Tandem Internal Carotid Artery/Middle Cerebral Artery Occlusion
An Independent Predictor of Poor Outcome After Systemic Thrombolysis

Marta Rubiera, MD; Marc Ribo, MD, PhD; Raquel Delgado-Mederos, MD; Esteban Santamarina, MD; Pilar Delgado, MD; Joan Montaner, MD; José Alvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD

Background and Purpose—Although tandem internal carotid artery/middle cerebral artery (MCA; TIM) occlusion has been associated with low recanalization rate after IV tissue plasminogen activator (tPA), its independent contribution on stroke outcome remains unknown. Moreover, whether the relative resistance to thrombolysis in tandem lesions varies depending on the location of MCA clot remains uncertain.

Methods—Two hundred and twenty-one consecutive stroke patients with an acute MCA occlusion treated with IV tPA were studied. Emergent carotid artery ultrasound and transcranial Doppler (TCD) examinations were performed in all patients before treatment. Recanalization was assessed on TCD at 2 hours of tPA bolus. National Institutes of Health Stroke Scale (NIHSS) scores were obtained at baseline and after 24 hours. Modified Rankin Scale score was used to assess outcome at 3 months.

Results—Median prebolus NIHSS score was 16 points. On TCD, 156 (71.6%) patients had a proximal and 65 (29.4%) a distal MCA occlusion. TIM occlusion was identified in 44 (19.9%) patients. Eighteen (41.9%) patients with and 123 (69.5%) without TIM lesions achieved an MCA recanalization (P = 0.01). In a logistic regression model, hyperglycemia >140 mg/dL (odds ratio [OR] 3.3, 95% CI, 1.6 to 6.8) and the presence of TIM occlusion (OR 2.8, 95% CI, 1.1 to 6.9) emerged as independent predictors of absence of recanalization. However, the independent contribution of TIM lesions on poor response to thrombolysis varied depending on the location of MCA occlusion. TIM occlusion independently predicted resistance to thrombolysis in patients with proximal (OR 4.63, 95% CI, 1.79 to 11.96), but not in those with distal MCA occlusion. Patients with TIM occlusion had worse short- (P < 0.0001) and long-term (P < 0.0001) clinical outcome.

Conclusions—TIM occlusion independently predicts poor outcome after IV thrombolysis. However, its impact varies depending on the location of MCA clot. Therefore, emergent carotid ultrasound plus TCD examinations may improve the selection of patients for more aggressive reperfusion strategies. (Stroke. 2006;37:2301-2305.)

Key Words: tandem ▪ thrombolysis ▪ ultrasonography

Intravenous thrombolysis is the only approved treatment in patients with acute ischemic stroke presenting in a narrow time window of <3 hours of symptom onset.1 However, in the best case-scenario, early complete recanalization is achieved in only 30% to 40% of patients, and <50% of treated patients become independent at long-term.2 Several factors may influence the response to intravenous thrombolysis in terms of recanalization, including time-to-treatment, size and location of arterial occlusion and stroke subtype.3 Information on early predictors of recanalization resistance may be useful for selecting patients for more aggressive reperfusion strategies.

Previous studies have shown that despite similar stroke severity on admission, patients with tandem cervical internal carotid artery (ICA)/middle cerebral artery (MCA; TIM) occlusion have lower likelihood of MCA recanalization and poorer outcome than those with isolated MCA occlusion.3–6 In the context of TIM lesions, site of the intracranial artery occlusion may represent not only a surrogate of clot burden but also may reflect different hemodynamic conditions and exposure to the thrombolytic agent, which may alter the response to systemic thrombolysis.

Therefore, we hypothesized that the relative resistance to thrombolysis in patients with TIM occlusion varies depending on the location of MCA clot. In the present study we sought to investigate clinical and hemodynamic predictors of poor response to systemic thrombolysis and to evaluate whether response to thrombolysis in patients with TIM occlusion differs depending on the location of MCA clot.

Subjects and Methods

All patients with an acute ischemic stroke admitted in our hospital within the first 6 hours after symptoms onset were prospectively studied. Stroke onset was defined as the last time the patient was known to be without any neurological symptoms. Five-hundred and thirty-three consecutive patients with a <6-hour nonlacunar ische...

