on the symptomatic side with AI equal to \(-49\%\) on the third examination (day 5 after ictus). MRA was performed at the time of the first TCD for 3 patients and at the time of the second TCD for 14 patients. In all cases, no intracranial occlusive disease was observed on MRA. In 5 patients, however, MRA showed stenosis of the extracranial part of the ICA on the symptomatic side, including the patient in whom the serial TCD revealed deterioration of the MCA flow.

Patients With Absent Flow in a Symptomatic MCA
For 10 patients, initial TCD revealed absent MCA flow on the symptomatic side. All these patients met TCD criteria for definite MCA occlusion with signs of flow diversion to ipsilateral ACA or PCA. MRI showed acute cerebral ischemia in the MCA distribution for all patients.

In this group, results of the follow-up TCD examinations were highly variable (Figure 2). For 3 of 10 patients, recanalization was observed between the first and second TCD examination. In these cases, on the first TCD examination, MCA blood flow was blunted or undetectable, whereas on the second examination, we observed increased flow velocity in combination with a reduced PI. In 1 patient, signal in the symptomatic MCA transformed from absent to dampened flow; on the third examination, flow velocities returned to normal limits. MRA was done at the time of the second TCD study and was normal. In the other 2 patients, we observed greatly increased flow velocity at the time of the second TCD (stenotic pattern). On the subsequent third and fourth TCD examinations, the flow velocity in recanalized MCA returned to normal limits for 1 patient (transient hyperemia) who also had normal MRA. For the third patient, flow velocities in the symptomatic MCA remained high (mean flow velocity, 130 to 140 cm/s) over all follow-up TCD examinations. MRA performed at the time of the second TCD examination demonstrated the presence of proximal MCA stenosis.

For the other 7 patients, the second TCD examination (24 to 48 hours after ictus) showed the same results as the first study. MRA of these patients at the time of the second TCD examination confirmed the presence of MCA occlusion in all cases. At the time of the third and fourth TCD examinations, the MCA remained occluded for 4 patients without significant changes in hemodynamics. For the other 3 patients, there were significant differences between the second and third studies. For 1 of these 3 patients, initially blunted flow signal deteriorated to absent flow on the third TCD examination with further increase in flow velocity in the contralateral MCA. In contrast, for 2 patients, blood flow in the symptomatic MCA significantly improved between the second and third TCD examination (from 3 to 8 days after ictus).

Patients With Absent Flow in a Symptomatic PCA
In 2 patients, the initial TCD examination showed no flow in ipsilateral PCA associated with increased MCA velocity on the symptomatic side (AI 51% and 63%). These cases were...
Patients With Initial Decreases in Flow Velocities in a Symptomatic MCA

We observed initially decreased blood flow velocities in MCA on the symptomatic side at the first TCD examination in 11 patients. On the basis of results of initial and follow-up TCD studies, we divided these patients into 3 subgroups.

For 2 patients, initial TCD revealed dampened flow signal in the symptomatic MCA without signs of flow diversion. Subsequent TCD revealed a pattern of gradual increases in MCA flow velocities to normal limits (Figure 3B). MRA at the time of the second TCD was interpreted as normal. In 1 patient, follow-up TCD revealed increasing flow velocities in both patients.

Nevertheless, in all patients MRI demonstrated acute ischemic stroke in the distribution of the MCA, where TCD showed initially increased flow velocity.

In the other 4 patients, initial TCD also revealed increased blood flow velocities in MCA on the symptomatic side. For these patients the flow velocity increases were associated with ICA/MCA ratio >1:3.5 and signs of flow diversion to ipsilateral ACA or PCA. In contrast to the previous 3 patients, flow velocities remained elevated during the TCD follow-up (Figure 3C). These findings are consistent with MCA stenosis. MRA confirmed the presence of MCA stenosis, and MRI showed acute infarction in the distribution of the symptomatic MCA in all 4 patients.

Patients With Initial Increases in Flow Velocities in a Symptomatic MCA

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For 2 patients, initial TCD revealed dampened flow signal in the symptomatic MCA without signs of flow diversion. Subsequent TCD revealed a pattern of gradual increases in MCA flow velocities to normal limits (Figure 3B). MRA at the time of the second TCD was in both cases normal, and MRI showed acute ischemic stroke in the distribution of the symptomatic MCA.

