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 Centre at Wakakusa Daiichi Hospital in Japan used computed tomography perfusion (CTP) to select 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 haemorrhage 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 ischaemic lesions were treated immediately with catheter thrombolysis after the CTP study. The occlusion vessels and collateral vessels were confirmed by CTA. 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]

Patients

As a result of severe motion artefact or defects of maps, seven cases were defaulted and 15 of the 22 patients were selected for inclusion in the study (see *Table 1*). 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.

Catheter Angiography and Thrombolysis

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

Imaging Analysis

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

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 1*). Catheter thrombolysis therapy was successful in 12 of 15 patients. However, haemorrhage occurred in six of the 12 patients after thrombolysis. Excluding one case, haemorrhage occurred in the CBV reduction areas. Only in 11 cases did haemorrhage 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 haemorrhage. 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 recanalisation during the catheter thrombolysis therapy was almost equal to the prolonged MTT area. Another ICA occlusion patient had broad haemorrhage after recanalisation. The remaining three patients of 15 could not obtain recanalisation. The infarct was found in the corresponding site of prolonged MTT areas with MCA occlusion patients. However, in ICA occlusion patients without recanalisation 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 recanalisation of MCA and BA occlusion, ADL at the time of discharge from hospital was favourable, showing MRS of 0 to II, except for two patients (case six and case 15) who had haemorrhage at the basal ganglia or pons. Patients without recanalisation of MCA occlusion and ICA occlusion patients had a poor outcome, showing MRS of IV or V.

Table 1: 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 Haemorrhage	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 infarction	– hemisphere	IV	Poor

CTP = computed tompgraphic 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 recanalisation; 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. Haemorrhage at putamen, anterior peduncle of the internal capsle and external capsle.
b. Hemorrhage due to interventional radiological technique (IVR).

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 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 recanalisation by catheter thrombolysis, the prolonged MTT areas were almost equal to the final infarction sites. CTA examination of the patients with failure of MCA recanalisation 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 recanalisation 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 haemorrhage or infarct, irrespective of recanalisation 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 haemorrhage 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 recanalised 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 recanalisation by the catheter thrombolysis, pontine haemorrhage occurred and the patient died.

When a decreased CBV area in the prolonged MTT areas is noticed before thrombolysis, mortal pontine haemorrhage after recanalisation 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 favourable in cases of successful thrombolysis except for two cases, even though partial haemorrhage occurred, as the sites of haemorrhage and final infarct were small.

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

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

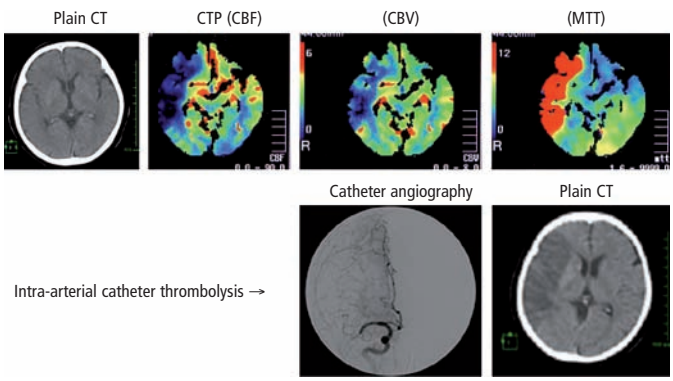
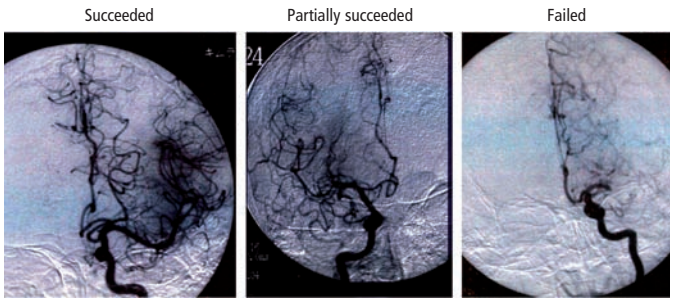


Figure 2: Estimation of the Intra-arterial Catheter Thrombolysis



prolonged MTT areas are large in size on CTP study, 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.[29–34] In summary, the current CTP study with the box-MTF method for hyper-acute stroke patients suggests that when recanalisation of CBV reduction areas in the prolonged MTT areas is achieved by catheter thrombolysis therapy, haemorrhage or infarct can occur, although it is limited to a localised 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 haemorrhage after thrombolysis should be considered carefully. However, the outcome after catheter thrombolysis with full or partial recanalisation 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 recanalisation is not achieved. ■

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