Triphasic Perfusion Computed Tomography in Acute Middle Cerebral Artery Stroke

A Correlation With Angiographic Findings

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Objective: To evaluate the usefulness of triphasic perfusion computed tomography (TPCT) in diagnosing middle cerebral artery (MCA) occlusion and in assessing the perfusion deficit and collateral circulation in patients with acute ischemic stroke.

Background: Conventional angiography is the criterion standard for the diagnosis of MCA occlusion and for the assessment of perfusion deficit and collateral blood supply. The risk of hemorrhagic transformation after revascularization of occluded arteries by thrombolytic therapy is considered high when pretherapeutic residual flow is markedly reduced.

Patients and Methods: In 8 patients within 3 hours of onset of acute MCA stroke, precontrast computed tomographic scans were taken, and then TPCT was performed after power-injector controlled intravenous administration of contrast media. Sequential images of early, middle, and late phases were obtained. The whole procedure took 5 minutes. Perfusion deficit on TPCT was graded as "severe" or "moderate," depending on the state of collateral flow. Digital subtraction angiography (DSA) was performed in all patients within 6 hours of acute stroke. Direct intra-arterial urokinase infusion was begun immediately after the angiographic superselection of the MCA occlusion site in 6 of the 8 patients within 7 hours of onset (range, 4.3-6.2 hours).

Results: The DSA findings showed occlusion of the MCA stem (n=1) and at the bifurcation (n=4). The sites of proximal MCA occlusion could be identified on the early and middle images of TPCT in all 5 patients. On DSA findings, all 8 patients had a zone of perfusion deficit with markedly slow leptomeningeal collaterals and a zone of perfusion deficit with no collaterals. The zone of severe perfusion deficit on TPCT corresponded to the zone of perfusion deficit with no or few collaterals on angiography, and the zone of moderate perfusion deficit on TPCT corresponded to that of perfusion deficit with markedly slow leptomeningeal collaterals. Early parenchymal hypodensity on precontrast computed tomography was confined to the zone of severe perfusion deficit on TPCT. The initial National Institutes of Health Stroke Scale score correlated better with the total extent of severe perfusion deficit and moderate perfusion deficit on TPCT than that of severe perfusion deficit alone. After direct intra-arterial thrombolysis within 7 hours of onset, symptomatic hemorrhagic transformation did not develop in 4 patients with small severe perfusion deficit (33% or less of the presumed MCA territory). However, the remaining 2 patients with large severe perfusion deficit (more than 50% of the presumed MCA territory) deteriorated to death with hemorrhagic transformation.

Conclusions: Triphasic perfusion computed tomography is useful for diagnosing proximal MCA occlusion and assessing perfusion deficit and collateral circulation as reliably as DSA. The zone of severe perfusion deficit on TPCT may be presumed to be the ischemic core, and that of moderate perfusion deficit, the penumbra zone. Triphasic perfusion computed tomography may be used as a rapid and noninvasive tool to make thrombolysis safer.

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Conventional angiography is the criterion standard for diagnosing MCA occlusion, and also for assessing perfusion deficit and collateral blood supply. Mag-
SUBJECTS AND METHODS

