Role of CT Angiography in Patient Selection for Thrombolytic Therapy in Acute Hemispheric Stroke

Susanne Wildermuth, MD; Michael Knauth, MD; Tobias Brandt, MD; Ralph Winter, MD; Klaus Sartor, MD; Werner Hacke, MD

Background and Purpose—It has been shown that thrombolytic therapy can improve clinical outcome in a subgroup of patients with acute cerebral ischemia. This subgroup was characterized by certain clinical and imaging findings (eg, moderate to severe neurological deficit for less than 3 to 6 hours, occlusion of the middle cerebral artery, lack of extended infarct signs on CT, and efficient leptomeningeal collaterals). Although not part of published prospective randomized rtPA trials, information about the status of the brain vessels would be helpful in the selection of patients who may benefit the most. Our purpose was to determine the feasibility of CT angiography (CTA) in patients with acute hemispheric ischemia and to evaluate its relevance for thrombolytic therapy.

Methods—CTA was performed in 40 consecutive patients (11 women and 29 men; age range, 19 to 80 years) with moderate or severe symptoms (National Institutes of Health Stroke Scale score of ≥8) of acute hemispheric ischemia. CTA findings were compared with Doppler ultrasonography (US; n = 22) and intra-arterial digital subtraction angiography (DSA; n = 7). Twenty patients received thrombolytic therapy, the remaining patients received intravenous heparin.

Results—Images and 3-dimensional reconstructions of diagnostic quality could be obtained in all patients. Thirty-four patients had a vessel occlusion. The extent of leptomeningeal collaterals correlated significantly with the outcome after thrombolytic therapy (r_s = 0.46, P < 0.05). The evaluation of diagnostic accuracy showed a high agreement with US (22 of 22) and DSA (6 of 7).

Conclusions—CTA can provide important information for the initiation of therapy in patients with acute hemispheric ischemia. Identification of patients with autolyzed thrombi, occlusion of the internal carotid artery bifurcation, and poor leptomeningeal collaterals is feasible with the use of CTA. These patients may have little potential for benefit from thrombolytic therapy. (Stroke. 1998;29:935-938.)

Key Words: angiography ■ computed tomography ■ ischemia, cerebral ■ stroke ■ thrombolytic therapy

Several encouraging studies have demonstrated the potential of thrombolytic therapy to improve the clinical outcome in patients suffering from acute cerebral ischemia.1-3 A particular subgroup of patients with distinct characteristics may have potential for greatest benefit; this subgroup is defined by a moderate or severe persisting neurological deficit for less than 3 to 6 hours,1,4-6 an occlusion of the MCA because of better recanalization rates compared with ICA occlusions,7,8 an initial CT without extended infarct signs as defined by Hacke et al in 1995,1 and efficient collateral circulation.1,10 Until now, the initial workup has been based mainly on clinical examination and CT. An additional vascular evaluation (eg, conventional intra-arterial DSA, US, or MRA) would be helpful to gather information about the site of the occlusion and the extent of collateral circulation. Furthermore, if spontaneous lysis of the occluding thrombus has already taken place, administration of thrombolytic agents may still do some harm.

Recent progress in CT technology, especially the spiral scanning technique with intravenous bolus administration of contrast agents, offers insight into the vascular status and the extent of the parenchymal lesion. The purpose of this study was to determine the feasibility of CTA in patients with clinically suspected acute hemispheric ischemia and to evaluate its potential in the decision for thrombolytic therapy. The extent of leptomeningeal collaterals was determined and correlated with clinical outcome. The diagnostic accuracy of CTA was compared with those of US and DSA in a subgroup of patients.