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mic stroke involving the vascular territory of the MCA were evaluated between March 2001 and February 2005. Of these, 516 (96.8%) underwent emergent carotid ultrasound (CUS) and transcranial Doppler (TCD) examination. Patients with an insufficient acoustic temporal window, with terminal ICA occlusion on TCD, who were taking anticoagulants, who had a dramatic spontaneous neurological improvement or had an infarction higher than 33% of MCA territory in the CT or MRI were excluded. Finally, 221 (50.3%) patients with an acute MCA occlusion were included in the study and treated with intravenous tissue-type plasminogen activator (IV tPA) in a standard 0.9 mg/kg dose <3 hours of stroke onset. Informed consent was obtained from all patients or their next-of-kin. The study protocol was approved by the local ethics committee.

Clinical Assessment
All patients underwent a standard neurological examination, ECG, blood chemistry, CUS and contrast CT or emergent MRI before treatment. A detailed history of vascular risk factors was obtained from each patient. To establish the stroke etiology, special coagulation tests, echocardiography and ECG-holter were performed when necessary, and a cerebral MR angiography was performed when extracranial carotid artery disease was suspected. Finally, patients were classified according to modified Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria in different stroke subtypes. Large-vessel disease was defined as >50% stenosis or occlusion of the carotid artery ipsilateral to the MCA occlusion in the absence of source of cardiac embolism. Cardioembolic stroke was defined as the presence of atrial fibrillation, myocardial infarction in the past 6 months, or a high-risk source of embolism on echocardiogram according to TOAST criteria. When no etiologic source could be identified, patients were categorized as having a stroke of undetermined etiology.

Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS) score which was performed at baseline and 24 hours after stroke onset. Stroke severity and neurological improvement or worsening was defined as a decrease or increase of ≥4 points in the NIHSS. An intracranial hemorrhage was considered as symptomatic if the patient had clinical deterioration causing an increase of ≥4 points on the NIHSS and if the hemorrhage was likely to be the cause of neurological deterioration. At the 3-month follow-up, patients were interviewed in the outpatient clinic (90%) or by telephone (10%) to evaluate clinical outcome in terms of level of independence in activities of daily living. If the patients were unable to answer the questions, information was obtained from a relative or caregiver. Favorable outcome at 3 months was defined as modified Rankin Scale score ≤2.

TCD and CUS Protocols
A standard TCD examination was performed in the emergency room on admission before tPA administration using 1-channel 2-MHz equipment (TCD 100 mol/L, Spencer Technologies, and DWL Multipod ×4). A standard set of diagnostic criteria was applied to diagnose arterial occlusion. Proximal MCA occlusion was defined as the absence of flow or the presence of minimal flow signal throughout the MCA at an insonation depth between 45 to 65 mm, accompanied by flow diversion in the ipsilateral anterior cerebral artery and posterior cerebral artery, according to the Thrombolysis in Brain Ischemia (TIBI) grading system. Distal MCA occlusion was defined as blunted or dampened signals (TIBI 2 or 3) in the symptomatic artery with <30% flow than the contralateral MCA, and flow diversion signs in ipsilateral neighboring arteries. These pathological signs of occlusion and recanalization on TCD have shown a sensitivity and specificity values >90% against conventional angiography.

On admission all patients underwent emergent carotid artery ultrasound (5 and 10-MHz linear probes, Aplo-80, Toshiba) examination before tPA administration. The presence and severity of stenosis or occlusion was defined by means of peak systolic velocity and end-diastolic velocity. A severe stenosis (≥70%) presented with peak systolic velocity >230 cm/s and end-diastolic velocity ≥100 cm/s, and a complete occlusion was defined by the absence of flow in the extracranial internal carotid artery.

The presence of TIM occlusion was determined based on previous published criteria. Briefly, in the presence of a stenosis ≥70% or occlusion in the extracranial carotid artery, TIM required an abnormal wave form (TIBI 0 to 3) on the ipsilateral MCA associated to collateral flow signals (anterior and posterior communicating arteries, reverse flow in the ipsilateral anterior cerebral artery and ophthalmic artery), flow diversion signs and compensatory velocity increase (≥20% increase in the contralateral hemispheric vessels or vertebralbasilar arteries).

After the site of MCA occlusion was identified, continuous monitoring of the residual flow signals was performed with a Marc 500 head frame (Spencer Technologies) or DWL metal head frame to maintain tight transducer fixation and a constant angle of insomation. Continuous TCD monitoring of recanalization was conducted during tPA administration and 1 hour after. Changes on TCD in each patient were determined by a rater using direct visual control of monitoring display. The same rater carried out an additional TCD recording at 2 hours of tPA bolus to assess the degree of recanalization. Again, a new TCD examination was performed if a neurological worsening was detected within the 24 hours after stroke onset.