PATIENT PROTOCOL

The 8 patients with acute MCA territory stroke were prospectively recruited for this study from April 1996 to August 1997. Our hospital ethics committee approved this study. Precontrast CT and TPCT were done within 3 hours after the onset of stroke in all patients. Digital subtraction angiography (DSA) was started in all patients within 6 hours of onset. Before TPCT and DSA, we confirmed that the serum creatinine level was 124 µmol/L or lower (≤1.4 mg/dL) in all patients. The criteria for intra-arterial thrombolytic therapy were (1) informed consent given by the patient or his/her relatives, (2) clinical diagnosis of acute MCA territory stroke, (3) absence of hematological disease, (4) absence of hemorrhage as documented by precontrast CT findings, and (5) angiographic demonstration of the appropriate MCA stem, bifurcation, division, and branch occlusion consistent with the patient’s clinical presentation. Patients with acute ischemic stroke with signs of early ischemia such as subtle parenchymal low density, loss of gray-white matter distinction, or sulcal effacement on precontrast CT findings were also included in this study. The urokinase infusion was begun immediately after the angiographic superselection of arterial occlusion in 6 patients within 7 hours of onset (range, 4.3-6.2 hours). Twenty-four hours later, we anticoagulated the blood of these 6 patients with heparin, and subsequently with coumadin. In the remaining 2 patients, the catheter could not be introduced not just in front of the embolus but to the proximal portion from the occluded MCA. Superselective intra-arterial thrombolysis was not performed in these patients. We anticoagulated both patients immediately after angiography. For measuring clinical outcome, we evaluated the patients with the National Institutes of Health Stroke Scale (NIHSS) score before performing TPCT, after thrombolysis, on the first, third, and seventh day after the onset of stroke, and with the modified Rankin scale at 3 months after the onset.

IMAGING TECHNIQUE

A TPCT protocol using a helical CT scanner (High-Speed Advantage; GE Medical Systems, Milwaukee, Wis) was developed by one of us (D.G.N.), which is described in detail elsewhere.21 After precontrast CT imaging of the whole brain, contrast-enhanced TPCT was performed in all patients. Ninety milliliters of 68% nonionic contrast material (Optiray 320; Mallinckrodt Medical, Quebec, Canada) was administered by a power injector into an antecubital vein (18-gauge intravenous cannula) at a rate of 3 mL/s. Early, middle, and late phase images were then obtained with scan delays of 18, 30, and 80 seconds, respectively. Scanning began from the level of 1 cm below the caudal proximal MCA identified on precontrast CT and continued toward the vertex. Six slices of images were obtained at the early phase and 10 slices of images were obtained at the middle and late phases. All images of unenhanced and enhanced CT scans were obtained with 10-mm collimation and at a 10-mm/s table speed; the images were reconstructed at 3-mm intervals. The total scanning time for completion of 3 acquisitions was 90 seconds; the total time for scanning (1 second per slice) and reconstruction of images (3 or 4 seconds per image) was less than 3 minutes.

IMAGE INTERPRETATION

Initially, each precontrast CT and TPCT image was interpreted by 2 neuroradiologists who were blind to the results of the DSA. However, the 2 observers were notified that TPCT was performed in patients with acute ischemic stroke. The 2 interpreters determined the presence of early signs of ischemia on precontrast CT, such as hyperdense MCA sign, suble parenchymal hypodensity, loss of gray-white matter distinction, and sulcal effacement. The interpreters determined the presence of proximal MCA (stem or bifurcation) occlusion with hyperdense MCA sign on precontrast CT and the presence of nonenhancing arterial segment on the early and middle phase images of TPCT. The interpreters also observed the presence of zone of perfusion deficit on TPCT (decreased arterial enhancement on the early phase images; poor perfusion on the middle phase images; and poor perfusion and delayed, asymmetric arterial enhancement on the late phase images). After completion of the analysis of occlusion signs on the initial TPCT, 2 observers independently assessed the perfusion and collateral circulation on TPCT, and then reviewed the findings of DSA and the follow-up CT or magnetic resonance imaging (MRI).

The extent of perfusion deficit and collateral blood supply was assessed semiquantitatively from DSA findings after the symptomatic carotid arteries had been visualized and graded as 0 (no collaterals), 1 (only collaterals with markedly slow blood flow), or 2 (many relatively fast leptomingeal collaterals).11 The arterial enhancement of the collateral vessels of the MCA branches distal to the occlusion site was assessed on the 3-phase images. The assessment of collateral vessels on TPCT was compared with the findings of DSA in all patients. The perfusion deficit was graded as either “severe” or “moderate.” Severe perfusion deficit meant that the ischemic zone of the affected MCA territory had decreased attenuation relative to contralateral normal parenchyma with no or few collaterals visible on the early, middle, and late phase images of TPCT scan. Moderate perfusion deficit meant that the ischemic zone of the affected MCA territory had either (1) decreased attenuation on the early phase images of TPCT and normal attenuation with only markedly slow collaterals on the middle and late phase images or (2) decreased attenuation on the early and middle phase images of TPCT and normal attenuation with only markedly slow collaterals on the late phase images. The extent of the severe perfusion deficit and moderate perfusion deficit was estimated as a percentage of the presumed MCA territory by using 3 categories: “33% or less (small),” “more than 33% but no more than 50% (medium),” and “more than 50% (large).”
Intravenous thrombolysis with recombinant tissue plasminogen activator is recommended for patients with acute ischemic stroke within 3 hours of onset.9

