Clinical and Tissue Response to Intravenous Thrombolysis in Tandem Internal Carotid Artery/Middle Cerebral Artery Occlusion
An MRI Study

Götz Thomalla, MD; Anna Kruetzelmann, MD; Susanne Siemonsen, MD; Christian Gerloff, MD; Michael Rosenkranz, MD; Joachim Röther, MD; Jens Fiehler, MD

Background and Purpose—The benefit of intravenous thrombolysis in tandem internal carotid artery (ICA)/middle cerebral artery (MCA) occlusion remains unclear. We studied clinical and imaging outcome of intravenous thrombolysis in MRI-selected patients with tandem ICA/MCA occlusion as compared to isolated MCA occlusion.

Methods—We analyzed data of MRI-selected acute ischemic stroke patients treated with intravenous tissue plasminogen activator within 6 hours. Initial perfusion and diffusion lesion volumes were calculated. Final infarct volume was assessed on follow-up imaging after 5 to 8 days. Recanalization/reperfusion was assessed after 24 hours using MRA. Favorable outcome was defined as a modified Rankin scale score of 0 to 1 after 90 days.

Results—Of 38 patients with proximal MCA occlusion, 14 (37%) had a tandem ICA/MCA occlusion. Median NIHSS on admission (15 vs 15), initial perfusion (246 vs 246 mL), and diffusion lesion volume (22 vs 21 mL), final infarct volume (30 vs 39 mL), and the proportion of patients with a favorable outcome after 3 months (50% vs 46%) were similar in tandem ICA/MCA occlusion versus isolated MCA occlusion.

Conclusion—The presence of tissue at risk appears to play a key role for the likelihood of clinical recovery after intravenous tissue plasminogen activator treatment in acute stroke patients with tandem ICA/MCA occlusion. There appears to be no evidence to exclude patients with tandem ICA/MCA occlusion from intravenous thrombolysis. (Stroke. 2008;39:1616-1618.)

Key Words: acute ischemic stroke ■ carotid artery occlusion ■ magnetic resonance imaging ■ middle cerebral artery occlusion ■ outcome ■ thrombolytic therapy

There has been some debate on the possible lack of response to intravenous thrombolysis with tissue plasminogen activator (IV-tPA) in the case of tandem occlusion of the internal carotid artery (ICA) and middle cerebral artery (MCA).1–4 We compared clinical outcome and MRI findings after IV-tPA treatment within 6 hours after symptom onset between MRI-selected patients with a tandem ICA/MCA occlusion and patients with an isolated occlusion of the MCA main stem.

Methods

Patients
We analyzed data of MRI-selected patients with an occlusion of the MCA trunk with and without additional occlusion of the ICA proximal to the bifurcation of the ICA treated with IV-tPA treatment ≤6 hours. Patients with an occlusion of the bifurcation of the intracranial ICA (carotid-T) were excluded. Patients treated with intra-arterial thrombolysis or those enrolled in trials of neuroprotective agents or thrombolytic drugs were also excluded from the analysis. The treatment protocol has been described in detail previously.5

Clinical Assessment
Severity of neurological deficit was assessed on admission and after 24 hours using the NIHSS.6 Outcome was assessed 90 days after stroke using the modified Rankin scale.7

MRI Protocol and Analysis
MRI studies were performed on a 1.5-T scanner equipped with a 20- to 40-mT/m gradient system (Magnetom Symphony/Sonata; Siemens) using a standardized stroke MRI protocol as reported previously.8 Diagnosis of vessel occlusion was based on time-of-flight MRA of the intracranial arteries, and additional contrast-enhanced MRA in doubtful cases. Lesion volumes on initial diffusion-weighted imaging and perfusion imaging were calculated. Final infarct volume was delineated on follow-up MRI or CT after 5 to 8
days. Recanalization of the MCA was assessed on follow-up MRI after 12 to 24 hours using both perfusion imaging and MRA. Modified Thrombolysis in Myocardial Infarction criteria were used as previously suggested.\(^9\) Statistical analysis was performed using SPSS 13.0 (SPSS Inc, Chicago, Ill).

### Results

Of 38 patients, 14 (37%) presented with a tandem occlusion of the ICA and the MCA main stem. The Table shows clinical and imaging baseline and outcome parameters. Patients with tandem ICA/MCA occlusion were slightly younger and less likely to be female than those with isolated MCA occlusion. Both groups were similar regarding the severity of neurological deficit on admission, onset to treatment time, initial diffusion-weighted imaging and perfusion imaging lesion volumes, as well as perfusion imaging/diffusion-weighted imaging mismatch volume and ratio. Clinical outcome, recanalization, and final infarct volume were similar for patients with tandem ICA/MCA occlusion and those with isolated MCA occlusion.

### Discussion

Within a homogeneous sample of MRI-selected patients treated by IV-tPA, we found no difference in recanalization rates (see Figure), MRI lesion volumes, and clinical outcome parameters between patients with tandem ICA/MCA occlusion and those with isolated MCA occlusion.

