Intra-arterial thrombolysis in 24 consecutive patients with internal carotid artery T occlusions

M Arnold, K Nedeltchev, H P Mattle, T J Loher, F Stepper, G Schroth, C Brekenfeld, M Sturzenegger, L Remonda

Objective: To determine the safety, efficacy, and predictors of favourable outcome of intra-arterial thrombolysis in acute stroke attributable to internal carotid artery “T” occlusion.

Methods: The authors analysed 24 consecutive patients with T occlusions of the internal carotid artery treated by local intra-arterial thrombolysis using urokinase.

Results: The median baseline National Institutes of Health Stroke Scale was 19. The average time from symptom onset to treatment was 237 minutes. Four patients (16.6%) had a favourable (modified Rankin Scale score (mRS≤2)) and 10 patients (41.7%) a poor outcome (mRS 3 or 4) after three months. Ten patients (41.7%) died. One symptomatic intracerebral haemorrhage (4.2%) occurred. Partial recanalisation of the intracranial internal carotid artery was achieved in 15 (63%), of the middle cerebral artery in four (17%), and of the anterior cerebral artery in eight patients (33%). Complete recanalisation never occurred. Sufficient leptomeningeal collaterals as seen on arteriography (p=0.02) and age <60 years (p=0.012) were the only predictors of favourable clinical outcome.

Conclusions: Acute stroke attributable to carotid T occlusion remains a condition with a generally poor prognosis even when intra-arterial thrombolysis is performed. Favourable outcome was seen only in patients with sufficient leptomeningeal collaterals.

Local intra-arterial thrombolysis (IAT) was shown to be effective in acute stroke attributable to middle cerebral artery (MCA) occlusion. However, whether stroke patients with occlusions of other vessels benefit from IAT as well, is open. For this reason we performed an analysis of our patients with internal carotid artery “T” occlusions (CTO) who had been treated with IAT.

METHODS

Twenty-four consecutive acute stroke patients with CTO, who were treated with IAT between December 1992 and December 2001, were analysed. Six of them had also the inclusion criteria for IAT reported in a previous study. In the same period 181 additional patients with acute stroke following occlusions of other cerebral vessels underwent IAT.

The neurological status at admission was quantified using the National Institutes of Health Stroke Scale (NIHSS) score. After neurological evaluation all patients underwent computed tomography (CT).

Early CT signs of ischaemia were defined according to von Kummer et al. Diagnostic intra-arterial digital subtraction angiography and IAT were performed on a biplane, high resolution angiography system as reported previously. A CTO was diagnosed, if the intracranial ICA, the ipsilateral MCA, and the ipsilateral A1 segment of the anterior cerebral artery (ACA) were occluded or absent. There were 15 patients with occlusion of the intracranial part of the ICA only and in nine patients the extracranial ICA was occluded as well. In four of them an endovascular dilatation of the extracranial ICA was performed and in two of them a stent was inserted. Urokinase was infused directly into or near the proximal end of the occluding thrombus over 60 to 90 minutes. A mean dose of 837 000 IU (range 250 000 to 1 100 000 IU) was given. Recanalisation was analysed by a control arteriogram immediately after IAT and classified according to TIMI grades. Two TIMI grades 2 or 3 were considered sufficient and grades 0 or 1 insufficient recanalisation. Recanalisation of each vessel (ICA, MCA, and ACA) was analysed.

Leptomeningeal collaterals from the anterior and posterior cerebral arteries were classified in two groups: poor, if none or minimal leptomeningeal anastomoses were present and no sufficient reversed filling of the occluded vessel territory was visible; and good if moderate or maximal leptomeningeal anastomoses with sufficient filling of the occluded vessel territory was observed, including opacification of a parenchymal and venous phase in the brain area supplied by leptomeningeal anastomoses.

