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Cerebral Blood Flow Study by Xenon-Enhanced Computed Tomography in Acute Cerebral Artery Occlusion

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Abstract The hemispheric cerebral blood flow (CBF) in 32 patients with acute cerebral artery occlusion was measured by means of xenon-enhanced computed tomography. Eighteen patients were treated with endovascular thrombolysis by intra-arterial administration of thrombolytic agents and occluded arteries were recanalized, while 14 patients were treated conservatively. The CBF and cerebrovascular reserve capacity in the well recovered or moderately disabled patients were higher than those in patients of vegetative state or death. The mean CBF in the patients with both internal carotid artery and middle cerebral artery occlusion was significantly lower than that in the patients with middle cerebral artery occlusion only. CBF study by means of xenon-enhanced computed tomography will be useful to determine candidates for local thrombolysis and to guess the prognoses of patients.

Key words : Xenon-enhanced computed tomography (Xe-CT), cerebral blood flow (CBF), acute cerebral artery occlusion

Introduction

Cerebral blood flow (CBF) and/or brain metabolism has been measured by means of single photon emission computed tomography (SPECT), xenon-enhanced computed tomography (Xe-CT) or positron emission tomography (PET)[1)2)]. Xe-CT CBF study is the simple quantitative study with high degree of spatial resolution and anatomical correlation[3)4)5)].

In patients with acute ischemic stroke, early treatment with thrombolytic agents would permit reperfusion of ischemic neurons and promote recovery of normal functions[3)]. Recently local thrombolysis with urokinase, streptokinase or tissue-type plasminogen activator (t-PA) was performed in the acute stage of ischemic stroke[6)7)8)]. In spite of successful thrombolysis, a few patients became severe or fatal. Endovascular thrombolysis was not always safe, because hemorrhagic infarction sometimes occurred after administration of thrombolytic agents. Therefore, indication of endovascular thrombolysis is still now obscure[9)], so that simple and reliable parameter will be expected for making decision of therapeutical strategy.

In this study the author measured CBF and cerebrovascular reserve capacity (CRC) by means of Xe-CT in acute stage of cerebral artery occlusion and evaluated correlation between the CBF and both the prognoses of patients and angiographical findings. The utility of Xe-CT in decision of the candidates for local thrombolysis was discussed.

Patients and Methods

Xe-CT CBF studies were done in 32 patients (25 men and 7 women) with acute neurological deficits caused by angiographically-proven occlusion of the main cerebral artery. The age of patients varied from 43 to 83 years (mean 68 years). Occluded arteries were middle cerebral artery (MCA) in 20 patients, internal carotid artery (ICA) in 7 patients, anterior cerebral artery in one patient and both ICA and MCA in 4 patients. Mean age of their groups were 69.8, 67.3, 57 and 64.5 years old, respectively. The CBF value by means of Xe-CT was measured within 6 hours after the onset of ischemic stroke.

While patients inhaled a 30% xenon/50% oxygen/50% oxygen/20% nitrogen gas mixture through face mask, using a 3-min wash-in/3-min wash-out inhalation protocol method[10], CT images were obtained every minute for 6 min. After measuring resting CBF, patients were received intravenous administration of 1,000 mg acetazolamide. CBF value was obtained again 15 min after administration of acetazolamide. The total time for CBF study was approximately 30 minutes.

The cerebrovascular reserve capacity (CRC) was defined as the difference between the acetazolamide-induced CBF and resting CBF. As the regions of interest (ROIs), affected hemisphere except ventricular system was selected at the level through bilateral basal ganglia. Eighteen patients were treated with local thrombolysis by means of endovascular surgery and 14 patients treated conservatively without it. The dose of urokinase for intra-arterial thrombolysis varied from 720,000 to 1,640,000 unit (mean 943,000 unit).

