Thrombolysis in Stroke Mimics
Frequency, Clinical Characteristics, and Outcome

David T. Winkler, MD, PhD; Felix Fluri, MD; Peter Fuhr, MD; Stephan G. Wetzel, MD; Philippe A. Lyrer, MD; Stephan Ruegg, MD; Stefan T. Engelter, MD

Background and Purpose—Intravenous thrombolysis for acute ischemic stroke is usually based on clinical assessment, blood test results, and CT findings. Intravenous thrombolysis of stroke mimics may occur but has not been studied in detail.

Methods—We determined frequency, clinical characteristics, and outcome of mimic patients versus patients with stroke treated with intravenous thrombolysis using data of a prospective, single-center thrombolysis data bank.

Results—Among 250 patients, 243 (97.2%) had strokes and 7 (2.8%) were mimics. Seizure was the most frequent diagnosis among mimics. There was a trend toward lower National Institutes of Health Stroke Scale scores in mimics (9.9 ± 4.2) compared with strokes (13.7 ± 5.4; P = 0.06). Global aphasia without hemiparesis was the presenting symptom in 3 (42.9%) mimics versus 8 (3.3%) strokes (P = 0.002). Orolingual angioedema, symptomatic intracranial hemorrhage, and asymptomatic intracranial hemorrhage occurred in 3 (1.2%), 13 (5.3%), and 30 (12.3%) patients with stroke, but were absent in mimics. After 3 months, 6 (85.7%) mimics and 86 (35.4%) strokes had a modified Rankin Scale score of 0 to 1 (P = 0.01).

Conclusions—Only few patients receiving intravenous thrombolysis did eventually have a final diagnosis other than stroke, ie, mostly seizures. Their outcome was favorable. Although clinical features differed between the stroke and the mimic groups, the differences were not distinctive enough to allow assigning individual patients to either of the groups. Multimodal neuroimaging or electroencephalographic recordings may be helpful for this assignment. However, their potential benefit has to be weighed against the potential harm of delayed thrombolysis. (Stroke. 2009;40:1522-1525.)

Key Words: epilepsy □ global aphasia without hemiparesis □ stroke □ stroke mimics □ thrombolysis

The rate of false-positive diagnoses of ischemic stroke labeled "stroke mimic" ranges from 1.3% to 25%1-3 in patients not treated with thrombolysis. IV thrombolysis (IVT) for acute ischemic stroke is usually based on clinical assessment, blood test results, and CT findings.4 Thrombolysis of stroke mimics thereby may occur.5,6 The current report aimed to determine the frequency, clinical characteristics, and outcome of mimic patients versus patients with stroke treated with IVT in an experienced stroke center.

Methods
The Basel Stroke Unit program includes a prospective registry and defines management pathways. IVT has been applied using current guidelines with the intention to start IVT as soon as possible within 3 hours after symptom onset.4 All patients were clinically assessed by a resident neurologist and a board-certified neurologist experienced in treating patients with stroke. All patients had nonenhanced brain CT scans.4 IVT application and monitoring for 24 hours were performed on an intensive care unit. After 24 to 72 hours, all patients had follow-up scans (CT or MRI). For each patient, baseline characteristics, complications, and functional outcome have been obtained prospectively and were recorded in the thrombolysis data bank.

For the current study, all consecutive patients treated with IVT were selected (June 1998 to May 2007). There is no general agreement as to the definition of stroke mimics.2,3 Thus, we distinguished stroke from mimic adapting the criteria reported from Hand et al2 and Ay et al3 as follows.

Stroke mimics comprise patients having eventually a final diagnosis other than stroke. A stroke was assumed in all patients with history, examination, and disease course typical for vascular brain damage plus signs of brain ischemia or hypoperfusion on CT scans before and/or on CT/MRI scans after thrombolysis. Patients, in whom an ischemic etiology was eventually the best explanation of their symptoms despite the absence of radiological proof, were labeled probable stroke. Patients in whom supportive investigations failed to establish a diagnosis of stroke or alternative diagnosis were considered as possible stroke.

From the database, we used the following variables: age, gender, National Institutes of Health Stroke Scale scores, clinical stroke syndrome according to the Oxfordshire Community Stroke Project classification, risk factors, blood pressure at admission, and history of antiepileptic treatment. The presence of global aphasia with minimal or without hemiparesis (GAWH) was based on the National Institutes of Health Stroke Scale score indicating global aphasia with scores ≤ 1 for the tested motor items.7

Outcome measures were favorable (modified Rankin Scale ≤ 1) versus poor outcome (modified Rankin Scale ≥ 2), death, occurrence
of orolingual angioedema, and intracranial hemorrhage (asymptomatic/symptomatic by National Institute of Neurological Diseases and Stroke trial definition).