The second subgroup included 6 patients, in whom initially decreased flow velocities in a symptomatic MCA were associated with a variety of signs of flow diversion, suggesting proximal stenosis. The signs included reversed and low-resistance flow in ophthalmic artery (1 patient), anterior cross-filling (4 cases), and low-resistance flow in posterior communicating artery with increased flow velocity in the PCA (1 case). For 5 patients, MRA and carotid Doppler showed ICA occlusion (2 patients) or tight ICA stenosis. For the last patient, MRA and carotid Doppler showed no abnormalities. Intracerebral arteries in all patients were normal in appearance. In this subgroup, TCD follow-up showed stable hemodynamic patterns for 4 of 6 patients. However, in 2 cases we observed changes in patterns of collateralization at the time of the second TCD study. In 1 of these cases, changes were consistent with development of reversal of blood flow in the A1 segment of ipsilateral ACA not evident on the first examination. This was associated with an increase in mean flow velocity in the symptomatic MCA from 16 to 24 cm/s. In the second case, there was transformation of initially present anterior cross-filling to collateralization through the posterior communicating artery.

The last 3 patients with dampened flow in a symptomatic MCA at the time of the first TCD examination met TCD criteria for distal MCA occlusion. In all patients, decreased (23±5.7 cm/s) and low-resistance M1 MCA flow velocities were observed, together with blunted MCA waveforms in distal MCA (depth, 40 to 50 mm) with signs of flow diversion to ipsilateral ACA. MRA-suspected distal MCA branch occlusions were shown in 2 patients; in the third patient MRA was normal. In 1 patient, follow-up TCD revealed increasing MCA flow velocity on the symptomatic side up to the normal
range. In a second patient, however, initially dampened flow signal in symptomatic MCA gradually progressed to blunted flow at the time of the third TCD study at day 6 after stroke (Figure 3D). Mean flow velocity decreased from 27 to 9 cm/s. For the last patient with normal MRA, dampened flow in symptomatic MCA persisted unchanged on all follow-up TCD examinations.

Discussion

Our control data regarding the mean flow velocities and their SDs in the basal arteries are consistent with previously published results.15–17 No sex-related variations in the flow velocities were observed. Ringelstein et al16 reported decreasing cerebral artery flow velocities with greater reduction of flow at the end of adolescence with decreasing flow velocity especially beyond the sixth decade of life. In our population, we also observed a trend toward lower flow velocities in older people (Figure 1). Like others,15,16 we observed small side-to-side differences of the flow velocities, characterized by AI values in the control group. The consistent character of control mean flow velocities and side-to-side asymmetry in different publications suggests that variations in these parameters may be a reliable instrument for evaluation of hemodynamic pattern changes.

The major finding of the present work is the demonstration of the value of TCD in the evaluation of hemodynamic patterns after acute stroke that were not evident on a single MRA. Serial TCD examinations revealed an evolution of intracranial hemodynamics in 16 patients (34%) after acute stroke. These hemodynamic changes might be expected to cause either improvement or deterioration of brain tissue perfusion. Even when serial TCD studies do not demonstrate evolution of intracerebral hemodynamics, detection of a stable reduction of regional brain perfusion could be clinically important. For example, the subgroup of patients with MCA (5 cases) or PCA (1 case) occlusion in whom no recanalization was observed may speculatively represent cases in which intracerebral vascular occlusion carries a poorer prognosis.

Striking changes in MCA hemodynamics were observed. It is well known that steno-occlusive disorders in the MCA are critically important in stroke pathophysiology. However, our data demonstrate that a single MRA examination performed within days after stroke may not demonstrate important dynamic changes in MCA perfusion. In particular, we observed 3 cases of MCA recanalization that occurred before MRA. At the time of the MRA study, the second TCD documented restoration of flow in a previously occluded MCA with or without transient hyperemia. This sequence is consistent with recanalization, which may be associated with reactive postischemic hyperemia.5,18,19 MRA performed after recanalization was normal, lacking the information about previous occlusion. In another case, the absence of flow in a symptomatic MCA on the initial TCD examination transformed to a high-velocity, low-resistance flow signal that persisted on subsequent examinations. This may be consistent with previously thrombosed atherosclerotic stenosis of the MCA or residual stenosis after partial recanalization.2,19 MRA performed at the time of the second TCD examination confirmed the presence of MCA stenosis. However, without serial TCD examination, the possibility of a transient MCA occlusion would have been overlooked.