Perfusion deficit and collateral blood flow are important factors associated with the safety and efficacy of thrombolytic therapy for acute MCA stroke.10,11 Hemorrhagic transformation of cerebral infarct is a major concern in thrombolytic therapy. The risk of hemorrhagic transformation after recanalization by thrombolytic therapy is high when pretherapeutic residual cerebral blood flow is markedly reduced.12,13 The use of thrombolytic agents increases the risk of intracerebral hemorrhage that can be severe and fatal in patients with acute MCA stroke with poor leptomeningeal collaterals.10,13,15 Effective collateral blood flow and reperfusion seem to be important factors associated with a small infarct volume and good clinical outcome in thrombolytic therapy.10,11

However, precontrast CT and conventional contrast–enhanced CT cannot provide enough information on perfusion deficit and collateral circulation, which is crucial for early, safe, and effective thrombolytic therapy for acute MCA stroke. The recent introduction of helical CT increased the utility of CT as an imaging method for acute ischemic stroke and increased the potential of helical CT for functional assessment of cerebral blood flow.16-20 We posit that triphasic perfusion CT (TPCT) with bolus injection of contrast material can demonstrate sequential enhancing features of intracranial arteries and the ischemic areas, depending on the degree of perfusion deficit and collateral circulation, by comparing with contralateral normal parenchyma.21 This TPCT provides the potential for detecting arterial occlusion and assessing perfusion deficit and collateral blood flow in the ischemic areas.

The European Cooperative Acute Stroke Study (ECASS) investigators14,15,22 recently reported that intravenous recombinant tissue plasminogen activator increased the chance of good outcome in patients with a small hypoattenuating area (33% or less of the presumed MCA territory) on precontrast CT who received treatment within 6 hours of onset of acute ischemic stroke. In contrast, intravenous recombinant tissue plasminogen activator had no beneficial effect but increased risk for fatal brain hemorrhage in patients with a large hypoattenuating area (more than 33% of the presumed MCA territory). Moreover, hypodensity covering more than 50% of the MCA territory had an 85% positive predictive value for fatal clinical outcome after thrombolysis within 6 hours.2

In the review of ECASS I, patients with normal CT findings outnumbered those with findings of small and large areas of hypoattenuation.14,22 Even if precontrast CT findings are normal in the hyperacute phase of stroke, however, TPCT may disclose the variable perfusion deficit and collateral blood flow in the ischemic areas before appearance of parenchymal hypodensity on precontrast CT. Subsequent treatment strategies may be individualized according to the perfusion deficit and collateral circulation based on TPCT. The aim of our study was to evaluate the usefulness of TPCT in diagnosing MCA occlusion and also in assessing perfusion deficit and collateral blood flow with a correlation between TPCT and angiographic findings in patients with acute MCA stroke.

Findings of DSA showed occlusion of the MCA stem (n=1), at the bifurcation (n=4), and in the superior/inferior division and/or branch (n=3). The site of occlusion could be identified by showing the nonenhancing arterial segment on the early and middle phase images of TPCT in all 5 patients with the MCA stem and bifurcation occlusion and by hyperdense MCA sign on precontrast CT in 4 of these 5 patients. We failed to obtain optimal arterial enhancement on the early phase images in 1 patient with congestive heart failure (Figure 1 and Figure 2).

