High Rate of Recanalization of Middle Cerebral Artery Occlusion During 2-MHz Transcranial Color-Coded Doppler Continuous Monitoring Without Thrombolytic Drug

Pascal Cintas, MD; Anne Pavy Le Traon, MD, PhD; Vincent Larrue, MD

Background and Purpose—Experimental evidence indicates that ultrasound can accelerate thrombolysis. We report our findings on early recanalization during transcranial color-coded Doppler (TCCD) continuous monitoring in acute stroke patients with middle cerebral artery (MCA) main stem occlusion.

Methods—We performed continuous TCCD monitorings in 6 consecutive patients with acute MCA main stem occlusion using a 2-MHz transducer. Patients were not treated with recombinant tissue plasminogen activator.

Results—Partial recanalization, defined as blunted waveforms, occurred during monitoring in 5 patients (83%). The mean time to beginning of recanalization was 17.2±9.6 minutes. Complete recanalization at 24 hours occurred in only 1 patient. The mean National Institutes of Health Stroke Scale score in the patients who recanalized during monitoring was 21.2±4.1 at baseline, 19.2±5 at 2 hours, and 15.6±3.4 at 24 hours (P=0.1).

Conclusions—In this short series of patients with acute MCA main stem occlusion, not treated with recombinant tissue plasminogen activator, we found a high rate of early partial recanalization during continuous exposure to 2-MHz ultrasound. (Stroke. 2002;33:626-628.)

Key Words: middle cerebral artery ■ thrombolysis ■ ultrasonography, Doppler, transcranial

Experimental evidence indicates that low-intensity ultrasound, in the range of values used for diagnostic purposes, accelerates thrombolysis by enhancing plasminogen activator-induced fibrinolysis.1,2 Recently, Alexandrov et al3 reported a high rate of recanalization in stroke patients treated with intravenous recombinant tissue plasminogen activator (rtPA) during 1-hour 2-MHz transcranial Doppler (TCD) monitoring, suggesting that ultrasound might have enhanced drug-induced fibrinolysis in these patients. We report our findings on recanalization during 2-MHz transcranial color-coded Doppler (TCCD) continuous monitoring in patients with acute middle cerebral artery (MCA) main stem occlusion who were not treated with rtPA.

Subjects and Methods

This study included consecutive patients admitted to our stroke unit with an acute ischemic stroke who could have a TCCD diagnosis of MCA main stem occlusion within 6 hours from symptom onset. All patients had a brain CT scan before inclusion to evaluate the hyperdense MCA sign. Patients were not treated with intravenous rtPA.

TCCD scanings were performed through the temporal bone window with a 2-MHz transducer (ATL Ultramark 9 HDI). We first used B-mode imaging to visualize the lateral fissure as a hyperechogenic structure, anterior and lateral to the hypoechogenic butterfly-shaped mesencephalic brain stem, in the orbitomeatal plane. A diagnosis of MCA main stem occlusion was made with the use of both color-coded imaging and pulsed-wave Doppler in case of lack of blood flow all along the lateral fissure, with persistent flow in both the ipsilateral anterior cerebral artery and posterior cerebral artery. Then the sample volume (10 mm in length) of the pulsed-wave Doppler was positioned in the initial part of the lateral fissure, where the MCA main stem runs (Figure 1). This allowed us to precisely focus the ultrasound beam on occluded MCAs. In a preliminary study, we found that this method could correctly identify the MCA main stem in 31 of 37 patients (83.8%) without cerebral artery occlusion and had 100% sensitivity compared with color-coded Doppler imaging.

The transducer was fixed with a head set, and pulsed-wave ultrasound was continuously delivered on the initial part of the MCA main stem to evaluate possible changes in flow. The spatial-peak temporal average intensity was 415 mW/cm2. The duration of monitoring was 30 minutes in 5 patients and 45 minutes in the remaining patient.

Other TCCD scanings (without monitoring) were performed 2 to 6 hours and 24 hours after the first one to evaluate possible delayed recanalization.

The clinical severity of stroke was evaluated at baseline, 2 hours, and 24 hours with the use of the National Institutes of Health Stroke Scale.

Results

Six patients (5 men and 1 woman; mean age, 54.3±14.7 years) were included. Four patients had a hyperdense MCA sign. All patients received aspirin 250 mg IV as part of their initial treatment.
The mean time from symptom onset to beginning of TCCD monitoring was 210 ± 86 minutes.

Recanalization of the initially occluded MCA main stem occurred during monitoring in 5 patients. Time to beginning of recanalization ranged from 5 to 30 minutes (mean, 17.2 ± 9.6 minutes) after the beginning of monitoring. Peak systolic velocities were reduced and waveforms were blunted (rounded systolic complex) in all cases (Table and Figure 1), suggesting that recanalization was only partial.4

On the second TCCD scan, performed 2 to 6 hours after the first one, all arteries had recanalized. Peak systolic velocities were reduced and waveforms were blunted in 5 patients, including the patient without recanalization during the monitoring. In the remaining patient, there was a stenotic pattern (focally increased peak systolic velocity and aliasing) of the initially occluded MCA (Table).