Immediately after IAT, 20 patients received aspirin (250 mg–500 mg). Four patients treated before publication of the International Stroke Trial results, were given heparin to double the activated thromboplastin time. Control CT was performed on day 1 after IAT and any time when clinical deterioration occurred. Stroke aetiology was classified according to the TOAST criteria. Outcome was assessed by clinical examination three months after IAT using the modified Rankin scale (mRS). For the analysis of predictors of outcome we considered clinical and radiological factors that may influence clinical outcome and recanalisation and divided patients into two groups (patients with good outcome (mRS≤2) compared with patients with poor outcome (mRS 3–5) or death (mRS 6).

The SPSS program was used for statistics. Comparisons were performed using Fisher’s exact test. Two sided p values <0.05 were considered significant.

RESULTS

Demographic, clinical, and radiological data

Twenty-four patients with CTO (11 men, 13 women, mean (SD) age 60 (13) years, range 26–75 years) were identified. The

Abbreviations: CTO, carotid artery T occlusions; NIHSS, National Institutes of Health Stroke Scale; ICA, internal carotid artery; MCA, middle cerebral artery; CT, computed tomography; mRS, modified Rankin scale; ACA, anterior cerebral artery
proximal beginning of the CTOs was extracranial in 9 and intracranial in 15, 11 times distal to the origin of the posterior communicating artery, twice between the ophthalmic artery and the posterior communicating artery and twice in the petrosal segment of the ICA. The median NIHSS on admission was 19 (range 12–27). The mean interval from symptom onset to treatment was 237 minutes. Clinical and radiological data are summarised in table 1.

### Outcome

Four patients (16.6%) had a favourable (mRS < 2) and 10 (41.7%) a poor outcome (mRS 3 or 4) after three months. Ten patients (41.7%) died (table 2).

### Predictors of outcome

Four of 12 patients (33%) with sufficient collaterals had a favourable outcome and all 12 with insufficient collaterals a poor outcome or died (p=0.02). Angiographic examples are

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**Table 1** Predictors of clinical outcome at three months

