

Computed Tomography Perfusion Maps and Final Infarction with Hyper-acute Stroke Patients Who Achieved Catheter Thrombolysis Therapy

a report by
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The Cerebral Stroke Center at Wakakusa Daiichi Hospital in Japan used computed tomography perfusion (CTP) for selecting candidates for catheter thrombolysis therapy from June 2002 to June 2005, until the treatment guidelines, which were for thrombolysis therapy by intravenous administration of recombinant tissue-type plasminogen activator (alteplase) for hyper-acute cerebral stroke patients, were established by the Japan Stroke Society.^{1,2} No previous study in Japan had investigated the correlation between the pre-treatment CTP maps and the outcome after intra-arterial catheter thrombolysis therapy with hyper-acute stroke patients.

Lev et al. described a correlation between cerebral perfusion volume reduction area and a final infarction lesion after catheter thrombolysis therapy in a perfusion-weighted CT study of hyper-acute cerebral stroke cases.³ However, they did not include an investigation of mean transit time (MTT) in the study.

Eastwood et al. reported that prolonged MTT areas are larger than cerebral blood flow (CBF) and cerebral blood volume (CBV) reduction areas.^{4,5} The collateral vessels have been reported to influence MTT.⁴ Prolonged MTT areas with the box-modified transfer function (box-MTF) method (deconvolution analysis CTP software) are known to include a tracer delay developed to circulate a roundabout route of collateral vessels.^{6,7}

In the current study, relationships between the location and site of the prolonged MTT areas as pre-treatment states and final infarction areas after intra-arterial catheter thrombolysis therapy with hyper-acute stroke patients were investigated using box-MTF analysis software. We also included evaluations of CBF and CBV reduction areas, collateral vessel development based on findings of CT angiography (CTA), outcome of thrombolysis therapy, presence of hemorrhage as a complication after therapy, and patient outcome after catheter thrombolysis.

Materials and Methods

Plain CT, CTP, and CTA were performed on 22 hyper-acute stroke patients who were brought to the emergency room of Wakakusa Daiichi Hospital within six hours of onset. All 22 patients with ischemic lesions were treated immediately with catheter thrombolysis after the CTP study. The occlusion vessels and collateral vessels were confirmed by CTA. Each CTP and CTA condition is shown in *Table 1*. Follow-up CT was performed to examine the presence of the final infarction after thrombolysis (see *Figure 1*). Image acquisition was performed according to the methods and scanning technique described by Yukari et al.⁸

Table 1: Conditions of Computed Tomography Perfusion and Computed Tomography Angiography

| Scan Parameters | CTP | CTA |
|--------------------------|---------------|-----------------|
| Tube voltage (kVp) | 120 | 120 |
| Helical pitch (mA) | 70 | 200 |
| Slice thickness (mm) | 8mm x 4 | 1mm x 4 |
| Scan mode | Interval scan | Helical scan |
| Delay time (seconds) | 5 | Real prep or 25 |
| Scan range (mm) | 32 | 73.5 |
| Injection speed (ml/sec) | 4 | 3 |

Patients

As a result of severe motion artifact or defects of maps, seven cases were defaulted and 15 of the 22 patients were selected for inclusion in the study (see *Table 2*). There were 10 males and five females, with ages ranging from 38 to 82 years (average 63.5 years). There were two intracranial artery (ICA) occlusion cases, nine middle cerebral artery (MCA) occlusion site cases, and five basilar artery (BA) occlusion cases. Patients were investigated by CTP study over 35–320 minutes after stroke onset. We evaluated the patients' outcome regarding activities of daily living (ADL) and the modified Rankin scale (MRS) at the time of discharge from hospital after receiving intra-arterial catheter thrombolysis therapy (see *Table 3*).

Catheter Angiography and Thrombolysis

Post-treatment arteriographic images were retrospectively analyzed regarding the achievement rate of recanalization as follows: successful—occluded vessels were recanalized and the peripheral vessels were delineated as expected; partly successful—occluded vessels were recanalized but irregular thicknesses of vascular walls were shown and the peripheral vessels were less delineated than normal; and failed—recanalization was not achieved (see *Figure 2*).

Imaging Analysis

The location and approximate size of prolonged MTT, decreased CBF and CBV in CTP study, and the final infarction areas on CT study were investigated with cerebral arterial territory.



