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Recanalization of the MCA should play an important role in dramatic recovery after t-PA therapy in patients with ICA occlusion

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ABSTRACT

Background and purpose: The intravenous t-PA thrombolysis is not thought to be effective in most patients with internal carotid artery (ICA) occlusion. However, we have sometimes observed dramatic recovery in patients with ICA occlusion after t-PA therapy. The aim of the present study was to investigate the mechanism of dramatic recovery in such patients.

Methods: Consecutive ICA occlusion patients treated with t-PA were prospectively studied. MRI, including MRA, was performed before and within 1 h and 24 h after t-PA thrombolysis. Patients were divided into 2 groups: dramatic recovery (D group) and non-dramatic recovery (ND group).

Results: The subjects consisted of 21 consecutive stroke patients (14 males; mean age, 76.5 ± 8.4 years). Six (28.6%) patients (D group) had dramatic improvement and 15 (71.4%) patients (ND group) did not. The frequency of partial or complete recanalization within 1 h and 24 h after t-PA infusion was 14.3% and 50.0% for the ICA, 9.5% and 40.0% for the MCA, and 23.8% and 65.0% for the ICA or MCA, respectively. There was no difference in the frequency of ICA recanalization 24 h after t-PA infusion between the 2 groups (66.7% for D group vs. 42.9% for ND group, $P = 0.629$); however, MCA recanalization was more frequent in the D group than in the ND group (100.0% vs. 14.3%, $P = 0.0004$).

Conclusion: Recanalization of the MCA, which provides collateral flow, appears to play an important role in dramatic recovery after t-PA therapy in patients with ICA occlusion.

1. Introduction

Intravenous administration of tissue plasminogen activator (t-PA) can improve clinical outcome in acute ischemic stroke patients [1,2]. However, several investigators reported that t-PA was not effective in patients with internal carotid artery (ICA) occlusion [3,4]. The reason for this was that the embolus responsible for ICA occlusion was larger than that responsible for other arterial occlusions, and such an embolus was likely to be resistant to t-PA. However, we have sometimes observed dramatic recovery in patients with ICA occlusion after t-PA therapy. The aim of the present study was to investigate the frequency of dramatic recovery after t-PA infusion in patients with ICA occlusion and the mechanism in such patients using magnetic resonance imaging (MRI), including MR angiography (MRA).

2. Subjects and methods

Consecutive patients with acute ischemic stroke treated with t-PA within 3 h of stroke onset between October 2005 and October 2008 were studied. Patients with ICA occlusion on MRA before t-PA infusion were enrolled in the present study. Patients with heart valve replacements, pacemakers, or clipping of cranial arteries were excluded, since MRI is contraindicated in such patients. Furthermore, patients with recurrence within 7 days of t-PA infusion were also excluded. The inclusion and exclusion criteria for intravenous t-PA that were used were in accordance with the Japan Alteplase Clinical Trial [5].

The following clinical data were collected from all patients: 1) age and gender; 2) NIHSS scores before and 24 h and 7 days after t-PA infusion; 3) DWI-ASPECTS on initial DWI before t-PA infusion; 4) recanalization of the ICA occlusion within 1 h, 24 h, and 7 days after t-PA infusion; 5) vascular risk factors, including hypertension (HT), diabetes mellitus (DM), and hyperlipidemia (HL); 6) presence of potential cardiac sources of emboli; and 7) modified Rankin scale (mRS) at 3 months after t-PA therapy.

A neurologist determined the NIHSS scores before and 24 h and 7 days after t-PA infusion. Three measures of clinical recovery based on modified methods used in previous studies were used [6]. "Dramatic improvement" was defined as a ≥10 point reduction in the total NIHSS score or a total NIHSS score of 0 or 1. "Good improvement" was defined as a ≥4 point reduction in the total NIHSS score. "Worsening" was defined as a ≥4 point increase in the total NIHSS score. The patients were divided into 2 groups: patients who had dramatic improvement 7 days after t-PA therapy (D group) and patients who did not have dramatic improvement (ND group). "Poor outcome" was defined as an NIHSS score ≥20 7 days after t-PA therapy. Symptomatic cerebral hemorrhage was defined as a ≥4 point

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increase in the total NIHSS score. Favorable and poor outcomes at 3 months after t-PA therapy were defined as an mRS 0–3 and >3 or death, respectively.