Recanalization on TCD was diagnosed as partial when blunted or dampened signals appeared in a previously demonstrated absent or minimal flow. Complete recanalization on TCD was diagnosed if the end-diastolic flow velocity improved to normal or elevated values (normal or stenotic signals). No change in the abnormal waveforms indicated that no recanalization had occurred.

Reocclusion (RO) was defined as a worsening in ≥1 grade in the TIBI flow grading system after a previously documented recanalization. RO was considered as symptomatic when a clinical deterioration (increase of ≥4 points in NIHSS score) occurred at the time of RO on TCD.

Imaging Protocol
On admission, all patients underwent a CT scan or a standard multiparametric MRI protocol within the first 3 hours after stroke onset. A CT scan was repeated after 24 to 36 hours or earlier when rapid neurological deterioration occurred. CT scan and MRI exams were reviewed by neuroradiologists with extensive experience in acute stroke, whom were blinded to the clinical and TCD details. Patients with TIM underwent a cervical MRI angiography to confirm the presence and severity of the carotid artery disease.

Statistical Analysis
The analysis was performed with the use of SPSS 12.0 software (SPSS Inc). Statistical significance for intergroup differences were assessed by the 2-tailed Fisher exact test and Pearson χ² test for categorical variables and Student t test and Mann–Whitney U test and Kruskal-Wallis test for continuous variables. A level of P<0.05 was accepted as statistically significant.

Results
Two-hundred and twenty-one patients (109 men and 112 women) with an acute ischemic stroke attributable to MCA occlusion treated with IV tPA were studied. Demographic data, risk factor profile, and baseline clinical findings are shown in Table 1. Mean age was 70.5±11.1 years (range 24 to 92 years). Median NIHSS score on admission was 16 points (interquartile range 13 to 18 points). Patients with TIM occlusion were more frequently males, younger, smokers, with higher baseline diastolic blood pressure, had more likely proximal occlusion and less frequent atrial fibrillation as compared with those without TIM occlusion. The time elapsed between symptom onset and drug administration was 150.5±32 minutes (range: 60 to 185 minutes). The door-to-needle time was 59.2±22.1 minutes, ranging from 47 to 109 minutes.

One-hundred and nineteen (53.8%) patients were considered to have a cardioembolic stroke, 53 (24%) had a stroke attribut-
TABLE 1. Demographic Data, Risk Profile and Basal Clinical Findings of the Series

<table>
<thead>
<tr>
<th>Variable</th>
<th>IMCA-O, n=177</th>
<th>TIM-O, n=44</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71.1±11.1</td>
<td>66.9±9.7</td>
<td>0.026*</td>
</tr>
<tr>
<td>Sex, male</td>
<td>80 (48.8%)</td>
<td>29 (69%)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>77 (49.7%)</td>
<td>23 (63.9%)</td>
<td>0.088</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32 (20.3%)</td>
<td>9 (25%)</td>
<td>0.335</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>19 (13.7%)</td>
<td>12 (41.4%)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>41 (26.1%)</td>
<td>15 (41.7%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>73 (45.9%)</td>
<td>5 (13.5%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>CHD</td>
<td>28 (17.9%)</td>
<td>6 (16.7%)</td>
<td>0.537</td>
</tr>
<tr>
<td>Time-to-treatment</td>
<td>148.1±32.8</td>
<td>158.1±29</td>
<td>0.071</td>
</tr>
<tr>
<td>Baseline NIHSS</td>
<td>15 (13–18)</td>
<td>16 (14–17)</td>
<td>0.202</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>137.9±6</td>
<td>126.9±6</td>
<td>0.062</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>153.9±23</td>
<td>162.2±24</td>
<td>0.064</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>80.3±12.8</td>
<td>87.5±12</td>
<td>0.003*</td>
</tr>
<tr>
<td>Platelets count</td>
<td>230.9±80</td>
<td>230.7±111</td>
<td>0.993</td>
</tr>
<tr>
<td>Proximal MCA-0</td>
<td>118 (67.1%)</td>
<td>38 (86.4%)</td>
<td>0.008*</td>
</tr>
<tr>
<td>ICA stenosis 70%–99%</td>
<td>13 (29.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA occlusion</td>
<td>31 (70.5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IMCA-O indicates isolated MCA occlusion; TIM-O, tandem ICA/MCA occlusion; CHD, coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure.

able to large-vessel disease and 49 (22.1%) patients without identified cause of stroke were regarded as undetermined stroke.