Statistics comparing stroke versus mimic patients include t tests and Fisher exact tests where appropriate.

**Results**

**Study Population**

Among 250 patients (mean age, 67.8±14.55 years; 59% males), 7 of 250 (2.8%) were stroke mimics and 243 of 250 (97.2%) had strokes, including 2 probable and 3 possible strokes (Table 1). Epileptic seizure was the most frequent diagnosis among mimics (n=6; Table 2). Seizures were attributable to old ischemic lesions (n=3) and a glioblastoma multiforme (n=1).

**Comparison of Strokes Versus Mimics**

Gender, age, and risk factors did not differ between strokes and mimics. The majority of the mimics (6 of 7 [85.7%]) but only 50.6% of the strokes were left hemispheric (123 of 243 [50.6%]; P=0.12). GAWH was present in 3 of 7 (42.9%) mimics versus 8 of 243 (3.3%) strokes (P=0.002). Mimics...
One in 30 patients treated with IVT for assumed stroke had GAWH.5 GAWH was 10 times more frequent in the mimic than in the stroke group. Yet, this clinical feature seems not distinctive enough to assign individual patients to one or the other group. Still, in IVT-treated patients with GAWH, the final diagnosis cost time, which is critical in patients with stroke awaiting IVT.4 In addition, electric epileptic activity can be expected in every sixth patient with acute stroke.8 Thus, the risk to use IVT inadver-
tently in stroke mimics seems low in a stroke unit converting current guidelines.4

Epileptic seizures were the most common cause for stroke-mimicking symptoms. This observation confirms previous stud-
ies2,3 and extends it to IVT-treated patients. Epileptic foci were attributable to pre-existing ischemic lesions in most patients.

GAWH was 10 times more frequent in the mimic than in the stroke group. Yet, this clinical feature seems not distinctive enough to assign individual patients to one or the other group. Still, in IVT-treated patients with GAWH, the final diagnosis was more often stroke (8 of 11) than mimic (3 of 11). Interestingly, a recent case of IVT in a patient with glioblastoma mimicking stroke presented with GAWH.5

MRI/MR angiography, CT angiography, or electroencephalography can offer additional information, potentially useful to identify stroke mimics. However, these investigations cost time, which is critical in patients with stroke awaiting IVT.4 In addition, electric epileptic activity can be expected in every sixth patient with acute stroke.8 Thus, the clinical significance of additional studies to distinguish mimics from strokes before IVT is unclear.

Functional outcome was better in mimics than in strokes. More importantly, stroke mimics had neither intracranial hemorrhage nor angioedema. However, a case report about an intracranial hemorrhage in a patient with glioblastoma treated with IVT for assumed stroke illustrates that complications in IVT-treated stroke mimics may occur.5

We are aware of the following limitations. First, due to the lack of a consensus about the diagnostic criteria, the definition of stroke mimics used is arbitrary to some degree. If we consider possible strokes as mimics, as done by others,2,3 the