Evolution of pulsed-wave Doppler in this patient is shown in Figure 2.

A third TCCD scan performed 24 hours later in 5 patients showed no further change. The mean National Institutes of Health Stroke Scale score in the 5 patients with recanalization during initial monitoring was 21.2 ± 4.1 at baseline, 19.2 ± 5 at 2 hours, and 15.6 ± 3.4 at 24 hours ($P = 0.1$, ANOVA).

### Discussion

In this study of patients with acute MCA main stem occlusion, who were not treated with rtPA and who were scanned within 6 hours of symptom onset, we could document early recanalization in 5 of 6 patients (83%). Recanalization began after a few minutes of continuous exposure to low-intensity ultrasound. In previous studies of early spontaneous recanalization in similar patients not continuously exposed to ultrasound, the rates of recanalization were much lower. Thus, in a recent series of 32 patients with proximal MCA occlusion first seen between 40 minutes and 5.3 hours from the onset of symptoms, only 2 (6.3%) had recanalized on a repeated TCD performed at 6 hours.5 Similarly, in the Duplex Sonography in Acute Stroke (DIAS I) study, among 12 patients with M1 occlusion first scanned within 6 hours of symptom onset, none had recanalized on a control TCCD performed 2 hours after inclusion.6 Finally, in the Prolyse in Acute Cerebral Thromboembolism (PROACT I and PROACT II) studies, which included patients with angiographically proven M1 or M2 occlusion within 6 hours of symptom onset, the recanalization rates at 120 minutes for control patients were 14.3% and 18%, respectively.7,8

Several in vitro studies have established that ultrasound at low intensity enhances enzymatic fibrinolysis, while it has no effect on clot dissolution without plasminogen activator.1,2,9

### Table 1. Characteristics of Recanalization

<table>
<thead>
<tr>
<th>Pt</th>
<th>Recanalization During TCCD 1</th>
<th>Time to Beginning of Recanalization, min</th>
<th>MCA Waveforms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>...</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>23</td>
<td>Blunted</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>16</td>
<td>Blunted</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>5</td>
<td>Blunted</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>12</td>
<td>Stenotic, Stenotic</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>30</td>
<td>Blunted</td>
</tr>
</tbody>
</table>

TCCD 1 indicates initial monitoring; TCCD 2, 2 to 6 hours after initial monitoring; TCCD 3, 24 hours after initial monitoring; and ND, not done.

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**Figure 1.** TCD focused on MCA main stem in the lateral fissure, with the use of B-mode imaging. Note the partial recanalization with localized color-coded blood flow and blunted waveforms on Doppler.

**Figure 2.** Evolution of recanalization in patient 5. a, Initial partial recanalization 12 minutes after beginning of monitoring. b, Increase in peak flow velocity with persistent blunted waveforms 30 seconds later. c, Stenotic flow signal 6 hours later with increased peak systolic velocity up to 300 cm/s.
Recently, in an in vitro model using the same 2-MHz ultrasound system as in the present study, we found that 30-minute insonation of whole blood clots enhanced rtPA-induced thrombolysis by 47% ($P=0.01$). Mechanisms whereby low-intensity ultrasound increases enzymatic fibrinolysis include acoustic microstreaming at clot/blood flow boundary and reversible changes in fibrin structure, which both result in increased plasminogen activator binding to fibrin and transport into the clot.

In the present study patients were not treated with rtPA. Thus, if we assume that our findings are not coincidental, the high rate of early recanalization and the close temporal relationship between the beginning of continuous exposure to ultrasound and recanalization suggest that low-intensity ultrasound focused on the occluded MCA main stem under control by B-mode imaging may have enhanced endogenous enzymatic fibrinolysis. However, early recanalization was only partial in all patients. Previous work with angiographic correlation suggests that blunted waveforms correspond, at best, to partial deobstruction with delayed filling of distal branches. This may explain, at least in part, why the clinical improvement in patients with early recanalization did not reach statistical significance in our study.

The present study has several limitations. The sample size was small, we did not use a control group, and the assessment of MCA patency at the end of monitoring was unblinded. Thus, the findings should be interpreted with caution.

In conclusion, in a short series of consecutive patients with acute MCA main stem occlusion, not treated with rtPA, we found a high rate of early recanalization during continuous exposure to low-intensity, 2-MHz ultrasound. The findings suggest that ultrasound may have played a role in thrombolysis. These findings need to be confirmed in other laboratories before a prospective, controlled study is considered.

References

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