Early Recanalization After Intravenous Administration of Recombinant Tissue Plasminogen Activator as Assessed by Pre- and Post-Thrombolytic Angiography in Acute Ischemic Stroke Patients

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Early Recanalization After Intravenous Administration of Recombinant Tissue Plasminogen Activator as Assessed by Pre- and Post-Thrombolytic Angiography in Acute Ischemic Stroke Patients

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Background and Purpose—Recanalization rates after the intravenous (IV) recombinant tissue plasminogen activator (rt-PA) treatment have been poorly studied in acute stroke.

Methods—CT angiography was performed before IV rt-PA in all patients and digital subtraction angiography was undertaken for intra-arterial thrombolysis in cases of no improvement after rt-PA infusion.

Results—Forty-five patients were treated with IV rt-PA. Initial CT angiography showed relevant arterial occlusions in 35 patients. Recanalization after rt-PA therapy was demonstrated by digital subtraction angiography in 7 of the 31 patients with the occlusion on initial CT angiography: 2/16 in the internal carotid or proximal middle cerebral artery, 3/11 in the distal middle cerebral artery and 2/4 in the basilar artery occlusion.

Conclusions—The early recanalization rate after IV rt-PA use was very low in cases with large proximal arterial occlusions. CT angiography before IV rt-PA may be useful for the prediction of its efficacy. **(*Stroke*. 2007;38:192-193.)**

Key Words: CT angiography ■ thrombolysis ■ tissue plasminogen activator

Recanalization rates after intravenous (IV) recombinant tissue plasminogen activator (rt-PA) therapy were estimated in stroke patients treated by combined IV and IA (intra-arterial) thrombolysis and in those with transcranial Doppler (TCD) monitoring during IV thrombolysis. Rates were reported as being between 16.8% and 38%.[1–3] However, in the Interventional Management of Stroke study,[1] the dose of rt-PA used was two-thirds of that used for conventional therapy, the duration of the infusion was reduced by a half, and the arterial occlusion before IV rt-PA was not determined. TCD itself may augment the thrombolytic effect of rt-PA.[3] Therefore, the exact recanalization rate by conventional IV rt-PA has remained uncertain.

Subjects and Methods

Patients with an acute ischemic stroke who were subjected to thrombolysis were retrospectively analyzed. The inclusion criteria for thrombolysis appear in our previous reports.[4] All CT angiography (CTA) examinations were performed on a 16-channel (Somatom Sensation 16; Siemens) system. The source images and the 3-D reconstructed images at 0.75-mm thickness with 0.3-mm increments were used for image analysis. After initial brain CTs, a total dose of 0.9-mg/kg rt-PA was given for 60 minutes. Patients showing no responses to IV rt-PA at the end of infusion (1 hour after the bolus; improvement of National Institutes of Health Stroke Scale [NIHSS] score <4) were subjected to further IA thrombolysis.[4] When an arterial occlusion was documented by digital subtraction angiography, IA thrombolysis with urokinase was performed.

Recanalization status was classified according to the Thrombolysis in Cerebral Infarction (TICI) classification[5] (Grade 0, no perfusion; Grade 1, penetration with minimal perfusion; Grade 2a, partial filling ⅔ of the entire vascular territory; Grade 2b, complete filling, but the filling is slower than normal; Grade 3, complete perfusion).

Results

Forty-five patients were treated with IV rt-PA within 3 hours of symptom onset. The initial CTAs showed relevant arterial occlusion in 35 and arterial stenosis in 3 patients. Eight patients showed rapid clinical improvement after IV rt-PA infusion. Four of them showed arterial occlusion (supplemental Table I, available online at http://stroke.ahajournals.org). Digital subtraction angiographies were performed in the remaining 37 patients. The median time from the IV rt-PA bolus to the visualization of the occluded arteries by digital subtraction angiography was 120 minutes (60 to 365 minutes). Early recanalization after IV rt-PA (TICI ≥2) was achieved in 7 of the 31 patients (22.6%) whose arterial occlusion had been found on initial CTAs. The early recan-