Subjects and Methods

We studied of 40 consecutive patients with clinical signs of moderate or severe acute hemispheric ischemia (NIHSS score of at least 8 without a tendency to improve) admitted to our emergency room (Department of Neurology, University of Heidelberg) within 6 hours of symptom onset.
A total of 1740 patients with ischemic stroke were admitted from July 1995 through December 1996, and 44% of them were seen within 6 hours after onset. Of these 767 patients, 274 had an NIHSS score of at least 8. Patients with aphasia (n=153) were excluded because of lack of informed consent, and patients with symptoms of infratentorial ischemia (n=34) were not included because of different diagnostic and therapeutic strategies. Forty percent of the remaining patients (n=35) were older than 80 years and were excluded as well. Twelve patients did not agree to the CTA examination and therefore were not included.

We included 11 women and 29 men (mean age, 58.2±13.7 years; range, 19 to 80 years). Thrombolytic therapy was considered in all. After history and physical examination, all patients were referred to CT and CTA. Informed consent was obtained from all patients or their relatives. Patients with a known history of hyperthyroidism, allergy to contrast agents, or acute renal failure were excluded. Additional extracranial and intracranial Doppler and duplex examinations were performed according to standard procedures in 25 of the patients (CDS 2-4, Medasonics Co). The Doppler examination was blinded regarding results of CTA and DSA (extracranial cw 4-MHz pencil probe, transcranial pw 2-MHz pencil probe; 5-MHz linear array, 128 XP4, Acuson Corp). On the basis of combined extracranial and intracranial US and duplex sonographic findings, results were graded into 4 groups: (1) complete ICA occlusions, (2) distal ICA occlusions including the intracranial ICA bifurcation and the MCA origin, (3) isolated M1 segment occlusions, and (4) distal M1 or M2 segment occlusions. Most of these US examinations lasted 10 to 20 minutes, and all were done within 3 hours of CT/CTA before initiation of thrombolytic therapy. In addition, 7 patients underwent conventional DSA.

A PQ 2000 CT (Picker International) was used for CT, with 8-mm slice thickness, throughout the neurocranium. CTA, involving spiral scanning with intravenous bolus administration of a nonionic contrast medium (Omnipaque 300; Schering), was performed on the same scanner immediately after the initial CT, without moving the patient. Slice thickness was 1.5 mm, with an index of 1.0 mm. Patients were scanned from the floor of the sella toward the vertex. The following scan parameters were used in all patients: spiral pitch, 1.25; 21 tube revolutions; tube voltage, 130 kV; and tube amperage, 125 mA. Total scanning time was 21 seconds. We injected 130 mL contrast medium into an antecubital vein (intravenous cannula >18 gauge) at an injection rate of 4 to 5 mL/s with a mechanical injection pump. Scan delay was 20 seconds in all patients.

The spiral data were transferred to an independent workstation (Picker Voxel Q), and the circle of Willis was reconstructed 3 dimensionally, as previously published. Since the 3-D volume-rendering algorithm does not require data segmentation, 3-D evaluation of the CTA data set took less than 10 minutes (including data transfer from the scanner to the workstation). Two experienced neuroradiologists (M.K. and K.S.), blinded to the other imaging modalities, evaluated independently occlusion site and presence and extent of LCBS. LCBS was graded according to the technique used by Knauth et al. Filling of the MCA branches in the Sylvian fissure was rated as “good” LCBS. “Moderate” LCBS meant that collaterals were visible but that the Sylvian MCA branches remained unchanged. No visible arteries beyond the occlusion was rated as “absent.”

The source images and the 3-D reconstructions were both used for the diagnosis of vessel obstruction and assessment of collaterals. In 20 patients we performed thrombolytic therapy in the following manner: local application of up to 1.5 million IU of urokinase in 4 patients and systemic application of recombinant tissue plasminogen activator (rtPA; 1.1 mg/kg body wt) in 16 patients. The remaining 20 patients received intravenous heparin (20 000 to 40 000 U IV qd). Clinical improvement was assessed at discharge according to the NIHSS and graded as no recovery (NIHSS score ≥8), moderate recovery (NIHSS score 4 to 7), and good to complete recovery (NIHSS score <4).

