Mild Neurological Symptoms Despite Middle Cerebral Artery Occlusion

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Background and Purpose—Only a small percentage of stroke patients are treated with thrombolytic therapy. We sought to determine whether vessel occlusion in mild strokes represented a new target population for interventional therapy.

Methods—We imaged 106 acute stroke patients with MRI. Patients were identified with evidence of middle cerebral artery (MCA) occlusion and mild or no stroke signs (National Institutes of Health Stroke Scale [NIHSS] ≤3). They were compared with patients with signs of stroke, NIHSS >3, and MCA occlusion.

Results—We identified 5 patients with absent flow on MRA in the MCA and mild or no stroke signs (NIHSS ≤3). All 5 were functionally independent at 3 months.

Conclusions—Caution should be exercised in considering thrombolytic therapy in these patients. Quantification of perfusion imaging is required to identify “at risk” mild stroke populations. (Stroke. 2004;35:469-471.)

Key Words: magnetic resonance imaging ■ stroke

The only therapeutic intervention available for the hyper–acute treatment of ischemic stroke is intravenous tissue plasminogen activator (tPA).1 We have previously identified that a large proportion of patients are not treated with tPA despite at the emergency department arriving early enough, because symptoms were deemed too mild (13.1%) or the patient was thought to be clinically improving (18.2%). A significant percentage of these patients go on to deteriorate in hospital, resulting in dependence or death.2 Similarly, a subgroup of transient ischemic attack patients are at particularly high risk for recurrent disabling ischemic events (5% within 48 hours) early after symptom onset, yet there is no reliable method of identifying or preventing such events.3 Recent work suggests that absent middle cerebral artery (MCA) flow signal on MRI correlates with poor clinical outcome.4 We assessed whether the presence of MCA flow abnormalities among mild stroke and transient ischemic attack patients identified a subset of patients who might deteriorate and be suitable for reperfusion strategies.

Subjects and Methods

Sequential patients with symptoms of acute stroke were prospectively included if they had both a CT scan completed in <6 hours and an MR scan within 7 hours of onset. Exclusion criteria were the presence of cerebral hemorrhage, preexisting significant nonischemic neurological deficits, or nonstroke diagnosis. Demographic data, stroke risk factors, and baseline National Institutes of Health Stroke Scale (NIHSS) were recorded prospectively by a stroke neurologist or trained stroke nurse. Mild neurological symptoms were defined as an NIHSS score of ≤3. The outcome measures were defined by the Rankin Scale score at 3 months, categorized into independence (0 to 2), dependence (3 to 5), and death. We identified patients with transient or minor neurological deficits (NIHSS ≤3) and evidence of a MCA occlusion on 3-dimensional time-of-flight MR angiography (MRA) at baseline.

MR images, obtained with a 3-T scanner (Signa, GE Medical Systems) equipped with high-performance gradients (40 mT/m, 184-μs rise time) and a standard quadrature head coil, included sagittal T1, axial T2, axial fluid-attenuated inversion recovery, diffusion-weighted imaging (DWI), perfusion-weighted imaging (PWI), and 3-dimensional time-of-flight MRA. One stroke neurologist with experience in interpreting MRA who was blinded to all clinical information except symptom side assessed the MRA in the anterior circulation for areas of reduced or absent flow signal in the distal internal carotid artery (ICA) and MCA. The MRA flow signal abnormality was categorized as follows: none or involving distal ICA, M1-MCA, M2-MCA, or distal MCA.

One stroke neurologist who was blinded to clinical details and outcomes retrospectively analyzed the images, looking for evidence of DWI-PWI mismatch, which was defined as present if the estimated volume of a PWI abnormality was greater than the DWI abnormality volume. Matching DWI and PWI images were placed on the MR workstation simultaneously. Functool (Functool 2000 User Guide, GE Medical Systems) was used to create the perfusion maps. A PWI abnormality was present if there was any visible abnormality on the relative mean transit time map when viewed on gray scale.

