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Potential of CT Angiography in Acute Ischemic Stroke

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PURPOSE: To study the ability of CT angiography to show intracranial arterial occlusion and collateral blood flow in patients with acute stroke. METHODS: Twenty-one patients with acute nonhemorrhagic stroke were studied prospectively with conventional CT, CT angiography, and digital subtraction angiography. On the basis of CT angiographic findings, two neuroradiologists independently assessed the site of arterial occlusion, the contrast enhancement in arterial branches beyond the occlusion as a measure of collateral blood supply, and the extent of diminished parenchymal enhancement; they then predicted the extent of ischemic infarction. RESULTS: Both raters correctly assessed all trunk occlusions of the basilar artery (n = 4), the internal carotid artery (n = 4), and the middle cerebral artery (n = 9). The chance adjusted intrarater agreement was $\kappa = .78$. The assessment of branch occlusions of the middle cerebral artery was less reliable. The agreement rate in judging the collateral state in 17 occlusions in the anterior cerebral circulation was 88%. The size of 21 (62%) of 34 hemispheric infarctions was predicted correctly. CONCLUSION: CT angiography quickly and reliably adds important information to conventional CT studies in cases of acute ischemic stroke. It shows the site of occlusion, the length of the occluded arterial segment, and the contrast-enhanced arteries beyond the occlusion as an estimate of collateral blood flow.

Index terms: Brain, infarction; Brain, computed tomography; Computed tomography, threedimensional


In acute intracranial arterial occlusion with sudden neurologic deficit, limited time is available to obtain information for carefully directed treatment, because of the relatively rapid onset of irreversible neuronal damage. Diagnosis based on both etiologic and pathophysiologic data is essential to enable therapeutic decisions to be made. Commonly, patients with acute stroke are examined with unenhanced computed tomography (CT) of the brain to exclude intracranial hemorrhage or other causes of the stroke. CT has also proved useful in assessing early sequelae of cerebral ischemia, such as parenchymal hypodensity and focal brain swelling, thus showing the volume of brain tissue most severely affected by ischemia (1–7). Unenhanced CT does not, however, show the arterial occlusion itself, except in patients with a hyperdense arterial sign (eg, the hyperdense middle cerebral artery [MCA] sign), which has high specificity but low sensitivity for an occluded cerebral artery (5, 8–10). Furthermore, conventional CT does not show the extent of disturbed cerebral perfusion, which is determined by the site of occlusion, collateral blood supply, and intracranial perfusion pressure. Finally, it does not allow the leptomeningeal collaterals to be seen. Conventional CT in acute arterial occlusion is thus incapable of showing the volume of viable tissue at risk from low perfusion, which is the target of thrombolytic treatment.

Because of these considerations, we evaluated whether CT angiography is capable of reliably showing the site of arterial occlusion, estimating leptomeningeal collateralization, and determining the extent of severe parenchymal perfusion deficit.
Patients and Methods

We examined with conventional cranial CT 21 patients with an acute (<6 hours), severe hemispheric syndrome (hemiparesis ≤ grade 2 and/or aphasia, where grade 2 hemiparesis is defined as a state in which a limb can be moved only when gravity is eliminated) in whom clinical symptoms showed no tendency toward improvement. Five patients had intracranial hemorrhage and were excluded from further study. Five patients with brain stem symptoms and clinically suspected basilar artery occlusion were examined by CT angiography, regardless of the time interval from symptom onset. We thus selected 16 patients with suspected acute arterial occlusion in the anterior cerebral circulation and five patients with suspected basilar artery occlusion for CT angiography immediately after unenhanced conventional cranial CT. Thirteen patients were men and eight were women; mean age was 59.8 years (SD ± 14.2).

Informed and signed consent was obtained from the patients or their relatives. For conventional CT, 8-mm-thick axial sections were used throughout the brain. For CT angiography, spiral scanning during intravenous bolus administration of nonionic contrast medium was done on the same scanner immediately after the initial CT study without moving the patient. Section thickness was 1.5 mm (index, 1.0 mm) for the patients with suspected occlusion in the anterior cerebral circulation and 2.0 mm (index, 1.5 mm) in cases of suspected basilar occlusion. This difference in scanning parameters was necessitated by the fact that in the patients with suspected basilar artery occlusion a wider scan range must be covered. Patients with suspected occlusion in the anterior cerebral circulation were scanned from the sellar floor toward the vertex, whereas in patients with suspected basilar occlusion, spiral scanning extended from the foramen magnum to the tip of the basilar artery. The following scan parameters were used in all patients: 1.25 spiral pitch, 130 kV, and 125 mA. Total scanning time was 21 seconds (1 second per revolution). We injected 130 mL of the nonionic contrast medium into an antecubital vein (intravenous cannula ≥ 18 gauge) with an injection rate of 4 to 5 mL/s using an injection pump. Scan delay was 20 seconds in all cases.