The prognoses of patients were classified into 5 groups according to Glasgow outcome scale (GOS), as good recovery, moderate disability, severe disability, persistent vegetative state and death. The relationship

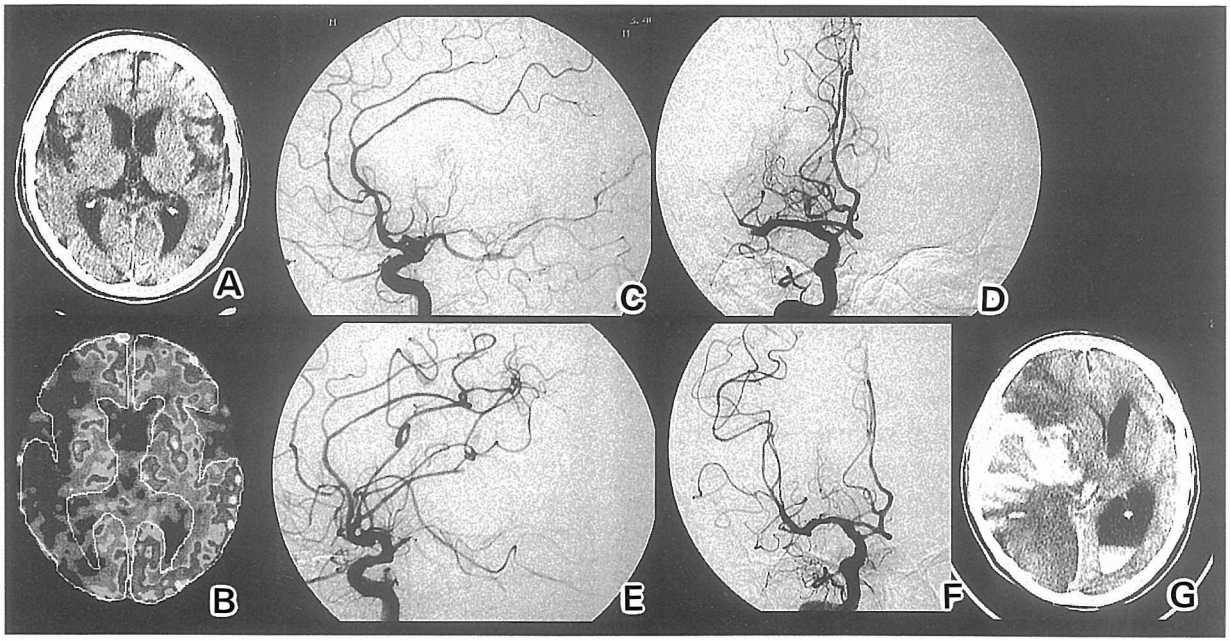

Fig 1. CT image, Xe-CT and angiograms of 74-year-old man with occluded right middle cerebral artery. A : CT image on admission showing no abnormal findings. B : Xe-CT. The white areas indicate high CBFs, and the dark ones low CBFs. The CBF is reduced in right MCA territory. C-D : The right carotid angiography on pre-thrombolysis showing right middle cerebral artery occlusion. C : lateral view, D : antero-posterior view. E-F : The right carotid angiography on post-thrombolysis showing recanalization of occluded middle cerebral artery. E : lateral view, F : antero-posterior view. G : CT image at 22 hours after recanalization showing large hemorrhagic infarction in right hemisphere with midline shift.

between the CBF, CRC and GOS was evaluated. Two patients with occlusion of the middle cerebral artery were demonstrated briefly as representative cases.

An unpaired t-test was used for comparison of the hemispheric CBF value of patients of different occlusive site. Difference at $p<0.05$ was considered significant.

Results

Angiographical recanalization by endovascular thrombolysis

A 74-year-old man had sudden onset of left hemiparesis and drowsiness and was then brought to the emergency room. Plain CT images demonstrated no abnormal findings. Xe-CT CBF study was immediately performed. Resting CBF and CRC in the affected right hemisphere were 8.3 ml/100 g/min and 3.8 ml/100 g/min, respectively. Angiograms demonstrated the right middle cerebral artery occlusion and poor collateral circulation through leptomeningeal anastomosis (Fig. 1). Endovascular thrombolysis using 720,000 unit urokinase was performed and was followed by subsequent large hemorrhagic infarction after recanalization. He was dead 3 days after the onset.

A 71-year-old man had sudden onset of left hemiparesis and drowsiness. His CBF and CRC were 13.0 and 10.8 ml/100 g/min, respectively. He was treated with local thrombolysis using 960,000 unit urokinase. As the occluded MCA was successfully recanalized without hemorrhagic infarction (Fig.2), motor paresis was resolved in a few days and he had no neurological deficits one month later.