On DSA results, all patients had perfusion deficit zones of grade 0, grade 1, and grade 2. The TPCT revealed zones of severe perfusion deficit and moderate perfusion deficit in all 8 patients (Table). The zone of grade 0 perfusion deficit on DSA was about the same as the zone of severe perfusion deficit on TPCT (Figure 3 and Figure 4) in terms of site and extent; that of grade 1 perfusion deficit on DSA corresponded to the zone of moderate perfusion deficit on TPCT. Triphasic perfusion CT could not detect the zone of grade 2 perfusion deficit on DSA. The asymmetrical arterial enhancement in perfusion deficit areas on the middle and late phase images of TPCT represented markedly slow collateral collaterals on DSA. In patient 7, the zone of moderate perfusion deficit with only markedly slow collaterals on TPCT was larger than a zone of grade 1 perfusion deficit because we performed carotid angiography only, and the leptomeningeal collaterals from the posterior cerebral artery were not visualized on DSA (Figure 5 and Figure 6).

On precontrast CT, low-density areas and/or loss of gray-white matter distinction was found in 6 patients. These areas were confined to a zone of severe perfusion deficit on TPCT. A zone of severe perfusion deficit on TPCT is usually more evident than low-density areas on precontrast CT. Severe perfusion deficit involving basal ganglia occurred in 4 patients. The extent of severe perfusion deficit was less than 33% of basal ganglia.

Superselective intra-arterial urokinase infusion was started in 6 of the 8 patients within 7 hours (range, 4.3-6.2 hours) after the onset of acute stroke (Table). The total dose of urokinase was 450000 to 1 million units. The total amount of injected nonionic contrast material was 90 to 160 mL for angiography. After thrombolytic therapy, 2 patients deteriorated to death (cases 1 and 2) with hemorrhagic transformation within 24 hours after partial recanalization (Figures 1 and 2). Both had a large extent of grade 0 perfusion deficit on DSA and of severe perfusion deficit on TPCT (more than 60% of the presumed MCA territory). Of the remaining 4 patients with a small extent of grade 0 perfusion deficit on DSA and severe perfusion deficit on TPCT (33% or less of the presumed MCA territory), 1 had complete recanalization (case 4); 1, a partial recanalization (case 5); 1, no recanalization (case 3); and 1 had a new embolism, probably due to a complication of DSA (case 6). There was no symptomatic hemorrhagic transformation in these 4 patients.
after thrombolytic therapy within 7 hours of onset. Patient 4 with complete recanalization showed a more than 4-point improvement in the NIHSS score within 24 hours (Figures 3 and 4). In patient 3 with partial recanalization, there was only a 2-point improvement of the NIHSS score within 24 hours of thrombolytic therapy. Patient 6 deteriorated because of a new embolism that occurred as a complication of angiography. The occluded MCA was recanalized completely without clinical improvement. The patient died of pneumonia 1 month after the onset of stroke.

Thrombolytic therapy could not be done in 2 patients because of superselection failure of the occluded MCA site (cases 7 and 8). In patient 7, who did not undergo thrombolytic therapy, an infarction was noted on follow-up MRI in the zones of both severe perfusion deficit and moderate perfusion deficit (Figures 5 and 6).

Overall, the initial NIHSS score correlated with the total extent of severe perfusion deficit and moderate perfusion deficit and with severe perfusion deficit alone (Table). The initial NIHSS score was 12 for patient 7, who had a large extent of moderate perfusion deficit (more than 50% of the presumed MCA territory) and a small extent of severe perfusion deficit (less than 10% of the presumed MCA territory). The patient improved without thrombolytic therapy and had a good clinical outcome at 3 months (Table). In this patient, the initial NIHSS score correlated better with the total extent of severe perfusion deficit and moderate perfusion deficit than with the extent of severe perfusion deficit alone.
Findings of Precontrast Computed Tomography and Triphasic Perfusion Computed Tomography, Clinical Scales, Treatment, and Outcome*