In eight of 16 patients with suspected occlusion in the anterior cerebral circulation and in three of five patients with suspected basilar occlusion, cerebral digital subtraction angiography (DSA) was performed within 1 hour after CT angiography. All but one patient had a follow-up CT study within 24 ± 12 hours of the initial CT examination. The spiral data were transferred to an independent medical workstation and three-dimensional reconstructions of the circle of Willis (or the basilar artery) were performed. Since the 3-D volume-rendering algorithm used does not require data segmentation, 3-D evaluation of the CT angiographic data set took less than 10 minutes (including data transfer from the scanner to the workstation). The quality of two CT angiographic data sets was diminished because of patient motion during spiral scanning; however, the five to seven sections that showed the circle of Willis were spared from motion artifacts. Thus, the CT angiographic data set was still diagnostic, but we were unable to reconstruct three-dimensionally the data sets that were degraded by motion artifacts.

Data Evaluation

The 3-D reconstructions of the circle of Willis were calculated by using a volume-rendering algorithm. A region of interest was defined in the MCA on the CT angiographic source images. The mean gray value of the region of interest was measured and taken as the center, the standard deviation as the width of the window for the 3-D reconstructions. The 3-D reconstructions of the circle of Willis were depicted as in the real world (ie, when the circle of Willis was viewed from above, the left MCA was on the left side). Calcification of the vessels may cause problems with the 3-D reconstructions, but it is easily detected on the CT angiographic source images. Therefore, it is necessary to use both the source images and the 3-D reconstructions for diagnosis. We did not use maximum intensity projections because the proximity of the vessels to the skull base would have required segmentation of the data sets, which would have delayed the diagnostic procedure.

Two experienced neuroradiologists, blinded to the patients’ clinical, DSA, and CT findings, evaluated the CT angiographic studies independently. The neuroradiologists were aware, however, that CT angiography had been performed for suspected vessel occlusion. Their evaluation was based solely on the CT angiographic source images and 3-D reconstructions. Occlusions were distinguished in the basilar artery, the intracranial internal carotid artery bifurcation, the proximal MCA trunk, the distal MCA trunk, and the MCA branch. Their assessment of arterial occlusion was compared with the findings on DSA (11 of 21) and/or the pattern of cerebral infarction on the follow-up CT study.

In the patients with vessel occlusion in the anterior cerebral circulation, the leptomeningeal collateral blood supply (LCBS) was rated on a semiquantitative scale. The number of arteries visible beyond the occlusion and supplied with contrast agent by collaterals was categorized and the LCBS was rated as “good” if there was filling of the MCA branches in the sylvian fissure, as “moderate” if collaterals were visible but the sylvian MCA branches remained unenhanced, or as “none” if no arteries beyond the occlusion were visible. In addition, the two neuroradiologists described the pattern and proportion of brain tissue without parenchymal enhancement as an estimate of severe perfusion deficit.

On the basis of the site of occlusion and the LCBS rating they tried to predict the extent of cerebral infarction on the follow-up CT scan. They predicted whether infarction would include the basal ganglia, the MCA territory (in part or complete), or the anterior cerebral artery territory. Answers could be combined, for example, “basal ganglia and partial MCA territory.” The predictions were compared with the extent of cerebral infarction on the follow-up CT scan.
We describe interobserver agreement by agreement rates and $\kappa$ statistics. The $\kappa$ statistic is chance corrected and measures the observed amount of agreement adjusted for the amount of agreement by chance alone. A $\kappa$ value greater than .6 was considered to indicate substantial to excellent agreement, as has been described by others (11).

Results

The two neuroradiologists found four basilar artery occlusions in five patients and 15 occlusions in the anterior circulation of 16 patients. Interestingly, they detected an additional proximal MCA occlusion that was not suspected clinically in one of the patients with basilar artery occlusion (Fig 1). Therefore, 20 arterial occlusions were observed in 19 patients (Table 1). In one patient with clinically suspected basilar artery occlusion, neither rater found an occlusion at CT angiography. Follow-up examination showed that this patient was intoxicated and did not develop brain stem or cerebellar infarction. We counted this rating as true-negative.

In another patient, neither rater was able to diagnose arterial occlusion by CT angiography, but the follow-up CT study showed partial infarction of the MCA territory, suggesting MCA branch occlusion (Fig 2). We counted this rating as false-negative.

DSA confirmed the site of occlusion as seen at CT angiography in the 11 patients in whom it was performed (Figs 1 and 3). In the remaining patients, the diagnosed occlusions were consistent with the extent and pattern of the infarction on follow-up CT scans. Altogether, one rater correctly judged 21 (95%) of 22 intracranial arterial occlusions and the other rater 20 (91%) of 22 occlusions. With regard to the exact site of arterial occlusion, the two neuroradiologists agreed in 21 of 22 assessments (95%, $\kappa = .78$) (Table 1). They disagreed in one case of MCA branch occlusion (Fig 4).