Hemispheric CBF, CRC and Glasgow outcome scale

Four of five patients of good recovery (80%) had more than 20 ml/100 g/min in

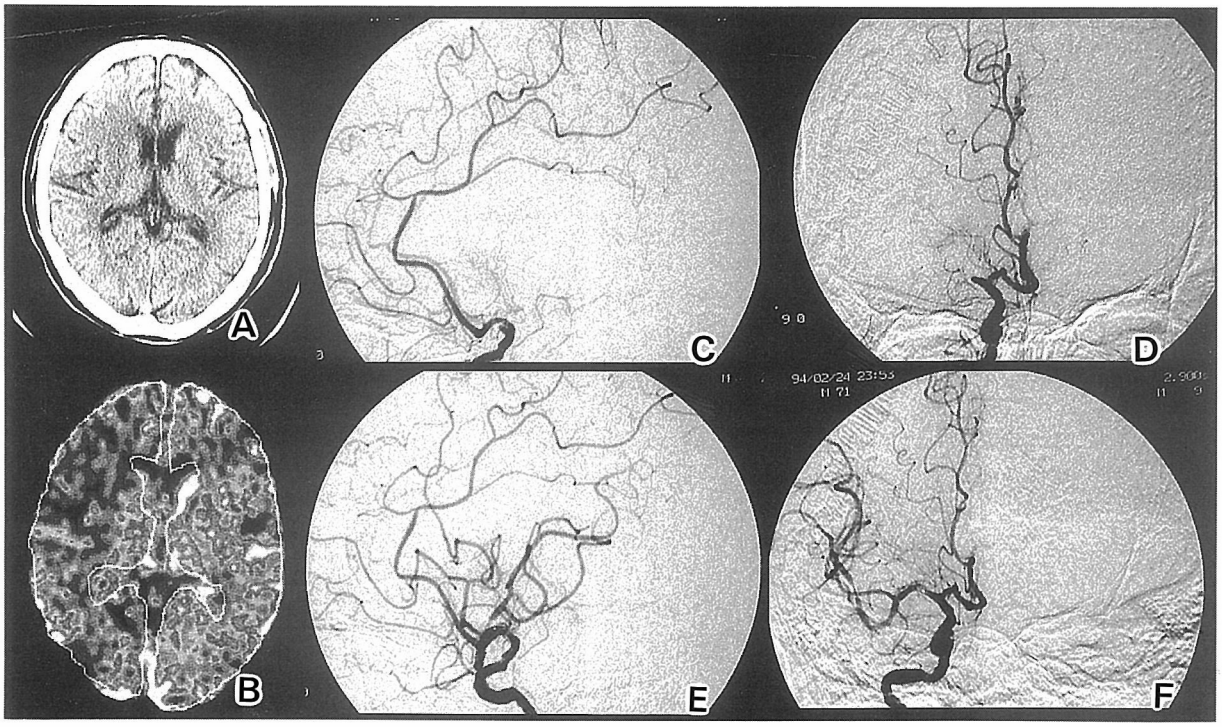

Fig 2. CT image, Xe-CT and angiograms of 71-year-old man with occluded right middle cerebral artery. A: CT image on admission showing no abnormal findings. B: Xe-CT. The CBF is reduced in right MCA territory. C-D: The right carotid angiography on pre-thrombolysis showing right middle cerebral artery occlusion. C: lateral view, D: antero-posterior view. E-F: The right carotid angiography on post-thrombolysis showing recanalization of occluded middle cerebral artery. E: lateral view, F: antero-posterior view.

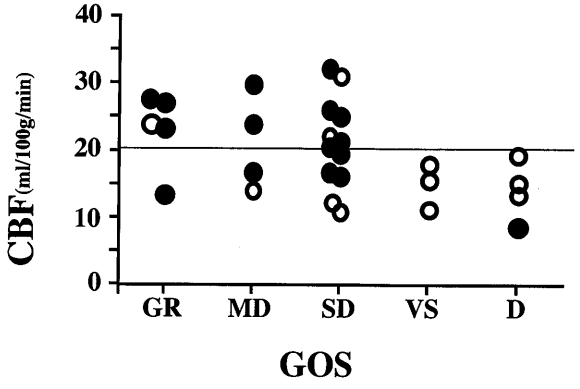

Fig 3. Relationship between resting CBF or CRC and Glasgow outcome scale. A; Between CBF and GOS. B; Between CRC and GOS.
Abbreviations: GR, good recovery; MD, moderate disability; SD, severe disability; VS, persistent vegetative state; D, death; Closed circle: patients who were treated with thrombolysis; Open circle: patients who were treated conservatively.

Fig 3 A: The border line is 20 ml/100 g/min CBF. All cases of VS and D had hemispheric CBF below 20 ml/100 g/min.