<table>
<thead>
<tr>
<th>Patient No./Age/Sex</th>
<th>Low Density on PCT (Time Lapse, h)†</th>
<th>Occlusion Site on TPCT</th>
<th>Extent of SPD, %</th>
<th>Extent of MPD, %</th>
<th>Initial NIHSS Scores</th>
<th>Urokinase Dose, $\times 10^3$ U (Time Lapse, h)†</th>
<th>Recanalization</th>
<th>Parenchymal Hematoma</th>
<th>Early Improvement‡</th>
<th>MRS at 3 mo</th>
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<tr>
<td>1/80/M + (2)</td>
<td>Bilocation</td>
<td>&gt;80</td>
<td>&lt;10</td>
<td>22</td>
<td>1000 (5.3)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Death</td>
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<tr>
<td>2/60/M + (2.7)</td>
<td>Bilocation</td>
<td>60-70 + ACA</td>
<td>&lt;10</td>
<td>22</td>
<td>500 (5.8)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Death</td>
</tr>
<tr>
<td>3/55/M + (1.2)</td>
<td>Bilocation</td>
<td>20-33</td>
<td>20-33</td>
<td>12</td>
<td>1000 (5.2)</td>
<td>No§</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td>4/51/M + (3)</td>
<td>Stem</td>
<td>20-33</td>
<td>20-33</td>
<td>14</td>
<td>450 (4.3)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>1</td>
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<tr>
<td>5/72/F - (1)</td>
<td>Superior/inferior division</td>
<td>&lt;10</td>
<td>10-20</td>
<td>4</td>
<td>1000 (5.3)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2</td>
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<tr>
<td>6/80/M + (2.5)</td>
<td>Superior division</td>
<td>&lt;10</td>
<td>10-20</td>
<td>5</td>
<td>500 (6.2)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Death§</td>
</tr>
<tr>
<td>7/78/M – (1.8)</td>
<td>Bilocation</td>
<td>&lt;10</td>
<td>&gt;50</td>
<td>12</td>
<td>Not done</td>
<td>No§</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>1</td>
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<tr>
<td>8/67/F + (1.2)</td>
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<td>&lt;10</td>
<td>10-20</td>
<td>6</td>
<td>Not done</td>
<td>No§</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2</td>
</tr>
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</table>

*PCT indicates precontrast computed tomography; TPCT, triphasic perfusion computed tomography; SPD, severe perfusion deficit; MPD, moderate perfusion deficit; NIHSS, National Institutes of Health Stroke Scale; MRS, modified Rankin scale; plus sign, presence of parenchymal low density or loss of gray-white matter distinction with sulcal effacement; ACA, anterior cerebral artery; and minus sign, absence of parenchymal low density.

†From onset of stroke to indicated procedure or intervention.
‡Improvement of 4 points or more from baseline in 1 day.
§Spontaneous recanalization was confirmed by magnetic resonance angiography 3 days after onset of stroke.
∥Patient 6 died of pneumonia 1 month after the onset of stroke.

Figure 2. Case 1.A, Occlusion at the MCA bifurcation on angiography. RT.ICA indicates right internal carotid artery angiography. B, Capillary phase image shows a large zone of grade 0 perfusion deficit with few collaterals and a small zone of grade 1 perfusion deficit with scanty, slow leptomeningeal collaterals. C, Partial recanalization of the occluded MCA after thrombolytic therapy. POST U.K(1,000,000) indicates after a 1 million-U intra-arterial urokinase infusion. D, Hemorrhagic transformation after thrombolysis.
Our TPCT identified the site of occlusion in all 5 patients with MCA stem or bifurcation occlusion on DSA. Hyperdense MCA sign was found in 4 of 5 patients on precontrast CT. Hyperdense MCA segments corresponded to the nonenhancing arterial segments on the early and middle phase images of TPCT. Given the substantial difference of attenuation between the normal-enhancing artery and less-enhancing occluded segments, there was no difficulty detecting a nonenhancing segment of MCA stem or bifurcation. However, it was difficult to trace these segments serially on the axial CT images owing to their oblique and tortuous directions.