Table 2. Summary of Stroke Mimics

<table>
<thead>
<tr>
<th>Patient No.; Age, Years</th>
<th>Presenting Symptoms</th>
<th>NIHSSS</th>
<th>Vascular Risk Factors</th>
<th>Main Comorbidities</th>
<th>CT/MRI After IVT</th>
<th>NIHSSS</th>
<th>EEG Findings</th>
<th>Complications</th>
<th>mRS at 3 Months</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1; F; 54</td>
<td>Global aphasia with right hemiparesis</td>
<td>18</td>
<td>None</td>
<td>Prior left middle cerebral artery stroke due to patent foramen ovale</td>
<td>MRA: chronic ischemic lesion in left parietal lobe</td>
<td>No</td>
<td>Left temporal intermittent rhythmic delta activity</td>
<td>None</td>
<td>1 (due to comorbidity)</td>
<td>Symptomatic focal epilepsy with recurrent complex partial seizures</td>
</tr>
<tr>
<td>2; M; 54</td>
<td>GAWH</td>
<td>6</td>
<td>Hypertension</td>
<td>Ethylism</td>
<td>MRA: normal</td>
<td>No</td>
<td>Left temporal slowing</td>
<td>Minor gastrointestinal bleeding</td>
<td>0</td>
<td>Secondarily generalized epileptic seizure with Todd’s paralysis</td>
</tr>
<tr>
<td>3; F; 75</td>
<td>GAWH</td>
<td>6</td>
<td>Diabetes mellitus, hypercholesterolemia</td>
<td>Depression</td>
<td>MRA: normal</td>
<td>No</td>
<td>Left temporal slowing with epileptiform discharges</td>
<td>None</td>
<td>0</td>
<td>Cryptogenic focal epilepsy</td>
</tr>
<tr>
<td>4; F; 78</td>
<td>Global aphasia with right hemiparesis</td>
<td>14</td>
<td>Hypertension, coronary heart disease, hypercholesterolemia</td>
<td>Schizophrenia</td>
<td>MRA: old microangiopathic lesions</td>
<td>No</td>
<td>Left temporal intermittent rhythmic delta activity</td>
<td>None</td>
<td>0</td>
<td>Symptomatic focal epilepsy</td>
</tr>
<tr>
<td>5; M; 53</td>
<td>Left hemiparesis</td>
<td>9</td>
<td>Diabetes mellitus hypertension, coronary heart disease</td>
<td>Prior right thalamic stroke, recurrent synapses of unknown origin, ethylism, bipolar disorder</td>
<td>MRA: chronic ischemic lesion in right thalamus</td>
<td>No</td>
<td>Normal</td>
<td>None</td>
<td>1 (due to comorbidity)</td>
<td>Conversion disorder</td>
</tr>
<tr>
<td>6; M; 74</td>
<td>GAWH</td>
<td>7</td>
<td>Hypertension</td>
<td>Hyperuricemia, lower back pain</td>
<td>MRA: DW- and T2-positive left temporal lesions</td>
<td>No</td>
<td>Recurrent nonconvulsive status epilepticus</td>
<td>None</td>
<td>5</td>
<td>Recurrent NCSE due to glioblastoma multiforme</td>
</tr>
<tr>
<td>7; M; 59</td>
<td>Motor aphasia, right hemiparesis, initial loss of consciousness</td>
<td>9</td>
<td>Diabetes mellitus atrial fibrillation</td>
<td>Myocardiopathy of unknown origin ethylism, prostate hyperplasia</td>
<td>CCT: microangiopathic lesions</td>
<td>No</td>
<td>Generalized background slowing</td>
<td>None</td>
<td>0</td>
<td>Secondarily generalized epileptic seizure with Todd’s paralysis</td>
</tr>
</tbody>
</table>

NIHSSS indicates National Institutes of Health Stroke Scale score; EEG, electroencephalography; F, female; M, male; DWI, diffusion-weighted imaging; NCSE, nonconvulsive status epilepticus.

tended to lower National Institutes of Health Stroke Scale scores (9.9±4.2) compared with strokes (13.7±5.4; P=0.06).

Orolingual angioedema, symptomatic intracranial hemorrhage, and asymptomatic intracranial hemorrhage occurred in 3 (1.2%), 13 (5.3%), and 30 (12.3%) strokes, respectively, but were absent in mimics (Table 1).

After 3 months, 6 (85.7%) mimics and 86 (35.4%) strokes had modified Rankin scale of 0 to 1 (P=0.01). None of the mimics but 34 of 243 (14.0%) of the strokes had died.

Discussion

This study about thrombolysis and stroke mimics had the following main findings. First, few patients receiving thrombolysis did eventually have a final diagnosis other than stroke. Second, mimics more often had global aphasia without hemiparesis than strokes. Third, IVT was not harmful in mimics.

One in 30 patients treated with IVT for assumed stroke had a stroke mimic. The confidence interval (2.8%; 95% CI, 1.1 to 5.7) includes rates from one in 100 to one in 17 patients. These rates are lower than the 7% misdiagnosis rate reported for emergency departments in which IVT was used without a stroke team evaluation.6 Thus, the risk to use IVT inadver-
tently in stroke mimics seems low in a stroke unit converting current guidelines.4
frequency of stroke mimics would increase from 2.8% to 4.2% with complications remaining absent. However, these rates may be higher in less experienced centers. Second, the small size of the mimic group bears the risk that some differences between both groups have occurred by chance. In particular, the absence of IVT-induced harm in the mimic group is not necessarily reassuring. Thus, our observations require confirmation in an independent large data set.

In conclusion, few patients receiving IVT for assumed stroke were eventually stroke mimics. None of the mimics was harmed by IVT.

Disclosures
None.

References


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