Intra-Arterial Thrombolytic Therapy in Peri-Coronary Angiography Ischemic Stroke

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Background—Intra-arterial thrombolysis (IAT) for peri-coronary angiography (CA) stroke may be safe and efficacious. However, IAT may increase the risk of intracranial hemorrhage (ICH).

Methods—A retrospective study was performed involving 3 university hospitals. All peri-CA IAT-treated cases were identified. Patient demographics, stroke severity, angiographic findings, thrombolytic use, modified Rankin Scale (mRS), ICH, and mortality were determined.

Results—A total of 21 patients with post–left CA stroke were treated with IAT (mean age 71.8±12.3 years). Arterial occlusion was found in 14 (66.7%) and 7 (33.3%) of the anterior and posterior circulation, respectively. Mean time-to-therapy was 36±12 minutes from the time the neurological deficit was noted. mRS ≤2 occurred in 10 of 21 (48%) patients. Patients with younger age and shorter time-to-IAT had more complete arterial recanalization and clinical recovery. Symptomatic ICH occurred in 3 (14%) cases, and 4 (19%) patients died.

Conclusions—Peri-CA IAT appears to be feasible and safe without increased risk of symptomatic ICH and death when compared with the previously reported IAT literature. (Stroke. 2005;36:1083-1084.)

Key Words: cardiac catheterization ■ cerebrovascular disorders ■ stroke ■ tissue plasminogen activator ■ thrombolysis

Coronary angiography (CA) is associated with a peri-procedural stroke rate of 0.3%. This risk is higher with interventional versus diagnostic CA. Peri-CA stroke may be related to air embolism, thrombus formation at the catheter tip, or thromboembolic material dislodged by the catheters or from the aortic arch. Fluoroscopic time and severity of coronary artery disease (CAD) may increase the risk of peri-CA stroke.

Peri-CA stroke represents a unique opportunity for immediate stroke interventional therapy with intravenous, catheter-based intra-arterial thrombolysis (IAT) or combined therapy using recombinant tissue plasminogen activator (rtPA), prourokinase, or urokinase (UK) because of very short time-to-treatment and readily available resources. We report multicenter experience of IAT of peri-CA stroke.

Subjects and Methods
Acute stroke treatment databases were reviewed from 3 university hospitals, selecting patients with peri-CA strokes treated with IAT between 1993 and 2004. Patients were considered for IAT if they did not receive fibrinolytic therapy for their underlying CAD and had normal baseline head computed tomography (CT) with no intracranial hemorrhage (ICH). Demographics, stroke risk factors, National Institutes of Health Stroke Scale (NIHSS), Coagulation studies, CT angiography, time-to-IAT, angiographic findings, thrombolytic agent, recanalization (as partial complete or none and thrombolysis in myocardial infarction [TIMI] scales), ICH, and clinical outcome as judged by modified Rankin scale (mRS) at discharge were collected. Symptomatic ICH was defined as worsening of neurological deficit by ≥4 points on NIHSS with well-defined hematoma on head CT.

Statistics
Analysis was performed with StatView 5.0 (SAS Institute). Bivariable comparisons were performed using Fisher’s exact test. Multivariable analysis with multiple comparison adjustment was performed.

Results
A total of 21 patients with left CA had peri-procedural acute stroke that was treated with IAT. The mean age was 71.8±12.3 years, 10 (48%) were men, 11 (52%) were women, and 15 (71%) were white. Cases were approximately equally divided between diagnostic (10) and interventional (11) CA. A total of 18 (85%) patients had hypertension, 19 (90%) had CAD, 5 (24%) had acute myocardial infarction (MI), and 5 (24%) had atrial fibrillation. Median initial NIHSS was 16 (interquartile range 13 to 24).

Head CT evidence of early ischemia was present in 3 (12.5%) patients: 1 with reduced white-gray matter differentiation and 2 with loss of insular ribbon. All patients had activated clotting time between 250 and 300 seconds.

The occluded vessel was M1–middle cerebral artery (MCA) in 3 (14%) patients, M2-MCA branch in 2 (10%), posterior
Clinical Outcome After IAT for Peri-CA Stroke

<table>
<thead>
<tr>
<th></th>
<th>mRS ≤2 (10)</th>
<th>mRS &gt;2 (11)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66.4±13.5</td>
<td>76.6±9.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Female</td>
<td>5/10</td>
<td>6/11</td>
<td>0.82</td>
</tr>
<tr>
<td>White</td>
<td>7/10</td>
<td>1/1</td>
<td>0.89</td>
</tr>
<tr>
<td>NIHSS (median, IQ range)</td>
<td>15 (12, 18)</td>
<td>18 (14, 26)</td>
<td>0.12</td>
</tr>
<tr>
<td>rtPA</td>
<td>5</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>Time-to-treatment (minutes)</td>
<td>98.7±11.2</td>
<td>137±15.3</td>
<td>0.06</td>
</tr>
<tr>
<td>ICH</td>
<td>0</td>
<td>3</td>
<td>0.04</td>
</tr>
</tbody>
</table>

IQ indicates interquartile.

cerebral artery in 4 (19%), basilar artery (BA) in 1(5%), vertebral artery in 2 (10%), and occlusion in 2 anterior circulation branches (MCA, anterior cerebral artery, or both) in 9 (43%).