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Table 2: Fifteen Patients with Hyper-acute Cerebral Infarction

| Case | Age/Sex | CTP Time After Onset (min) | Occlusion of Artery | Decreased CBF Area | Prolonged MTT area | CBV Change | Catheter Thrombolysis | Final Infarction (territory) | Cerebral Hemorrhage | Outcome (mRS) | Collateral Supply |
|------|---------|----------------------------|---------------------|--|--|---|-----------------------|---|-------------------------------------|---------------|---------------------------|
| 1 | 71/M | 300 | Rt ICA | Rt basal ganglia and Rt MCA | Rt basal ganglia and Rt MCA | Decrease: anterior 1/3 of Rt MCA and Rt basal ganglia | Succeeded | Rt hemisphere hemorrhagic infarction | Rt cerebral hemorrhage ^a | V | Poor |
| 2 | 63/M | 50 | Rt ICA | Bil ACA and Rt basal and Rt MCA ganglia | Bil ACA and Rt basal ganglia and Rt MCA | Decrease: anterior 1/3 of Rt MCA and Rt basal ganglia | Failed | Anterior 1/3 of Rt MCA and Rt basal ganglia | — | IV | Poor |
| 3 | 65/M | 60 | Rt MCA: proximal M1 | Rt MCA | Rt MCA | Decrease: anterior 2/3 of Rt MCA | Partially succeeded | Anterior 2/3 of Rt MCA | — | I | Poor |
| 4 | 38/M | 60 | Lt MCA: proximal M1 | Lt basal ganglia and Lt MCA | Lt basal ganglia and Lt MCA | Decrease: anterior 1/3 of Lt MCA and Lt basal ganglia | Partially succeeded | Lt basal ganglia and 2/3 of Lt MCA | Lt basal ganglia | II | Poor |
| 5 | 71/M | 125 | Lt MCA: proximal M1 | Lt MCA | Lt MCA | No decreased area | Succeeded | Lt caudate nucleus head | — | 0 | Poor |
| 6 | 59/F | 55 | Lt MCA: proximal M1 | Lt basal ganglia and Lt MCA | Lt basal ganglia and Lt MCA | Decrease: middle 1/3 of Lt MCA and Lt basal ganglia | Succeeded | Middle 1/3 of Lt MCA and Lt basal ganglia | Lt basal ganglia | IV | Poor |
| 7 | 82/F | 320 | Lt MCA: distal M1 | Lt basal ganglia and Lt MCA | Lt basal ganglia and Lt MCA | No decreased area | Failed | Lt basal ganglia and Lt MCA | — | V | Intermediate |
| 8 | 73/F | 60 | Rt MCA: M2 | Rt MCA | Rt MCA | Decrease: anterior 2/3 of Rt MCA | Failed | Rt MCA | — | IV | Intermediate |
| 9 | 60/F | 35 | Lt MCA: M2 | Lt MCA | Lt MCA | Decrease: anterior 1/3 of Lt MCA and Lt insular subcortical | Succeeded | Anterior 1/3 of Lt MCA | Lt insular subcortical | I | Good |
| 10 | 67/M | 50 | Rt MCA: M2 | Rt MCA | Rt MCA | No decreased area | Partially succeeded | Posterior 1/3 of Rt MCA | — | I | Poor |
| 11 | 57/M | 60 | Lt MCA: M2 | Posterior 2/3 of Lt MCA | Posterior 2/3 of Lt MCA | Decrease: posterior 1/3 of Lt MCA | Partially succeeded | Posterior 1/3 of Lt MCA | Lt basal ganglia ^b | II | Poor |
| 12 | 43/F | 90 | BA | Bil PCA | Bil PCA | Increase: Rt PCA | Partially succeeded | Lt PCA, Lt SCA | — | II | Poor |
| 13 | 20/M | 90 | BA | Bil PCA | Bil PCA | No decreased area | Succeeded | Lt thalamus and Lt PCA | — | II | Good |
| 14 | 70/M | 150 | BA | Bil PCA, Bil cerebellar hemisphere, pons | Bil PCA, Bil cerebellar hemisphere, pons | Increase: Bil PCA and Bil cerebellar hemisphere | Succeeded | Small pontine infarction | — | II | Rt PCA: good; Lt PCA Poor |
| 15 | 67/M | 50 | BA | Bil PCA, Bil cerebellar hemisphere, pons | Bil PCA, Bil cerebellar hemisphere, pons | Decrease: Pons; increase: Bil cerebellar hemisphere | Succeeded | Lt cerebellar hemisphere infarction | — | IV | Poor |

CTP = computed tomographic perfusion; CTA = CT angiography; M = male; F = female; Rt = right; Lt = left; Bil = bilateral; ICA = internal carotid artery; MCA = middle cerebral artery (MCA branch was divided into three portions: proximal M1, distal M1, and M2); BA = basilar artery; ACA = anterior cerebral artery; PCA = posterior cerebral artery; SCA = superior cerebellar artery; CBV=cerebral blood volume; MTT= mean transit time.