On baseline TCD assessment, proximal MCA occlusion was detected in 156 (70.5%) patients and distal occlusion in 65 (29.5%). TIM occlusion was seen in 44 (19.9%) patients. Among patients with a TIM occlusion, 38 (86.4%) had a proximal and 6 (13.6%) a distal MCA occlusion.

One hundred and forty-one (63.8%) patients recanalized during the first 2 hours of tPA bolus; 91 (41.2%) had a complete and 50 (22.6%) a partial recanalization. The rate of 2-hour recanalization was significantly lower (P=0.01) in patients with (n=18; 40.9%) compared with those without (n=123; 69.5%) TIM lesion. Only 10 (22.7%) patients with a TIM occlusion recanalized completely as compared with 78 (44.1%) in the isolated MCA occlusion group (P=0.03).

Factors associated with absence of recanalization on univariate analysis are shown in Table 2. Stroke severity on admission (P=0.023), baseline glucose level >140 mg/dL (P<0.001) and TIM occlusion (P=0.001) were factors significantly associated with a lack of recanalization. In a logistic regression model, only baseline glucose >140 mg/dL (odds ratio [OR] 2.84; 95% CI, 1.1 to 7.1) and TIM occlusion (OR 3.17; 95% CI, 1.5 to 6.5) remained as independent predictors of poor response to systemic thrombolyis.

Moreover, the impact of TIM occlusion on the success of recanalization varied markedly depending on the location of MCA clot. Among all patients with a proximal MCA occlusion, recanalization was significantly (P=0.001) less frequently seen in patients with (n=14; 31.8%) than without (n=79; 66.9%) TIM occlusion. In this group of patients, baseline glucose >140 mg/dL (OR 2.27; 95% CI, 1 to 5.1), systolic blood pressure >155 mm Hg (OR 3.36; 95% CI, 1.4 to 8.1) and TIM occlusion (OR 4.63; 95% CI, 1.8 to 11.9) independently predicted poor response to tPA in terms of recanalization. However, in patients with distal MCA occlusions, recanalization rate was not affected by the presence or absence of a TIM lesion (66.7% versus 71.2%, respectively; P=0.567). Among patients with distal MCA clot before treatment, only baseline glucose >140 mg/dL (OR 4.28; 95% CI, 1.2 to 15.4) emerged as independent predictor of resistance to thrombolysis in the logistic regression model.

RO was seen in 22 (9.9%) patients. RO was 4-fold more frequent in patients with TIM occlusion (n=11; 25%) compared with those with isolated MCA occlusion (n=11; 6.2%; P<0.001).

Hemorrhagic transformation on CT (symptomatic and asymptomatic) was detected in 57 (25.8%) patients, 13 (29.5%) with and 44 (24.9%) without TIM occlusion (P=0.56). Symptomatic intracranial hemorrhage was seen in 5 (0.4%) patients, all of them in the isolated MCA occlusion group.

Figures 1 and 2 illustrate early clinical course and long-term outcome in patients with and without TIM lesion before systemic thrombolysis. Patients with TIM occlusion had worse early clinical course and only 10 (22.7%) patients with TIM versus 101 (57.1%) with isolated MCA occlusion improved ≥4 points in the NIHSS after 24 hours from tPA treatment (P<0.0001; Figure 1). Similarly, after 3 months, only 8 (18.2%) TIM patients were independent (modified Rankin Scale ≤2) versus 84 (47.5%) with isolated MCA occlusion (P<0.001).

Thirty-nine (17.6%) patients died, 12 (27.3%) with and 27 (15.2%) without TIM occlusion, but the difference did not reach statistical significance (P=0.06).

Discussion

The present study demonstrates that detection of a TIM occlusion before systemic thrombolysis is associated with a low recanalization rate, high rate of early arterial RO and independently predicts poor clinical outcome. However, the impact of TIM occlusion on thrombolysis response varies depending on the location of MCA clot. TIM occlusion independently predicted poor response to thrombolysis in patients with proximal, but not in those with distal MCA occlusion. Patients with tandem ICA/distal MCA occlusion exhibited similar recanalization rates than patients with an isolated distal MCA occlusion.