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Good (mRS 0–2)</th>
<th>Poor or death (mRS 3–6)</th>
<th>Total (n)</th>
</tr>
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<tr>
<td>Patients [n]</td>
<td>4 (17)</td>
<td>20 (83)</td>
<td>24</td>
</tr>
<tr>
<td>Mean age [y] (SD)</td>
<td>47 (4)</td>
<td>63 (13)</td>
<td>60 (13)</td>
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<tr>
<td>Age ≤60</td>
<td>4 (33)</td>
<td>8 (67)</td>
<td>12</td>
</tr>
<tr>
<td>Age &gt;60</td>
<td>0 (0)</td>
<td>12 (100)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0 (0)</td>
<td>9 (100)</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>4 (27)</td>
<td>11 (73)</td>
<td>15</td>
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<tr>
<td>Diabetes</td>
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<td>5 (100)</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>4 (21)</td>
<td>15 (79)</td>
<td>19</td>
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<td>Smoking</td>
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</tr>
<tr>
<td>Yes</td>
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<td>2 (67)</td>
<td>3</td>
</tr>
<tr>
<td>No</td>
<td>3 (14)</td>
<td>18 (86)</td>
<td>21</td>
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<tr>
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<td>1 (25)</td>
<td>3 (75)</td>
<td>4</td>
</tr>
<tr>
<td>No</td>
<td>3 (15)</td>
<td>17 (85)</td>
<td>20</td>
</tr>
<tr>
<td>Hypertension</td>
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<td></td>
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<tr>
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<td>11</td>
</tr>
<tr>
<td>No</td>
<td>3 (23)</td>
<td>10 (77)</td>
<td>13</td>
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<tr>
<td>NIHSS on admission ≤10</td>
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<tr>
<td>11–15</td>
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<td>3 (100)</td>
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<tr>
<td>&gt;15</td>
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<td>17 (85)</td>
<td>20</td>
</tr>
<tr>
<td>Time to treatment ≤4 hours</td>
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<td>11 (85)</td>
<td>13</td>
</tr>
<tr>
<td>&gt;4 hours</td>
<td>2 (18)</td>
<td>9 (82)</td>
<td>11</td>
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<tr>
<td>CT Dense artery</td>
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<tr>
<td>Yes</td>
<td>3 (19)</td>
<td>13 (81)</td>
<td>16</td>
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<tr>
<td>No</td>
<td>1 (13)</td>
<td>7 (87)</td>
<td>8</td>
</tr>
<tr>
<td>CT early signs of ischaemia</td>
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<tr>
<td>Yes</td>
<td>1 (9)</td>
<td>11 (91)</td>
<td>12</td>
</tr>
<tr>
<td>No</td>
<td>3 (25)</td>
<td>9 (75)</td>
<td>12</td>
</tr>
<tr>
<td>Extension of ICA occlusion</td>
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<td></td>
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<tr>
<td>Extracranial and intracranial</td>
<td>2 (22)</td>
<td>7 (78)</td>
<td>9</td>
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<tr>
<td>Intracranial only</td>
<td>2 (15)</td>
<td>13 (85)</td>
<td>15</td>
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<td>Recanalisation ICA</td>
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<tr>
<td>TIMI 0 or 1</td>
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<td>8 (89)</td>
<td>9</td>
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<tr>
<td>TIMI 2</td>
<td>1 (25)</td>
<td>3 (75)</td>
<td>4</td>
</tr>
<tr>
<td>TIMI 3</td>
<td>2 (18)</td>
<td>9 (82)</td>
<td>11</td>
</tr>
<tr>
<td>Recanalisation MCA</td>
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<td></td>
</tr>
<tr>
<td>TIMI 0 or 1</td>
<td>2 (10)</td>
<td>18 (90)</td>
<td>20</td>
</tr>
<tr>
<td>TIMI 2</td>
<td>2 (50)</td>
<td>2 (50)</td>
<td>4</td>
</tr>
<tr>
<td>TIMI 3</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Recanalisation ACA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI 0 or 1</td>
<td>3 (19)</td>
<td>13 (81)</td>
<td>16</td>
</tr>
<tr>
<td>TIMI 2</td>
<td>1 (13)</td>
<td>7 (87)</td>
<td>8</td>
</tr>
<tr>
<td>TIMI 3</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Collaterals</td>
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<td>Sufficient</td>
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<td>Stroke aetiology</td>
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<td>Cardioembolic</td>
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<td>7 (100)</td>
<td>7</td>
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<tr>
<td>Unknown</td>
<td>1 (20)</td>
<td>4 (80)</td>
<td>5</td>
</tr>
<tr>
<td>Large artery disease</td>
<td>3 (27)</td>
<td>8 (73)</td>
<td>11</td>
</tr>
<tr>
<td>Others</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>1</td>
</tr>
</tbody>
</table>

Data shown as mean (SD) and number (%). mRS, modified Rankin scale score; NIHSSS, National Institute of Health Stroke Scale score; TIMI, thrombolysis in myocardial infarction; p, difference between subgroups by Fisher’s exact test.

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**Table 2** Outcome according to the modified Rankin scale (mRS) at three months

<table>
<thead>
<tr>
<th>mRS 2</th>
<th>mRS 3</th>
<th>mRS 4</th>
<th>mRS 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>8</td>
<td>33</td>
<td>42</td>
</tr>
</tbody>
</table>

Data shown as percentages.
shown in figures 1 and 2. Patients younger than 60 years were more likely to have a favourable outcome (p=0.012). There was no association between baseline NIHSS, time to treatment, vascular risk factors, dense artery sign, early CT signs of ischaemia, extent of the occlusion on arteriography, stroke aetiology, and grade of recanalisation with outcome (table 1).

Recanalisation
Partial recanalisation of the intracranial ICA was achieved in 15 (63%), of the MCA in four (17%), and of the ACA in eight patients (33%). Complete recanalisation (TIMI 3) of the ICA was achieved 11 times (46%), but never occurred for the ACA and the MCA.

Complications
One symptomatic intracerebral haemorrhage (ICH) (4.2%) and one haematoma (4.2%) at the puncture site of the femoral artery occurred.