Thrombolysis: Succeeded = distant artery appeared and achieved recanalization; Partially succeeded = distant artery was obscurely appeared; Failed = distant artery did not appear.

Outcome (modified Rankin Scale [mRS]): 0 = no symptoms at all; I = no significant disability despite symptoms; able to carry out all usual duties and activities; II = slight disability; unable to carry out all previous activities but able to look after own affairs without assistance; III = moderate disability requiring some help, but able to walk without assistance; IV = moderate severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance; V = severe disability; bedridden, incontinent, and requiring constant nursing care and attention, VI = death.

a. Hemorrhage at putamen, anterior peduncle of the internal capsule and external capsule.

b. Hemorrhage due to interventional radiological technique (IVR).

Table 3: Evaluation for Activities of Daily Living

| | |
|-----|---|
| 0 | No symptoms at all |
| I | No significant disability despite symptoms: able to carry out all usual duties and activities |
| II | Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance |
| III | Moderate disability requiring some help, but able to walk without assistance |
| IV | Moderate severe disability: unable to walk without assistance and unable to attend to own bodily needs without assistance |
| V | Severe disability: bedridden, incontinent, and requiring constant nursing care and attention |
| VI | Death |

Results

Abnormal perfusion areas detected by the box-MTF study were shown with CTP maps of CBF, CBV, and MTT in all of the 15 hyper-acute stroke patients (see *Table 2*).

Catheter thrombolysis therapy was successful in 12 of 15 patients. However, hemorrhage occurred in six of the 12 patients after thrombolysis. Excluding one case, hemorrhage occurred in the CBV reduction areas. Only in 11 cases did hemorrhage occur by the interventional technique. Final infarction was seen in all of the 15 patients. The decreased CBF areas showed nearly equal sites to the prolonged MTT areas in 15 patients. In all of the 15 patients the decreased CBV areas were identified in the prolonged MTT area and were smaller than the final infarct areas, although all of them resulted in either infarct or hemorrhage. The increased CBV areas were found in prolonged MTT areas only with BA-occluded hyper-acute stroke patients.

Among 12 patients with successful catheter thrombolysis, the final infarction areas were smaller than the prolonged MTT areas with two patients, including ICA occlusion (case one) and MCA occlusion (case four).

The final infarction area in case four with partial recanalization during the catheter thrombolysis therapy was almost equal to the prolonged MTT area. Another ICA occlusion patient had broad hemorrhage after recanalization. The remaining three patients of 15 could not obtain recanalization. The infarct was found in the corresponding site of prolonged MTT areas with MCA occlusion patients. However, in ICA occlusion patients without recanalization, the final infarction area was identified at the decreased CBV area, which was smaller than the prolonged MTT area. Regarding the comprehensive outcome of patients with recanalization of MCA and BA occlusion, ADL at the time of discharge from hospital was favorable, showing MRS of 0 to II, except for two patients (case six and case 15), who had hemorrhage at the basal ganglia or pons. Patients without recanalization of MCA occlusion, and ICA occlusion patients, had a poor outcome, showing MRS of IV or V.

Discussion

CTP can be performed soon after plain CT for emergent cases, which can show abnormal perfusion sites in a short time.^{4,7,9-13} In our investigation with the box-MTF method, we found that the locations and areas of CBF reduction sites were nearly identical to the prolonged MTT areas (see *Table 2*).

Although magnetic resonance perfusion and CTP studies do not have the same results with hyper-acute stroke patients, several papers have reported that prolonged MTT areas in perfusion studies were larger in size

Figure 1: Chart Flow of the Study for Hyper-acute Stroke Patients Pre-treatment Study

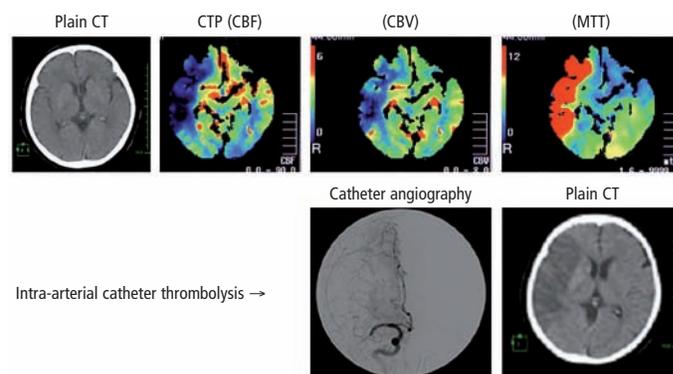
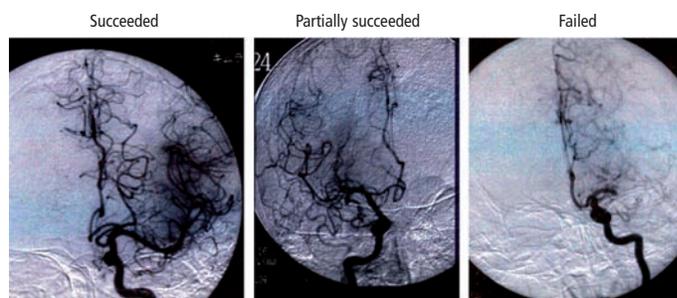