In all patients with suspected occlusions in the anterior cerebral circulation, the two neuroradiologists rated the LCBS with the use of a semiquantitative scale. They agreed in their assessment of 15 (88%) of 17 patients (Table 2). In two patients, LCBS was rated as “none” by one neuroradiologist and as “moderate” by the other.

The source CT angiographic images showed areas without parenchymal enhancement in eight (47%) of 17 patients with occlusion in the anterior cerebral circulation. In all cases, unenhanced brain parenchyma became hypodense on the follow-up CT scan (Figs 4 and 5). The minimum size of the ischemic lesion was represented consistently by the pattern of unenhanced tissue. The hypodense area of brain tissue on the unenhanced follow-up CT scans was either the same size or larger than the unenhanced tissue volume (Fig 5).

On the basis of their assessment of occlusion site and collateral blood supply, the two neuroradiologists tried to predict the size and pattern of hemispheric brain infarction in the 17 patients with occlusion in the anterior circulation. When compared with CT performed at 24 ± 12 hours after the stroke, their ratings were correct in 21 (62%) of 34 assessments. In five patients with “none” or “moderate” LCBS, the infarct pattern and size were estimated correctly 90% of the time (nine of 10 predictions), whereas this rate dropped to 50% (12 correct predictions) in patients with “good” LCBS. In nine of the 12 false predictions, the infarcted area on the follow-up CT study was larger than predicted.

<table>
<thead>
<tr>
<th>Rater 2</th>
<th>No Occlusion</th>
<th>ICA</th>
<th>M1 Prox</th>
<th>M1 Dist</th>
<th>M2</th>
<th>BA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rater 1</td>
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<td>2</td>
<td>0</td>
<td>0</td>
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<td></td>
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<tr>
<td></td>
<td>BA</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
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</tbody>
</table>

Note.—ICA indicates internal carotid artery; M1 prox, proximal middle cerebral artery (MCA) trunk; M1 dist, distal MCA trunk; M2, MCA branch; BA, basilar artery. Figure 4 shows the patient in whom the observers disagreed with regard to an MCA branch occlusion.
TABLE 2: Assessment of collateral blood supply at CT angiography by two raters

<table>
<thead>
<tr>
<th>Rater 1</th>
<th>None</th>
<th>Moderate</th>
<th>Good</th>
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<tr>
<td>Rater 2</td>
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<td>0</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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Discussion

Today, emergency CT is generally the first diagnostic step after physical examination in patients with acute focal neurologic deficit. CT is also currently used in major clinical trials to properly select patients for thrombolysis with remarkable results (12, 13). The European Cooperative Acute Stroke Study showed that the use of CT assessment to exclude patients with primary hemorrhage and larger ischemic lesions (>33% of the MCA territory) within the first 6 hours after the onset of symptoms markedly influenced patients' response to treatment (12).

Despite the enormous potential of magnetic resonance imaging in this regard (14), we presume that, because of its greater availability and practicability for mostly uncooperative patients, CT will continue to be the primary diagnostic tool in stroke in the foreseeable future. All major controlled trials thus far have used CT to check patient inclusion and exclusion. It is therefore important to know whether a new CT technology with spiral scanning during bolus injection of a contrast agent can reliably give additional and important information about the site of arterial occlusion and, thus, the vascular territory at risk from low perfusion.

So far, CT angiography has been used to evaluate vascular lesions at the carotid bifurcation and to search for aneurysms at the circle of Willis (15–17). More recently, cerebral CT venography has been used successfully to diagnose dural sinus thrombosis (18).

CT angiography of the intracranial vasculature adds only a few minutes to standard CT protocols and thus does not significantly delay initiation of treatment. In our study, motion by uncooperative patients was a minor problem. No patient had an adverse reaction to the contrast agent. The amount (130 mL) of nonionic contrast agent we injected is relatively high, but it does not preclude additional DSA if invasive angiography becomes necessary.

Pullicino and Kendall (19) reported a possible association between the use of ionic (and thus hyperosmolar) contrast agent and poor outcome in stroke patients. Although inconclusive, their findings resulted in a restrictive attitude toward the administration of contrast material in patients with cerebral ischemia. Surprisingly, no controlled study was performed to clarify a possible toxic effect of contrast agents in acute cerebral ischemia. At this point, we want to stress that we exclusively use nonionic (almost isosmolar) contrast media for CT angiography.

To obtain more information about potential risks of contrast infusion in acute stroke, we conducted an experimental study to investigate the effects of bolus injection of ionic and nonionic contrast agents on infarction size and clinical course in a rat model of acute focal cerebral infarction. Our results suggest that bolus administration of nonionic contrast agents even in the double clinical dose does not significantly influence infarction volume and clinical course in acute ischemic stroke (Doerfler et al, unpublished data).