Data are reported in frequency tables. Proportions were compared by use of Fisher’s exact test; continuous variables, with a Student’s t test; and ordinal variables, with a Mann-Whitney U test as appropriate. All tests were 2 sided, and conventional levels of statistical significance at 5% were used.
Results
A total of 106 consecutive patients were included. MR was begun within the 3 hours of onset in 42% of patients, and 79% of patients underwent CT scanning within 3 hours of symptom onset. An MRA was completed in 104 patients; 49 of these had evidence of flow abnormalities. Five patients were identified with both an NIHSS \( \leq 3 \) and diminished flow in inferior M2 division. DWI imaging initially showed no evidence of a lesion (B). PWI showed large area of mean transit time delay (C). He had fluctuating clinical course over next 24 to 48 hours, with NIHSS varying between 3 and 6. He was treated with volume therapy, did not deteriorate further, and at 30 days had follow-up scan. Fluid-attenuated inversion recovery (D) shows right insular infarction. He was functionally independent and had NIHSS of 2.

Discussion
Persistent ischemia in the absence of a severe neurological deficit has been previously suggested through the use of delayed SPECT. It is important to note that 1 patient (20%) fluctuated neurologically, but all 5 were independent at follow-up. These patients were all seen by the acute stroke team, considered for thrombolytic therapy, and not treated because of mild symptoms. The good prognosis in our study is important because MCA occlusion and good prognosis have not been previously associated. However, we advise caution in overinterpretation of these results on the basis of this small sample.

With the increasing availability of noninvasive imaging, we routinely have information about the site of vascular occlusion but do not have empirical evidence to guide translation of that information into effective clinical decisions. Most physicians would not offer thrombolysis to patients with mild stroke symptoms because of their expected good prognosis, but the National Institute of Neurological Disorders and Stroke (NINDS) tPA stroke study included patients with NIHSS scores as low as 1. Although we know that "mild" patients can deteriorate, our experience suggests that, despite vascular occlusion, these patients may not be the population of stroke patients who deteriorate and need thrombolytic therapy.

Vascular occlusion plays a major role in the prognosis of acute ischemic stroke, but the effect is likely mitigated by compensatory collateral blood flow. None of our patients recanalized within 24 hours, suggesting that collateral flow remains important for hours to days. The experience documented in the EC-IC Bypass Study emphasizes this concept. Reduced collateral blood flow assessed on CT angiography has previously been shown to identify those at risk for infarct expansion. In the setting of MCA occlusion with mild acute MR scan, and 2 patients had evidence of a mismatch between DWI and PWI. There was no statistical difference between presence of mismatch in the NIHSS \( \leq 3 \) with MCA occlusion patients (n=5) and the NIHSS >3 and MCA occlusion patients (n=24).

<table>
<thead>
<tr>
<th>Table 1. Demographic Characteristics of NIHSS ( \leq 3 ) + MCA Occlusion Group Compared With NIHSS &gt;3 + MCA Occlusion Group</th>
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<tbody>
<tr>
<td>NIHSS ( \leq 3 ) + MCA Occlusion</td>
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<tr>
<td>(n=5)</td>
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<tr>
<td>Mean age, y</td>
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<tr>
<td>Median NIHSS</td>
</tr>
<tr>
<td>tPA, IV or IA</td>
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<tr>
<td>Men, n</td>
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<tr>
<td>Left side of body event, n</td>
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<tr>
<td>Mean initial blood glucose, mg/dL</td>
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<td>Mismatch on MR, n</td>
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<td>M1-MCA occlusions, n</td>
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<td>M2-MA occlusions, n</td>
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None of the comparisons were statistically significant.
symptoms, good control of blood pressure with fluid replacement or even induced hypertension may be beneficial by improving collateral flow. A clinically useful tool to measure collateral blood flow might allow stratification of patients with vascular occlusion into those who require reperfusion and those who do not.

PET studies in primates and humans support the concept of perfusion thresholds that predict early, late, or no subsequent infarction. Analogous information is beginning to emerge with multimodal stroke MRI, but perfusion MR currently provides only semiquantitative data. PWI-DWI mismatch has been proposed as a tool to identify patients who are at risk of deterioration and have potentially salvageable brain tissue. Post hoc analysis suggests that patients with PWI-DWI mismatch do not uniformly do badly. Absolute quantification of blood flow with MR may be crucial in predicting patient outcome by allowing the clinician to visualize tissue at risk of infarction.

Further study with neuroimaging is needed to understand mechanisms for clinical deterioration and recurrent stroke in the mild stroke and transient ischemic attack population. We suggest caution in recommending thrombolysis to patients with mild symptoms and MCA occlusion.

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