Figure 2: Estimation of the Intra-arterial Catheter Thrombolysis



than the final infarct areas, and sometimes than CBF reduction areas, with or without thrombolysis therapy.¹⁴⁻²¹ In addition, in some reports, MTT indicated by the box-MTF method included tracer delay and overestimated true prolonged MTT areas, and thus CBF was underestimated.^{4-7,11,22-24} However, as was reported in a previous article,⁸ in cases with MCA occlusion without recanalization by catheter thrombolysis, the prolonged MTT areas were almost equal to the final infarction sites.

CTA examination of the patients with failure of MCA recanalization showed the infusion of contrast media from the posterior cerebral artery to the MCA occlusion area by way of collateral vessels. The box-MTF method applied in the study has shown no differentiation between the tracer delay areas and true prolonged MTT areas. We consider that if recanalization with MCA occlusion is not achieved in the prolonged MTT areas of the box-MTF method, vascular flow through collateral vessels may be disturbed in the timecourse, leading to the mechanism of CBV reduction beyond the compensatory range that Powers et al. and others stated, and resulting in final infarction.²⁵⁻²⁷

Almost the same mechanism and collateral vessel development might be suggested in BA or ICA occlusion cases but with different circulation factors.

The patients who had CBV reduction areas in the prolonged MTT areas had either hemorrhage or infarct, irrespective of recanalization after thrombolysis therapy. This agreed with the published papers. However, it was difficult to estimate whether CBV reduction areas of the prolonged MTT areas led to hemorrhage or infarct after thrombolysis therapy.

In case four, for whom catheter thrombolysis therapy partly succeeded, the prolonged MTT area and final infarction area coincided. Case four had no complications of cardiac disease and received traumatic dissection of the CA at the time of catheter thrombolysis therapy. A possibility of a creeping thrombus into the partly recanalized MCA or the formation of embolus was considered in this case.

In some cases of BA occlusion, increased CBV areas were identified in prolonged MTT areas. Final infarction areas were found only in the decreased CBV areas in the prolonged MTT sites. Although there was no report about CBV change in the prolonged MTT areas with BA-occluded hyper-acute stroke patients, these facts might correlate with the positive prognosis of BA-occluded patients. However, in case 15, who achieved recanalization by the catheter thrombolysis, pontine hemorrhage occurred and the patient died.

When a decreased CBV area in the prolonged MTT areas is noticed before thrombolysis, mortal pontine hemorrhage after recanalization should be considered carefully. In the patients, the outcome of MCA occlusion and BA occlusion, both in ADL and MRS at the time of discharge from hospital, was relatively favorable in cases of successful thrombolysis except for two cases, even though partial hemorrhage occurred, as the sites of hemorrhage and final infarct were small.

As reported by Ueda et al.,²⁸ ICA occlusion cases had poor prognosis even with recanalization. However, in cases of MCA or BA occlusion,

when prolonged MTT areas are large in size on CTP study, and with small decreased CBV area and sometimes with large increased CBV area, regarding collateral vessel development on CTA study, although careful consideration is necessary, catheter thrombolysis therapy is recommended.^{29–33}

In summary, the current CTP study with the box-MTF method for hyper-acute stroke patients suggests that when recanalization of CBV reduction areas in the prolonged MTT areas is achieved by catheter thrombolysis therapy, hemorrhage or infarct can occur, although limited to a localized CBV reduction area in size.

Therefore, if the site of the decreased CBV area is in the prolonged MTT area with BA occlusion on the brainstem, pontine hemorrhage after thrombolysis should be considered carefully. However, the outcome after catheter thrombolysis with full or partial recanalization with BA occlusion seems to end in a relatively positive outcome, with MRS from 0 to II after catheter thrombolysis.

In this study, in the case of unsuccessful thrombolysis therapy with MCA occlusion, final infarctions were identical to the prolonged MTT area. With the box-MTF method, the prolonged MTT areas included tracer delay and the true prolonged MTT areas, which could not be differentiated. It is considered necessary to investigate the possibility that an entire tracer delay area of MTT with MCA occlusion may result in final infarction when recanalization is not achieved. ■

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