Several factors may influence the differential response to thrombolysis among patients with TIM lesions. Experimental studies have demonstrated that effective delivery and distribution of tPA into the clot accelerates fibrinolysis and that fibrinolytic rate is dependent on the pressure gradient to which the clot is exposed. The presence of an extracranial carotid severe stenosis or occlusion leads to a regional decrease of cerebral perfusion pressure, which may not only hamper MCA clot dissolution but also favor blood-stasis, increasing the likelihood of rethrombosis after incomplete recanalization. In carotid atherothrombosis, the presence of an ipsilateral MCA occlusion usually is related to an artery-to-artery embolism, with a platelet-rich lytic-resistant clot proceeding from the carotid plaque. This large prospective study demonstrates that identification of a TIM occlusion independently predicts poor response to IV tPA in terms of
recanalization. The presence of a TIM occlusion before systemic thrombolysis increased in 2- and 4-fold the probability of persistent occlusion and early RO, respectively. Moreover, the sonographic detection of TIM occlusion was associated with a worse clinical course and poorer long-term outcome and with a trend toward higher mortality compared with patients with isolated MCA occlusion. Therefore, TIM occlusion may represent the worse case-scenario for standard thrombolytic therapy in terms of recanalization and outcome.

In the present study, the presence of a concomitant ipsilateral severe carotid artery disease independently predicted poor response to thrombolysis in patients with proximal, but not in those with distal MCA clot. Patients with tandem ICA/distal MCA occlusion showed similar recanalization rates than patients with an isolated distal MCA occlusion. Several mechanisms different than clot size may explain the better recanalization profile in patients with TIM lesions with distal MCA component. Unlike patients with proximal MCA occlusion, the hemo-

**TABLE 2. Univariate Analysis of Factors Associated With Lack of Recanalization According to the Location of MCA Occlusion**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All No RE</th>
<th>RE</th>
<th>Proximal MCA Occlusion No RE</th>
<th>RE</th>
<th>Distal MCA Occlusion No RE</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71±10.1</td>
<td>70±11.4</td>
<td>72.6±10.3</td>
<td>69.5±10.9</td>
<td>68.3±9.4</td>
<td>71.1±12.6</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>40 (50)</td>
<td>72 (51)</td>
<td>27 (44.3)</td>
<td>46 (48.4)</td>
<td>14 (73.7)</td>
<td>29 (639)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>49 (61.2)</td>
<td>66 (47)</td>
<td>38 (62.3)</td>
<td>45 (47.4)</td>
<td>10 (52.6)</td>
<td>23 (50)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>20 (25)</td>
<td>28 (19.8)</td>
<td>15 (24.6)</td>
<td>20 (21.1)</td>
<td>4 (21.1)</td>
<td>8 (17.4)</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>21 (26.2)</td>
<td>18 (12.7)</td>
<td>16 (26.2)</td>
<td>10 (10.5)*</td>
<td>3 (15.8)</td>
<td>10 (21.7)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>30 (37.5)</td>
<td>36 (25.5)</td>
<td>22 (36.1)</td>
<td>27 (28.4)</td>
<td>6 (31.6)</td>
<td>9 (19.6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>33 (41.2)</td>
<td>58 (41.1)</td>
<td>23 (37.7)</td>
<td>39 (41.1)</td>
<td>8 (42.1)</td>
<td>21 (45.7)</td>
</tr>
<tr>
<td>CHD</td>
<td>14 (17.5)</td>
<td>27 (19.1)</td>
<td>10 (16.4)</td>
<td>18 (18.9)</td>
<td>3 (15.8)</td>
<td>10 (21.7)</td>
</tr>
<tr>
<td>Time-to-treat</td>
<td>159.5±47</td>
<td>159.3±51</td>
<td>162.2±47</td>
<td>165.1±53</td>
<td>150.6±48</td>
<td>146.7±41</td>
</tr>
<tr>
<td>NIHSS &gt;16</td>
<td>54 (67.5)</td>
<td>68 (48.2)*</td>
<td>48 (78.7)</td>
<td>63 (66.3)</td>
<td>3 (15.8)</td>
<td>6 (13.1)</td>
</tr>
<tr>
<td>Glu&gt;140 mg/dl</td>
<td>45 (56.2)</td>
<td>37 (26)*</td>
<td>32 (52.5)</td>
<td>29 (30.5)*</td>
<td>10 (52.6)</td>
<td>9 (19.5)*</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>159.5±22</td>
<td>153.7±24</td>
<td>160.2±23</td>
<td>151.2±26*</td>
<td>157.1±22</td>
<td>159.3±21</td>
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<td>DBP, mm Hg</td>
<td>82.5±13.3</td>
<td>81.4±12.7</td>
<td>82.1±12.4</td>
<td>10.2±12.6</td>
<td>83.8±16.4</td>
<td>84.3±12.7</td>
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<tr>
<td>Platelets count</td>
<td>230.8±89</td>
<td>227.9±84</td>
<td>229.3±86</td>
<td>228.8±79</td>
<td>236±102</td>
<td>226.4±96</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>43 (53.7)</td>
<td>70 (49.6)</td>
<td>33 (54.1)</td>
<td>45 (47.4)</td>
<td>7 (36.8)</td>
<td>27 (58.7)</td>
</tr>
<tr>
<td>TIM-occ</td>
<td>26 (32.5)</td>
<td>18 (12.7)*</td>
<td>24 (39.4)</td>
<td>14 (15.6)*</td>
<td>2 (10.5)</td>
<td>4 (8.7)</td>
</tr>
<tr>
<td>ICA stn &gt;70%</td>
<td>7 (8.8)</td>
<td>6 (4.2)</td>
<td>7 (11.4)</td>
<td>4 (4.2)</td>
<td>1 (5.7)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>ICA occlusion</td>
<td>19 (23)</td>
<td>12 (8.5)</td>
<td>17 (27.8)</td>
<td>10 (10.5)</td>
<td>1 (5.7)</td>
<td>3 (6.6)</td>
</tr>
</tbody>
</table>