Prior to t-PA infusion, MRI studies, including DWI and MRA, were done to measure DWI-ASPECTS [7] and to identify the presence of arterial occlusion. ICA occlusion was defined as follows: MRA showed no delineation of the ICA (complete ICA occlusion) or partial delineation of the ICA without delineation of the top of the ICA (ICA top occlusion). Furthermore, the status of the MCA was also investigated and classified as complete MCA occlusion, partial MCA occlusion, or patent MCA. Subsequently, follow-up MRA was performed within 1 h and 24 h after t-PA administration to determine the presence or absence of recanalization of the ICA occlusion and the MCA occlusion. Recanalization was graded as complete, partial, or no recanalization, as follows: 1) complete recanalization, reappearance of the entire occluded artery and the distal vessel branches; 2) partial recanalization, from complete occlusion to partial occlusion, and restoration of part of the distal vessels supplied by the occluded artery; and 3) no recanalization, persistent complete and partial occlusion.

MRI was performed using a commercially available echo planar instrument operating on a 1.5-T unit (Signa EXCITE XL ver. 11.0; GE Healthcare, Milwaukee, WI, USA). DWI-ASPECTS was used to evaluate the affected middle cerebral artery territory. The experienced researcher (K.K.) who evaluated the MRA findings was blinded to patient clinical background and the initial presence of an occluded artery.

Using clinical, radiological, cardiac, and ultrasound test results, an experienced stroke neurologist assessed each patient according to modified Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria to determine stroke subtype. Large-vessel disease (LVD) was defined as >50% arterial stenosis or occlusion corresponding to neurological deficits in the absence of a source of cardiac embolism. Cardioembolic stroke was defined as the presence of potential cardiac sources of emboli. Lacunar stroke was defined as the presence of infarction <15 mm and absence of a source of cardiac embolism and >50% arterial stenosis. Undetermined stroke was used when no etiological source of emboli could be identified.

The clinical characteristics of the 2 groups were compared. Statistical analysis was performed using StatView version 5 statistical software. The significance of inter-group differences was assessed using Fisher's exact test for categorical variables and the Mann–Whitney *U* test and the Kruskal–Wallis *U* test for continuous variables. Values of $P<0.05$ were considered statistically significant. All study protocols followed the principles outlined in the Declaration of Helsinki, and written informed consent was obtained from all patients.

3. Results

Ninety-two consecutive stroke patients received t-PA treatment. The initial MRA demonstrated ICA occlusion in 22 patients, but 1 patient was excluded because of a recurrent stroke 24 h after t-PA infusion. Therefore, 21 patients with ICA occlusion (14 males, 7 females; mean age, 76.5 ± 8.4 years) were enrolled in the present study. The time from symptom onset to the initial MRI study was 93.5 ± 27.1 min, and the time from symptom onset to the t-PA bolus was 145.9 ± 25.7 min. Mean baseline NIHSS score was 19.5 ± 5.0 (9–27).

3.1. Initial MRA findings

Of 21 patients with ICA occlusion, 10 patients had complete ICA and MCA occlusion. One patient had complete ICA occlusion with partial MCA occlusion. Eight patients had ICA top occlusion with complete MCA occlusion. Two patients had ICA top occlusion with partial MCA occlusion.

3.2. Follow-up MRA 1 h after t-PA infusion

Overall, 16 patients had no recanalization, 4 patients had partial recanalization (3 patients in the ICA, 1 in the MCA), and 1 patient had complete recanalization of the MCA but persistent complete ICA occlusion.