Our TPCT revealed decreased perfusion areas in all 8 patients with acute MCA occlusion who had MCA territory infarction on follow-up CT or MRI. The first poor perfusion sign of the TPCT, namely, decreased enhancement of the affected MCA or its branches, could be depicted by obtaining images at the early or middle phase before maximum opacification of the distal MCA branches by collateral circulation. The second sign, perfusion deficit in the affected MCA territory, can be shown as low-density areas relative to contralateral normal parenchyma, especially on the middle and late phase images. The third sign, a delayed asymmetric arterial enhancement between markedly slow collateral arteries and con-
trilateral normal arteries, is the same mechanism as the enhancement of markedly slow collaterals on gadolinium-enhanced MRI in acute cortical ischemic stroke. All 3 poor perfusion signs were more evidently shown in patients with MCA stem or bifurcation occlusion than in MCA distal occlusion. The perfusion deficit can be graded as severe or moderate perfusion deficit as described earlier.

A precise and quick identification of reversible ischemic penumbra and irreversible ischemic core would provide the most important basis for ideal treatment without complication in patients with acute MCA occlusion.

Figure 4. Case 4. A, An arterial phase image of the right internal carotid artery angiography shows an occlusion on the right middle cerebral artery (MCA) stem with leptomeningeal collaterals from the anterior and posterior cerebral arteries (arrows). B, A capillary phase image of angiography shows prominent slow leptomeningeal collaterals on the frontoparietal cortex (zone of grade 1 perfusion deficit, small arrows) and a small zone with no collaterals on the insula (zone of grade 0 perfusion deficits, large arrow). C, Complete recanalization of the MCA on angiography after thrombolytic therapy. POST U.K(450,000) indicates after a 450000-U intra-arterial urokinase infusion. D, Recanalization of the MCA on the early phase images of follow-up T2CT (13 days after onset). E, Small infarction on the right insula and basal ganglia on magnetic resonance imaging 1 day after symptom onset.
At present, diffusion and perfusion MRI have been shown to be reliable and promising tools to obtain information on tissue viability and reversibility. Diffusion imaging can detect early ischemic change, and perfusion imaging can show the state of tissue perfusion. The region with perfusion deficit on perfusion imaging and without abnormality on diffusion imaging might represent the ischemic penumbra. However, the precise zone of ischemic penumbra cannot be easily determined with both diffusion and perfusion imaging, and this functional MRI also entails large gradient hardware requirements that are not widely available in clinical practice.

It is suggested that the zone of severe perfusion deficit on TPCT may be presumed as the ischemic core and that of moderate perfusion deficit as the penumbra zone. In our experience, and in that of von Kummer et al, an area of parenchymal hypodensity evident on precontrast CT has a low possibility of becoming normal even after thrombolytic therapy. In our study, there seems to be the most significant decrease of cerebral blood flow in the zone of severe perfusion deficit; this zone will eventually become an infarction. Low-density areas on precontrast CT were confined to the zone of severe perfusion deficit on TPCT. The zone of severe perfusion deficit in most cases seemed to be similar to the infarcted area on follow-up CT and/or MRI in terms of location and size. Therefore, this zone of severe perfusion deficit may be the ischemic core and may have a high possibility of irreversible ischemic damage.

The zone of moderate perfusion deficit on TPCT (normal attenuation on precontrast CT) may be presumed to be the penumbra zone from the following evidence from
patient 7 (Figures 5 and 6): (1) The infarction appeared on follow-up MRI not only in the zone of severe perfusion deficit but also in the zone of moderate perfusion deficit. (2) This patient, who had a large extent of moderate perfusion deficit (more than 50% of the presumed MCA territory) and a small extent of severe perfusion deficit (less than 10% of the presumed MCA territory) and whose initial NIHSS score was 12, had an improved and good clinical outcome at 3 months without thrombolytic therapy. (3) The initial NIHSS score correlated better with the total extent of moderate and severe perfusion deficit than that of severe perfusion deficit alone. These findings were consistent with recent reports regarding a correlation between clinical and functional MRI findings.36,37

We failed to get an optimal arterial enhancement at the early phase of TPCT in patient 1, who had congestive heart failure (Figures 1 and 2). This problem may have resulted from individual variation in the circulation time of blood flow, which is mainly influenced by cardiac function or, if present, bilateral carotid occlusive disease. Therefore, we could recognize the cardiac dysfunction based on the early phase findings in this patient.