The two neuroradiologists assessed the occlusion sites of the intracranial internal carotid artery, the basilar artery, and the MCA trunk with a 100% sensitivity and specificity. Their evaluation was less certain in three patients with MCA branch occlusion. They disagreed in one patient (Fig 4), and neither rater could see one particular occlusion that was presumably re-
sponsible for small cortical infarctions (Fig 2). We counted this assessment as false-negative, although recanalization at the time of CT angiography is another possibility. We did not repeat the CT angiography to study recanalization.

For ethical reasons we were not able to compare CT angiographic findings with the DSA standard of reference in all patients. For example, if CT angiography showed MCA trunk occlusion and the patient turned out to have contraindications for thrombolytic therapy, or if it was decided to perform systemic thrombolytic therapy, we could not perform DSA, which would have delayed therapy. In these cases we compared CT angiographic findings with the pattern of infarction on the follow-up CT study.

In all 11 patients who had both CT angiography and DSA, DSA confirmed the CT angiographic findings. Although the number of patients is small, we have become convinced by this experience that CT angiography reliably shows the clinically relevant occlusions of major cerebral arteries. As mentioned earlier, CT angiography is less reliable in showing MCA branch occlusions. However, the natural course of MCA branch occlusion is relatively benign, whereas occlusions of the MCA trunk, intracranial internal carotid artery, and basilar artery are associated with high morbidity and mortality.

Fig 2. A 75-year-old man with left-sided hemiparesis. Admission CT scan (A) and CT angiographic 3-D reconstruction of the circle of Willis (viewed from above) (B) and source image (C) are nondiagnostic. D, Follow-up CT scan shows areas of infarctions compatible with MCA branch occlusions (arrows).
(20–24) and are therefore considered the targets of thrombolytic treatment.

The mismatch between the territory of an occluded artery and the volume of ischemic lesion as shown by CT can be explained by collateral blood supply (25, 26). We found that CT angiography reliably showed the effect of collaterals, that is, enhancement of MCA branches beyond the site of occlusion. Although absence or reduction of this vascular enhancement was associated with a large infarction, the presence of collaterals did not necessarily guarantee a small infarction (Fig 5).

If the LCBS was judged “none” or “moderate,” the extent of the infarcted area was correctly predicted in 90% of the patients. By contrast, if the LCBS was judged “good,” the rate of correct predictions dropped to 50%. We suggest that this variation may be due to the potential instability of collateral blood flow. The judgment of “good” at the time of CT angiography does not mean that the collaterals will remain viable over time. In these patients there is still brain tissue to be lost. This view is supported by the fact that in nine of the 12 incorrect predictions in patients with “good” collaterals, the infarcted...
area was underestimated. Perhaps it is this group of patients that is most likely to benefit from early thrombolytic recanalization.

We considered the brain parenchyma that either was hypodense on the admission CT scan or showed missing parenchymal enhancement at CT angiography to be the core of infarction, because without exception this area became hypodense on the follow-up CT scans (Figs 4

A 47-year-old man with rightsided hemiparesis.

A, Admission CT scan shows no infarction.

B, CT angiographic 3-D reconstruction of the circle of Willis (viewed from above) does not show a vessel occlusion.

C, CT angiographic source image shows a circumscribed area with no enhancement (asterisk). This led one of the raters to the conclusion that an MCA branch was occluded.

D, Follow-up CT scan shows an infarction of this area. This was the only case in which there was interrater disagreement concerning the site of occlusion (Table 1).

We conclude from our experience that CT angiography in cases of acute stroke is safe and can add important diagnostic information to that obtained from conventional CT; namely, the site of arterial occlusion, an estimate of the capacity of the collaterals, and the pattern of unenhanced (poorly perfused) brain tissue. The diagnostic information gained from

...
A 69-year-old woman with MCA trunk occlusion.

A, Baseline CT study 5 hours after symptom onset already shows hypodensity of the left insular cortex and the posterior part of the lentiform nucleus (arrows).

B, CT angiographic 3-D reconstruction shows a trunk occlusion of the left MCA (arrow).

C, CT angiographic source image shows a circumscribed area of no parenchymal enhancement (asterisk). The collateral blood supply in this case was rated as “good” (arrowheads).

D, Follow-up CT scan 1 day later shows an infarction exactly matching the area of missing parenchymal enhancement on CT angiogram.

E, Three days later, the extent of infarction has increased considerably. This case is an excellent example of the finding that a “good” collateral blood supply at the time of CT angiography is necessary for, but does not guarantee, a small infarction.
conventional CT and CT angiography together may provide a rational basis by which to choose the optimal treatment for patients with acute stroke.

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References

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Please see the Commentary on page 1021 in this issue.