3.3. Follow-up MRA 24 h after t-PA infusion

One patient who died due to brain herniation 4 days after t-PA therapy did not undergo MRA. Thus, follow-up MRA was performed in 20 patients. Two patients had complete recanalization of both the ICA and the MCA, 11 had partial recanalization (5 patients in the ICA, 3 in the MCA, and 3 in both the ICA and the MCA), and 7 patients had no recanalization. Of the 11 patients who had partial recanalization, 2 had partial recanalization of the ICA with complete MCA recanalization, 3 had partial recanalization of the ICA but persistent MCA occlusion, 2 patients had complete ICA recanalization but persistent MCA occlusion, and 1 had complete ICA recanalization with partial MCA recanalization. Thus, the frequency of partial recanalization was 25.0% for the ICA, 15.0% for the MCA, and 0.0% for both the ICA and the MCA. On the other hand, the frequency of complete recanalization was 25.0% for the ICA, 25.0% for the MCA, and 10.0% for both the ICA and the MCA. Therefore, the frequency of partial or complete recanalization was 50.0% for the ICA, 40.0% for the MCA, and 65.0% for the ICA and the MCA.

3.4. Patient outcome 7 days and 3 months after t-PA therapy

Dramatic improvement, good improvement, and worsening at day 7 were observed in 6, 5, and 4 patients, respectively. Therefore, the D group had 6 patients, and the ND group had 15 patients. No patients had symptomatic cerebral hemorrhages. Table 1 shows the characteristics of the 2 groups. The initial NIHSS score, blood pressure, and glucose were lower in patients with dramatic improvement than in patients with no dramatic improvement. Seven days after t-PA therapy, 66.7% of patients with no dramatic improvement had an

Table 1
Univariate analysis: factors associated with dramatic recovery at 7 days.

	Dramatic recovery	Non-dramatic recovery	*P*
	N = 6	*N* = 15	
Age (years)	79.2 ± 8.1	75.5 ± 8.6	0.3115
Male	6 (100.0%)	8 (53.3%)	0.0609
Hypertension	4 (66.7%)	7 (46.7%)	0.6351
Diabetes mellitus	1 (16.7%)	3 (20.0%)	0.9999
Hyperlipidemia	1 (16.7%)	2 (13.3%)	0.9999
Atrial fibrillation (AF)	2 (33.3%)	11 (73.3%)	0.1462
TOAST classification			
Cardioembolic	1 (16.7%)	11 (73.3%)	0.0464
Atherothrombotic	3 (50.0%)	1 (6.7%)	0.0526
Undetermined/others	2 (33.3%)	3 (20.0%)	0.5975
Baseline DWI-ASPECTS score	7.7 ± 2.4	6.1 ± 2.7	0.1990
MRA			
ICA top occlusion	3 (50.0%)	7 (46.7%)	0.9999
Complete ICA occlusion	3 (50.0%)	8 (53.3%)	0.9999
Partial MCA occlusion	0 (0.0%)	3 (30.0%)	0.5263
Complete MCA occlusion	6 (100.0%)	12 (80.0%)	0.5263
NIHSS score at baseline	15.3 ± 5.9	21.1 ± 3.7	0.0391
24 h after t-PA infusion	6.8 ± 7.7	19.3.3 ± 4.8	0.0391
7 days after t-PA infusion	3.0 ± 3.5	21.9 ± 9.5	0.0005
NIHSS score ≥20 at 7 days	0 (0.0%)	10 (66.7%)	0.0057
Systolic blood pressure (mmHg)	143.3 ± 11.3	164.3 ± 15.6	0.0081
Diastolic blood pressure (mmHg)	72.8 ± 9.3	94.3 ± 16.8	0.0045
Time from symptom onset to treatment, min	139.3 ± 26.3	149.0 ± 26.5	0.1328
Glucose (mg/dl)	131.2 ± 30.2	151.7 ± 22.1	0.0199