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Angiographic Findings of the 31 Patients With Arterial Occlusion on Initial CTA

Occlusion Site	ICA or Proximal MCA	Distal MCA	Basilar Artery
No. of patients	16	11	4
Recanalization after IV rt-PA	2 (12.5%)	3 (27.3%)	2 (50%)
Final recanalization after combined IA UK	10 (62.5%)	7 (63.6%)	3 (75%)

IA UK indicates intra-arterial urokinase.

alization was least common in the occlusion of the internal carotid artery (ICA) or proximal middle cerebral artery (MCA; M1, 2/16, 12.5%). The recanalization rate was 27.3% (3/11) in patients with the distal MCA (M2 and distal) and 50% (2/4) in those with basilar artery occlusion. After IA thrombolysis, the final recanalization was achieved in 20 of 31 patients (Table). The median time from onset to successful recanalization among those treated with IA thrombolysis was 325 minutes (range 195 to 380 minutes, 13 patients). All of the 7 patients with initially normal CTAs exhibited acute cerebral infarctions on follow-up MRIs. Infarctions were in the perforating arterial territory in 3, and multiple and small in the MCA territory in 3 patients. There were multiple and bilateral cerebral and cerebellar infarctions in 1. Atrial fibrillation was diagnosed in 3 of those 4 patients with multiple infarctions.

The median baseline NIHSS score was 13 for 45 patients. At 30 days, it was 2 (assessed in 36 patients). Fifty percent (21 of 42 patients assessed) had a good functional outcome at 90 days, defined as modified Rankin Scale score $\leq$1. Eighteen of 39 patients with ICA territory infarction showed early ischemic changes (Alberta Stroke Program Early CT Score [ASPECTS] $<$10) on initial brain CT.[6] Although good functional outcomes were frequent in high ASPECTS, it was not statistically significant (ASPECTS $>$7 in 17/33 and ASPECTS $\leq$7 in 1/6, χ^2 test, $P=0.19$). Two of 7 patients who showed recanalization after IV rt-PA and 8 of 20 patients who showed recanalization after combined IV and IA thrombolysis had good functional outcomes. The mortality rate after 90 days was 13.3% (6 patients) attributable to an intracranial hemorrhage (1), massive cerebral infarctions (4) or an undefined cause after discharge (1). Symptomatic hemorrhage occurred in 3 patients (2 in the IV rt-PA group) and 1 of them who had distal ICA occlusion and treated with IV rt-PA died 3 days after thrombolysis.

Discussion

This study provides data on the efficacy of IV thrombolysis that is used in clinical practice with the currently recommended drug and dosage. The overall recanalization rate in this study was 22.6% soon after IV rt-PA therapy. It has been reported that thrombolytic agents administrated intravenously cannot readily lyse thrombi occluding a large artery. The recanalization rates evaluated by angiographies that were performed before and after IV 2-chain rt-PA treatment (0.12 to 0.75 MIU/kg) were 8% in the extracranial ICA, 26.1% in the proximal MCA, and 38.1% in the distal MCA occlusion.[7] A study using 100 mg of rt-PA demonstrated recanalization rates of 9% in the ICA, 38.8% in the proximal MCA, and 100% in the distal MCA occlusion.[8] Our data are consistent with those studies in that it shows very low recanalization rates in the ICA and proximal MCA occlusions.

The present study indicates that CTA at the time of initial evaluation might predict some of the patients who will respond poorly to IV rt-PA, and this information may be helpful in the decision of immediate individualized therapeutic planning. For example, in cases with occlusion at the distal ICA or proximal MCA segment on the initial CTA, additional treatment with IA thrombolysis or mechanical clot removal may be considered from the beginning. However, further studies are necessary because the number of patients in the present study was too small to provide conclusive data regarding recanalization rates in each arterial segment.

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Disclosures

None.

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