In our study, direct intra-arterial urokinase infusion was performed in 6 patients within 7 hours of onset. Two patients deteriorated to death with hemorrhagic transformation within 24 hours after intra-arterial thrombolysis. One had subtle sulcal effacement with loss of gray-white matter distinction (Figure 1), and the other had subtle parenchymal hypodensity on precontrast CT. However, both had a large extent of severe perfusion deficit (more than 60% of the presumed MCA territory) on TPCT. The remaining 4 patients with small severe perfusion deficit on TPCT (33% or less of the presumed MCA territory) did not develop any symptomatic hemorrhagic transformation. In the Prolyse in Acute Cerebral Thromboembolism trial,38 5 of the 40 treated patients displayed baseline evidence of injury exceeding 33% of the affected hemisphere on the initial CT scan. All 5 patients with those findings received intra-arterial recombinant pro-urokinase within 6 hours of the onset and developed hemorrhagic transformation within 24 hours. It is suggested that intra-arterial thrombolytic therapy within 6 hours of onset as well as intravenous thrombolytic therapy within 6 hours may increase the risk of fatal brain hemorrhage in patients with a hypoattenuating area larger than 33% of presumed MCA territory on precontrast CT or TPCT.10

In this study, precontrast CT findings obtained within 2 hours of onset in 4 patients were normal in 2 (patients 5 and 7; Figure 5) and showed subtle abnormalities in the other 2 (patients 1 and 2; Figure 1). Within 2 hours of onset, the increase in the tissue water was still too small to cause a visible decrease in radiograph attenuation.22 However, in all 4 patients, our TPCT taken at the same time as precontrast CT clearly showed the extent of severe perfusion deficit. Even if the initial precontrast CT finding is normal or shows subtle abnormality (Figure 1) in patients with acute ischemic stroke, thrombolytic therapy within 6 hours of onset seems potentially dangerous in patients with medium to large extent of severe perfusion deficit. If the extent of severe perfusion deficit is 33% or less of the presumed MCA territory, thrombolytic therapy may be safe within 7 hours of onset. If

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Figure 6. Case 7. A, An arterial phase image of the left internal carotid angiography (LT. ICA) shows occlusion of the left middle cerebral artery. B, A capillary phase image shows markedly slow arterial collaterals in the identical site with delayed arterial enhancement on triphasic perfusion computed tomography (TPCT). The zone of moderate perfusion deficit on TPCT is larger than that of grade 1 perfusion deficit because the leptomeningeal collaterals from posterior cerebral artery are not visualized. C, A fluid attenuated inversion recovery image of magnetic resonance imaging 9 days after symptom onset shows new infarcts in the zones of severe perfusion deficit (large arrow) and moderate perfusion deficit (small arrow) on TPCT.
the extent of severe perfusion deficit is very small and the extent of moderate perfor- 
dation deficit is large (more than 50% of the presumed MCA territory), patients like 
the one in case 7 may recover without thrombolytic therapy. Therefore, TPCT may be used to make throm- 
bolysis safer or to predict clinical outcome in patients with acute MCA ischemic stroke.

Triphasic perfusion CT has a disadvantage of using contrast material in patients with acute ischemic stroke. Some studies have reported potential neurotoxicity of hyper- 
perosmolar ionic contrast material in patients with acute infarction. However, nonionic low osmolar contrast ma- 
terial has lower neurotoxicity and little effect on the blood- 

In conclusion, TPCT can be performed easily and rapidly in conjunction with conventional precontrast CT for emergency imaging of acute ischemic stroke. It seems to be useful for diagnosing proximal MCA occlusion in patients with acute ischemic stroke. Furthermore, TPCT can demonstrate perfusion deficit and collateral circulation of the affected MCA territory. Thus, TPCT may be used as a rapid and noninvasive tool to make thrombo- 

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