Mean time-to-therapy was 106.7±38.3 minutes from last documented normal patient examination and 36±12 minutes from the time symptoms were initially observed. rtPA was used in 9 (43%) and UK and UK in 12 (57%) patient. Median rtPA dose was 23 mg (range 12 to 34). Median UK dose was 1 000 000 U (range 50 000 to 1 500 000). No heparin was allowed for 24 hours after IAT. Recanalization (TIMI 1, 2, and 3) occurred in 14 (66.7%) patients: complete (TIMI 3) in 5 (24%) and partial (TIMI 1 and 2) in 9 (43%); no recanalization (TIMI 0) occurred in 7 (33.3%) patients.

Two patients (4%) had good outcome at discharge, defined by mRS ≤2. Symptomatic ICH occurred in 3 (14%) patients, which was not related to intra-procedure anticoagulation. Four (19%) patients died: 1 related to ICH, 1 to large stroke, and 2 to CAD.

Younger age, shorter time-to-treatment, and lack of ICH showed a trend for improved outcome (Table). There was no statistically significant difference with regard to gender, race, thrombolytic agent used, or NIHSS, although patients with good outcome had numerically lower median NIHSS score than patients with bad outcome (15 versus 18). Multivariable analysis showed an association between age and time-to-treatment with better outcome (P value of 0.06 and 0.05, respectively; R-square 0.34).

Discussion

Peri-CA strokes often occur during or immediately after the procedure, whereas the femoral artery sheath is still in place, providing an opportunity for rapid initiation of IAT. To our knowledge, this is the largest multicenter study reporting use of IAT for peri-CA acute ischemic stroke. Previous studies were limited to single case reports and single small case series lacking significant details. One patient with acute BA occlusion during transbrachial CA was treated with UK, which led to complete recanalization and full clinical recovery. Full recovery after intravenous UK or rtPA has also been reported in isolated anterior and posterior circulation stroke during peri-CA period.5–8 These reports are vulnerable to selection bias and do not reflect actual safety and feasibility of fibrinolytic therapy. Single case series reported on 8 patients with peri-CA stroke treated with mixed treatment: 3 cases with intra-arterial UK, 2 cases with intra-arterial rtPA, one case with abciximab, and 2 cases with UK and abciximab. However, initial NIHSS, presenting symptoms, and coagulation studies were not provided. Their time-to-therapy is shorter than our study (mean of 31 versus 119.8 minutes). However, it was unclear whether the time-to-treatment in that study was estimated from when symptoms were first noticed or from the last time the patient was seen intact. Four patients (50%) had full recovery, 2 had minor residual, 1 had no change, and 1 had ICH with death.9

In our study, all centers had well-established brain attack protocol, with an experienced team of stroke neurologists and neurointerventionalists. All patients received full neurological evaluation, coagulation profile, and head CT scan. IAT was performed by experienced neurointerventionalists in specialized cerebral angiography suites. Ascertainment patients’ neurological status to be related to acute ischemic stroke rather than seizure, medication or hemodynamic compromise is of paramount significance before exposing patients to IAT.

Good outcome in our series may be related to rapid initiation of IAT. Other factors may include younger age and initial NIHSS. Our small sample size could not allow further exploration. Overall recanalization rate of 67% in our study was comparable to previous IAT studies. Complete recanalization occurred in 24%, which may be related to various types of clot and multiple distal small vessels occlusion that may be technically difficult to reach.

The rate of symptomatic ICH in our study was 14%, similar to other IAT studies,2–4 despite having aggressive anticoagulation in our study population for their CA intervention. Our mortality rate was 19%; 2 were related to ICH or stroke, and 2 were related to underlying CAD. This mortality rate is within the range of the previously published stroke thrombolysis literature, although considering that many of our patients had several comorbidities and some had acute MI.

In conclusion, IAT is a valid therapeutic option for peri-CA stroke. Symptomatic ICH and mortality were similar or lower than reported previously in IAT trials. Time-to-therapy, younger age, and initial NIHSS may influence clinical outcome.

References

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