Even in cases in which MRA documented MCA occlusion, the absence of serial examinations limits information regarding subsequent changes in the MCA perfusion. Among 7 patients with MRA-suspected MCA occlusion, subsequent TCD examinations demonstrated signs of recanalization in 2 cases. In 1 case, there was normalization of MCA flow, whereas in the second case, absent MCA flow transformed to dampened flow. The same sequence was observed in another patient in whom initial TCD and MRA evaluations revealed left PCA occlusion. It may be speculated that transformation of initially absent flow to blunted, then dampened flow signal is consistent with partial spontaneous recanalization or distal clot migration.5

Although we observed several cases of presumed MCA recanalization, it is likely that we missed some instances of recanalization during the initial hours after the ictus. It has been previously demonstrated that up to 30% of spontaneous recanalization occurs early after ischemic stroke.8 Nevertheless, TCD still may detect changes in MCA flow suggestive of previous occlusion. In 3 cases, initial TCD revealed transitory hyperemia that subsided in follow-up examinations. As noted above, this may represent reactive postischemic hyperemia or initial residual stenosis after partial recanalization. In another 2 cases, initially dampened flow signal improved on subsequent examination to normal flow signal. Such signals may be observed during recanalization when partial occlusion still persists before development of full recanalization with normalized flow.18 It is likely that in all of these cases TCD was performed after early recanalization, and although the TCD study could not document actual MCA occlusion, it still might provide a clue to ischemic stroke pathogenesis. MRA in all of these cases was normal and inconclusive regarding possible previous hemodynamic disorders. The fact that in all of these 5 patients MRI showed the presence of acute ischemic stroke corroborates the suggestion that MCA occlusion subsided before the initial TCD examination because even a brief MCA occlusion is known to produce focal brain ischemia.2,3

We observed several cases of worsening intracerebral hemodynamics on serial TCD. In 1 case, the initial TCD was normal although MRA revealed right proximal ICA stenosis (false-negative TCD examination). Subsequent TCD studies revealed progressive decreases in blood flow velocities in the right MCA. This suggests the possibility of artery-to-artery embolization. In 2 cases, the initial TCD and MRA examinations revealed MCA occlusion and distal MCA branch occlusion. Initially, there was significantly decreased flow signal in the proximal MCA, and subsequent TCD examinations revealed further progressive decrease. Similar cases were described by Toni et al,20 possibly representing thrombus propagation or lodging of new embolus next to initial occlusion. Again, although MRA examination suggested initial occlusive disease in these cases, it failed to document subsequent blood flow deterioration. The clinical significance of these findings remains unclear. Speculatively, they may explain worsening of neurological deficits, in some patients.
after acute ischemic stroke. It is possible that we missed some hemodynamic factors contributing to clinical deterioration (eg, continuous embolization, reocclusion) because of the limited number of TCD examinations. Continuous TCD monitoring may be more useful to document such changes.

The results of serial TCD examination in our population documented 4 cases of intracranial MCA stenosis. Evaluation of the ICA/MCA ratio and repeated TCD were shown to differentiate between stenosis and hyperemia. The value of combined TCD and MRA study in the presence of MCA stenosis is even greater because of the possibility of evaluating collateral circulation on the TCD examination. We observed several cases of proximal MCA stenosis with increased flow velocity in ipsilateral ACA or PCA suggestive of collateralization from the ACA or PCA territory into the MCA territory.

Similarly, in some cases of ICA occlusive disease the TCD examination may be complementary to MRA, documenting the presence and variants of collateralization as well as its changes in the postictal period. In our patients, we observed anterior cross-filling and collateralization through the PCA or ophthalmic artery. Distinguishing these types of collateralization may be of clinical importance. For example, collateralization via anterior circulation is likely to be a sign of well-preserved hemodynamic status, whereas flow via a posterior communicating artery may be a sign of deteriorating cerebral perfusion. It is of particular interest that in 2 cases the patterns of collateralization changed during follow-up. We observed development of flow reversal in the ACA A1 segment and transformation from anterior cross-filling to collateralization through the posterior communicating artery. Certainly, these findings are of limited value. Further investigations are needed to establish possible use of serial TCD examinations in evaluation of dynamics in patterns of collateral flow after acute ischemic stroke.

Our results confirm the value, previously suggested by other authors, of combining time-matched results of TCD and MRA after stroke. In patients with acute ischemic stroke, the timing of MRA and TCD may significantly influence the findings, leading to discrepant conclusions. In our study TCD was more sensitive for detecting steno-occlusive changes in MCA than for proximal ICA or distal MCA stenosis or occlusion, in accordance with previously published studies.

The present study is limited by the small number of patients with each category of hemodynamic abnormality. The time frame for the initial TCD evaluation was within 24 hours after symptom onset and presumably missed early modifications of intracerebral hemodynamics within hours after ictus. Moreover, 3 to 4 TCD examinations may not be sufficient to characterize delayed changes in hemodynamic patterns. Nevertheless, even such a limited study clearly suggests that the serial TCD study is a useful, inexpensive adjunct to MRA examination, transforming the static MRA picture of cerebral perfusion into a dynamic evaluation of cerebral circulation after acute stroke. Continuous or rapid, repeatable evaluations of cerebral hemodynamics may offer new insights into acute ischemic stroke pathogenesis and provide guidance for therapeutic interventions in relation to particular hemodynamic patterns.

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References

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