### Table. Baseline and Outcome Parameters

<table>
<thead>
<tr>
<th></th>
<th>ICA/MCA Occlusion, (n=14)</th>
<th>MCA Occlusion, (n=24)</th>
<th>Group Comparison, (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>62 (55–65)</td>
<td>69 (59–74)</td>
<td>0.033</td>
</tr>
<tr>
<td>Sex, female</td>
<td>1 (7%)</td>
<td>11 (46%)</td>
<td>0.027</td>
</tr>
<tr>
<td>NIHSS (aA)</td>
<td>15 (11–18)</td>
<td>15 (13–19)</td>
<td>0.792</td>
</tr>
<tr>
<td>OTT, min</td>
<td>195 (143–250)</td>
<td>165 (136–210)</td>
<td>0.554</td>
</tr>
<tr>
<td>DWI lesion, mL</td>
<td>22 (16–61)</td>
<td>21 (12–67)</td>
<td>0.606</td>
</tr>
<tr>
<td>PI lesion, mL</td>
<td>246 (111–331)</td>
<td>246 (196–303)</td>
<td>0.713</td>
</tr>
<tr>
<td>PI/DWI mismatch volume, mL</td>
<td>218 (86–258)</td>
<td>209 (137–286)</td>
<td>0.180</td>
</tr>
<tr>
<td>PI/DWI mismatch ratio</td>
<td>6.3 (3.0–14.2)</td>
<td>12.0 (4.5–23.2)</td>
<td>0.532</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRS d90</td>
<td>2 (1–4)</td>
<td>3 (1–4)</td>
<td>0.992</td>
</tr>
<tr>
<td>Favorable, outcome (MRS 0–1)</td>
<td>7 (50%)</td>
<td>11 (46%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Independent outcome (MRS 0–2)</td>
<td>8 (57%)</td>
<td>11 (46%)</td>
<td>0.737</td>
</tr>
<tr>
<td>Poor outcome (MRS (\geq)4)</td>
<td>4 (29%)</td>
<td>7 (29%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>2 (8%)</td>
<td>0.522</td>
</tr>
<tr>
<td>Recanalization after 24 hr (TIMI)(‡)</td>
<td>1 (0–2)</td>
<td>2 (0–3)</td>
<td>0.343</td>
</tr>
<tr>
<td>Any recanalization (TIMI 1–3)(‡)</td>
<td>7 (58%)</td>
<td>13 (65%)</td>
<td>0.724</td>
</tr>
<tr>
<td>Relevant recanalization (TIMI 2–3)(‡)</td>
<td>5 (42%)</td>
<td>10 (50%)</td>
<td>0.726</td>
</tr>
<tr>
<td>Complete recanalization (TIMI 3)(‡)</td>
<td>1 (7%)</td>
<td>7 (29%)</td>
<td>0.204</td>
</tr>
<tr>
<td>Final infarct volume, mL</td>
<td>30 (13–136)</td>
<td>39 (15–126)</td>
<td>0.725</td>
</tr>
</tbody>
</table>

\(aA\) indicates on admission; OTT, onset to treatment time; PI, perfusion imaging; DWI, diffusion-weighted imaging.

All values are presented as median (quartiles) for continuous variables and count (%) for categorical variables. Mann–Whitney \(U\) test was used for continuous variables and Fisher exact test was used for categorical variables.

*Data missing for 2 patients.
†Data missing for 3 patients.
‡Data missing for 6 patients.
sion and those with an isolated occlusion of the MCA main stem.

Our findings regarding clinical outcome are in line with those from previous studies, which reported no difference in functional outcome at 3 months between tandem and isolated MCA occlusion.1,2 Two studies, which reported a significant worse long-term functional outcome for patients with tandem occlusion,3,4 did not restrict the inclusion of patients to those with occlusion of the MCA main trunk but included patients with occlusions of MCA branches. Previous studies reported larger initial diffusion and perfusion lesions10 and lower recanalization rates1–3,10,11 after IV-tPA in patients with tandem ICA/MCA occlusion. We could not reproduce these findings in our sample. However, there is a key difference between our study and previous studies: as a result of the use of MRI for patient selection for tPA treatment in our study, virtually all patients presented with a relevant perfusion/diffusion mismatch. There is no doubt that patients with a confirmed relevant amount of tissue at risk of infarction will be more likely to benefit from reperfusion therapy.5 The selection of patients by MRI is very likely to account for some of the differences between our results and those of previous studies.

There are limitations to our study. The small sample size prevents us from generalizing the results. The sample might have been too small to detect possible differences between the 2 groups (type II error). Imbalances in age and sex (with patients in the tandem group being slightly younger and more likely to be male) might further affect our results. Late assessment of recanalization after 24 hours prevents us from differentiating between persistent occlusion and early reocclusion after initial recanalization.

To summarize, the results of our study indicate that the presence of a relevant amount of tissue at risk appears to play a key role for the likelihood of clinical recovery after IV-tPA treatment in acute stroke patients with tandem ICA/MCA occlusion. Tandem ICA/MCA occlusion is a frequent finding in acute ischemic stroke, and it appears not justified to exclude these patients from an effective treatment like intra-venous thrombolysis.

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Disclosures
None.

References
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