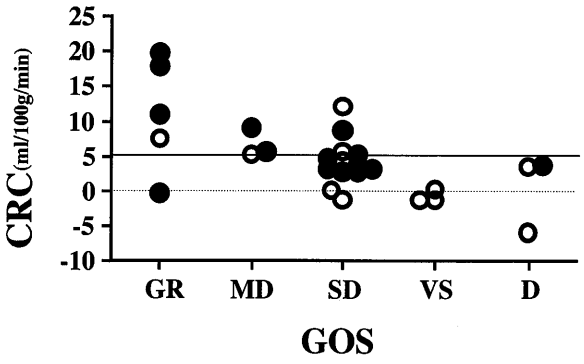

Fig 3 B: The border line is +5 ml/100 g/min CRC. All cases but one of GR and MD had CRC over +5 ml/100 g/min. All cases of VS and D had hemispheric CRC below +5 ml/100 g/min.

resting CBF (Fig.3 A) and more than 5 ml/100 g/min in CRC (Fig.3 B). All patients of vegetative state or death had less than 20 ml/100 g/min in resting CBF and less than 5 ml/100 g/min in CRC. All patients but one of

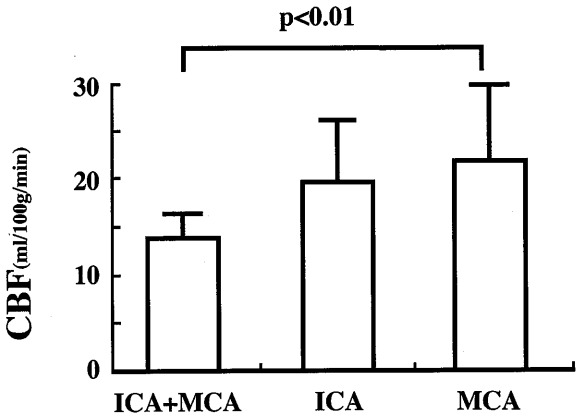

Fig 4. Relationship between occlusive site and resting CBF.
Abbreviations: ICA+MCA, both ICA and MCA; ICA, internal carotid artery; MCA, middle cerebral artery.
Mean CBF of patients with both ICA and MCA occlusions was significantly lower than that of patients with MCA occlusion. ($p<0.01$)

good recovery or moderate disability had CRC more than 5 ml/100 g/min (Fig.3 A, B). All patients who were treated with endovascular thrombolysis were in good recovery, moderate disability or severe disability of GOS, and only one resulted in death caused by hemorrhagic infarction after recanalization.

Hemispheric CBF among the different occluded artery

Mean resting CBF in patients with both ICA and MCA occlusions (13.8 ml/100 g/min) was the lowest (Fig.4). CBF in patients with MCA occlusion (21.8 ml/100 g/min) was lower than normal value of CBF.

Occluded artery and Glasgow outcome scale

Four patients with both ICA and MCA occlusions resulted in severe disability in 75% and vegetative state in 25%. No patients of this group had good recovery or moderately disabled state. Forty percent of patients with MCA occlusion were well recovered or moderately disabled (Fig.5).

Laterality of the occlusion and Glasgow outcome scale

The affected hemispheres were left in 12 patients and right in 20 patients. Mean CBF

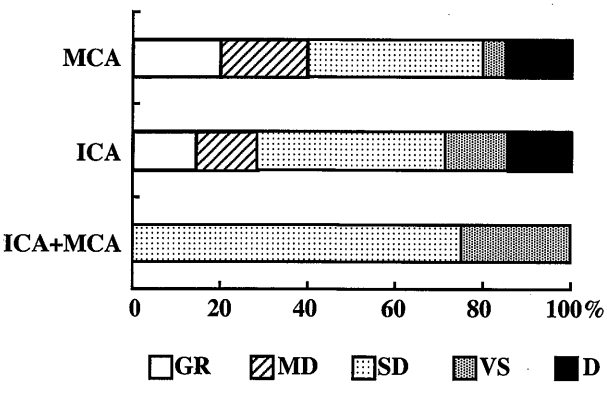

Fig 5. Relationship between occlusive site and Glasgow outcome scale. Forty percent of patients with MCA occlusion were GR and MD. None of patients with both ICA and MCA occlusions were GR and MD.