No RE indicates not recanalization; RE, recanalization. Percentages are indicated in parentheses. * Statistical significance (P<0.05).

**Figure 1.** Early clinical course in patients with and without TIM occlusion.

**Figure 2.** Long-term outcome after 3 months in patients with and without TIM occlusion.
dynamic impact of a concomitant cervical carotid stenosis or occlusion may be less relevant in distal MCA clots. In patients with tandem ICA/distal MCA occlusion the relative reduction of regional cerebral blood flow in the carotid artery territory may be more effectively compensated via leptomeningeal collateral circulation as compared with patients TIM lesions with a proximal MCA occlusion component.16 This may result in a higher pressure gradient to which the clot is exposed and a better delivery of tPA to a wider front of recanalization in patients with distal MCA occlusion.

In our study, admission hyperglycemia emerged as a robust predictor of thrombolysis resistance regardless occlusion location. Beside the deleterious effect of high glucose levels on ischemic brain tissue in acute stroke,17 previous clinical and experimental studies have demonstrated that acute hyperglycemia may hamper the recanalization process through mechanisms including inhibition of plasma fibrinolysis, increasing plasminogen activator inhibitor type-1, and decreasing tPA activity.18 Our study confirms, in a large number of patients, the role of high glucose levels in delaying reperfusion of the brain in acute stroke by impairing tPA-induced recanalization.19

Patients with terminal ICA occlusions (T occlusions) may exhibit larger clots and poorer pattern of collateral blood supply than patients with proximal MCA occlusion. Although patients with T occlusions were not included in this study, sonographic discrimination between proximal MCA occlusion and carotid T occlusion may be in some cases problematic and, therefore, we cannot rule out that some T occlusion patients were regarded as having proximal MCA occlusion. However, this would occur theoretically in both patients with and without TIM occlusions. On the other hand, in our series the number of patients with TIM, in particular those with distal TIM lesions was relatively small. Therefore, our observations require confirmation from a larger study population. Finally, the relative resistance of TIM lesion to lysis may vary depending on the hemodynamic effect of the extracranial ICA stenosis/occlusion. Although in our study recanalization rates were not influenced by whether the extracranial ICA was severely stenosed or occluded, this hypothesis requires further investigation in larger studies. The rate and timing of tPA-induced extracranial carotid artery recanalization is beyond the scope of this study.

In conclusion, TIM occlusion independently predicts poor outcome after IV thrombolysis. However, its impact varies depending on the location of MCA clot. Therefore, a rapid noninvasive neurovascular evaluation may improve the selection of patients for more aggressive rescue reperfusion strategies.

Disclosures

None.

References


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