DISCUSSION
Outcome and recanalisation
The main message of this study is that prognosis of CTO remains poor even after IAT. Only 4 of 24 patients (17%) had a favourable outcome after three months. Previous smaller series of CTOs treated with different thrombolitics and inclusion and outcome criteria were not more encouraging. Good or moderate outcomes ranged from 12.5% to 33% (table 3). In a series of 100 patients treated with intravenous rt-PA proximal ICA thrombosis ipsilateral to the stroke predicted a poor outcome as well. One possible reason for the disappointing results in our series is that complete recanalisation of the occluded intracranial vessels was never achieved, potentially because of the large bulk of thrombotic material in CTO or because the thrombolytic agent is drained away through the ophthalmic or the posterior communicating arteries before it can be effective.

A third of our patients showed partial recanalisation of the ACA and 17% of the MCA, however patients did not benefit clinically from this partial reperfusion. Perhaps in a larger series a small benefit could have been seen. The low recanalisation rates in our study are in concordance with previous reports (table 3). Jansen reported restoration of adequate antegrade blood flow in 2 of 16 CTO patients (12%) after intra-arterial and in 2 of 16 patients (12%) after intravenous thrombolysis. According to a meta-analysis of previous heterogeneous reports 7 of 64 patients (11%) recanalised (table 3).25

<table>
<thead>
<tr>
<th>Table 3</th>
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<tbody>
<tr>
<td><strong>Source</strong></td>
</tr>
<tr>
<td>Urbach9</td>
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<tr>
<td>Sasaki10</td>
</tr>
<tr>
<td>Bollaert11</td>
</tr>
<tr>
<td>Kucinski11/12</td>
</tr>
<tr>
<td>Zeumer13</td>
</tr>
<tr>
<td>Jansen14</td>
</tr>
<tr>
<td>Zeidat15</td>
</tr>
<tr>
<td>Present study</td>
</tr>
</tbody>
</table>

*In the original article recanalisation is indicated as "almost complete".
Predictors of favourable outcome

In this series, sufficient leptomeningeal collaterals and age <60 years were predictors of favourable outcome. All four patients with favourable outcome had sufficient collaterals. However, outcome was never favourable in any of the 12 patients with insufficient collaterals, even in the six of them who recanalised partially. The importance of leptomeningeal collaterals has been described in several reports of strokes in the territories of the carotid and basilar arteries. Adequate collaterals were found to be meaningful in IAT of CTO as well. Urbach reported a favourable outcome in three of four patients with good collaterals, whereas seven of eight patients with insufficient collaterals did poorly or died. Jansen published four good outcomes and 11 survivors in 12 patients with good collaterals compared with only one good outcome and 80% mortality in 20 patients with poor collaterals. Patients younger than 60 years had a better outcome than older patients, as has been noted in previous thrombolyis trials as well. There was no association between sex, vascular risk factors, stroke aetiology, baseline NIHSS score, early CT signs of ischaemia, HDAS on CT scan, time to treatment or recanalisation, and outcome in our patients. These results should be interpreted with caution because of the small sample size.

Complications

One symptomatic ICH (4%) occurred among our 24 patients, similar to other thrombolyis studies. The small numbers preclude a statement about safety of IAT in CTO. However, the low ICH rate is an indicator, though weak, that poor outcomes of CTO patients are not attributable to an exaggerated haemorrhage risk of IAT.

Conclusions

In conclusion, acute stroke attributable to CTO remains a condition with a generally poor prognosis, even when IAT is performed. The prognosis is especially gloomy when leptomeningeal collaterals are insufficient. From a pathophysiological point of view complete and fast recanalisation is still a goal promising good clinical outcomes. How to achieve this needs further research. Potential approaches are combined intravenous/intra-arterial thrombolysis, mechanical thrombascipiration, intracranial balloon angioplasty with or without stenting, and thrombolysis combined with ultrasound.

Authors’ affiliations

M Arnold, K Nedeltchev, H P Mattle, T J Loher, F Stepper, M Sturzenegger, Department of Neurology, University Hospital of Berne, Switzerland

G Schroth, C Brekenfeld, L Remonda, Department of Neuroradiology, University Hospital of Berne

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REFERENCES


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