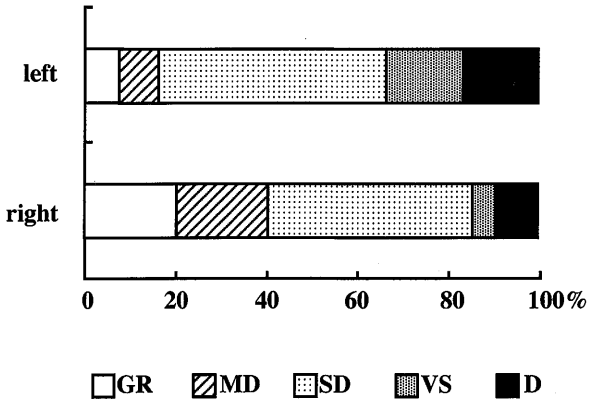

Fig 6. Affected side and Glasgow outcome scale. Patients with left affected brain tend to have worse GOS than patients with right affected brain.

were 19.4 and 20.9 ml/100 g/min, respectively. There was no significant difference. The good prognostic patients were 17 % in left affected case, while the ones were 40% in right (Fig.6).

Discussion

The endovascular thrombolysis by administration of urokinase, streptokinase or tissue-type plasminogen activator (t-PA) is recently done in acute stage of ischemic stroke. Hemorrhagic infarction may occur after thrombolysis and the patient may be severe or fatal. Even if the thrombolytic agents were given within 3 hours, the incidence of hemorrhagic infarction was higher in the administration of streptokinase or t-PA than that in the placebo group. However, cerebral blood flow was not studied in the previous reports[6)7)8)].

CBF was decreased not only in the infarcted area but also in the wide affected hemisphere as well as in the non-affected hemisphere[11)]. Therefore qualitative CBF study, e.g., single photon emission computed tomography (SPECT) does not provide enough information to evaluate truly the decreased CBF. Although two patients, presented in this paper, showed the same angiographical and neurological findings, their cerebral hemodynamics were different. Therefore it is greatly important to measure absolute value of hemispheric CBF in acute stroke in order to determine the therapeutical strategies as soon as possible.

Although PET has the very important ability of defining local metabolism, it is still currently limited to a few centers. Xe-CT CBF study is more readily available and more economical than other studies, e.g.,PET, because no equipment except Xe gas inhalator is required. Endovascular thrombolysis should be done as soon as possible from the onset in order to avoid hemorrhagic infarction. Xe-CT is the most available method, because it can be done immediately after first plain CT scan. The most valuable contribution of Xe-CT examination is ability to correlate local CBF directly with the anatomic locus. Although SPECT is the qualitative study, it does not provide absolute value of regional CBF. The degree of spatial resolution of SPECT is not higher than that of Xe-CT.

Mean CBF of the affected hemisphere in patients with occlusion of both ICA and MCA (ICA & MCA group) was significantly lower than that in patients with MCA occlusion. It would be caused by the poorest collateral circulation through the Willis circle. All patients of ICA & MCA group were severely disabled and vegetative. ICA & MCA group may be contra-indication for endovascular thrombolysis, if the CBF and CRC of affected hemisphere is less than 20 ml/100 g/min and 5 ml/100 g/min, respectively.

If the affected side would be left and domi-

nant, GOS may be worse. Because most Japanese patients are right handed, the affected left hemisphere results in right motor paresis as well as speech disturbance.

Since patients with severe disability had various CBF, it may be the most important problems how patients in this group should be treated.

Xe-CT CBF studies would provide many useful information about clinical decision -making process for management the patients with acute cerebral artery occlusion. The methods can not be replaced by SPECT and angiography in evaluation of CBF of the patients.

Patients are often drowsy or restless in acute stage of ischemic stroke. Xe-CT CBF study may be not suitable for measurement of CBF in restless patients, because the minimal head motion during the examination makes CBF data unreliable. However, the examination can be done safely with fixation of the head on the headrest. Moreover, sedative agents, e.g., diazepam, should not be administrated to restless patients in order to avoid minimal cerebral hemodynamic change. This is one of the disadvantage of Xe -CT CBF study for the patients in the acute stage of stroke.

In conclusion, endovascular thrombolysis in acute stage of cerebral artery occlusion may be indicated to the patients with resting CBF above 20 ml/100 g brain/min and/or CRC above 5 ml/100 g brain/min in affected hemisphere. The resting Xe-CT CBF and CRC will be useful in the identification of a high risk group of patients for acute endovascular thrombolysis.

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