Results
CTA was successfully completed in all patients without the occurrence of any side effects. CTA reconstructions were of diagnostic quality in all 40 patients. ICA occlusion was diagnosed in 3, occlusion of the ICA bifurcation in 4, occlusion of the MCA trunk (M1 segment; Figure 1) in 22, and occlusion of the distal MCA or a branch (M2 segment; Figure 2) in 5 patients. In 6 patients we did not find vascular occlusions. Collateral circulation was graded as “absent” in 6 patients, “moderate” in 5, and “good” in 29 cases.

Thrombolytic therapy was initiated in 20 patients, and the other 20 patients received intravenous heparin. Recovery from the ischemic insult was judged clinically according to the NIHSS. One patient receiving heparin died from intracerebral hemorrhage, and 3 patients receiving it were lost to follow-up. Of the remaining 36 patients, 10 showed no recovery, 12 a moderate recovery, and 14 a good to complete recovery (see Table 1). There was a significant positive correlation (see Table 2) of the extent of collateral circulation as estimated by CTA with the clinical outcome after therapy. The correlation was stronger for patients who received thrombolytic therapy compared with heparin-treated patients.

US was performed in 25 patients by an experienced sonographer. US examinations of 3 patients were technically insufficient because of poor ultrasound penetration. Twenty-two of 22 US results showed findings identical to those of CTA.

DSA showed results identical to those of CTA in 6 of 7 patients. In the seventh patient CTA and US both showed an ICA occlusion at the common carotid artery bifurcation. DSA was performed 1 hour after CTA and showed only wall irregularities consistent with embolic remainders but no occlusion.

Discussion
The quick initiation of thrombolytic therapy has been shown to be a critical determinant of therapeutic success in patients with acute hemispheric ischemia. Therefore, a rapid, reliable workup is required in these very sick patients. Physical examination and CT to rule out hemorrhage are standards for assessment of stroke patients in the emergency room.

Additional vascular studies would be helpful to determine site and extent of the vascular occlusion when a treatment plan is being determined, especially with respect to thrombolytic therapy. Today, there are several modalities for vascular assessment available that differ greatly in availability, invasiveness, time requirement, applicability, and cost. MRA yields high-quality images of the cerebral circulation. However, it is time consuming and may be hampered by movement artifacts in acutely ill stroke patients. The clinical
value of novel functional MR techniques (eg, perfusion and diffusion MR) remains to be evaluated in the future. US is comparatively time-consuming, examiner dependent, and sometimes technically infeasible (eg, in 12% of our cases). Intra-arterial DSA remains the gold standard for vascular assessment up to now. However, it is invasive and time consuming, and it sometimes requires sedation and intubation. Complications with permanent neurological deficits cannot be avoided totally, even by a skillful technique and an experienced angiographer. Although DSA is an integral part of local thrombolytic therapy, cost effectiveness, risk reduction, and the need to save time strongly favor other modes of vascular assessment, provided they reveal reasonably accurate information.

CTA is readily available and minimally invasive. It can be performed on all CT scanners with spiral capability and can be done immediately after standard CT imaging without moving the patient. Because of the narrow time window for initiation of successful thrombolytic therapy, it is important to note that CTA is a very fast procedure, requiring only an additional 5 minutes of examination time in the CT scanner and about 10 minutes of reconstruction time. The application of 130 mL nonionic contrast agent for CTA is no contraindication for a subsequent diagnostic or therapeutic DSA. Idiosyncratic reactions to iodinated contrast agents have been reported, but the use of nonionic agents minimizes the risk of moderate or severe incidents. There is no risk of arterial injury or embolization. In our experience, CTA can even be applied to severely ill and uncooperative patients owing to the speed of imaging. Patients who would have required general anesthesia for DSA have undergone CTA with no sedation or only mild sedation. Contrary to DSA and US, CTA yields only static images, but hemodynamic or functional information can be inferred by indirect parameters such as visibility of collaterals.

Figure 1. M1 segment occlusion (see arrows) in 3-D reconstruction and perfusion deficit (see arrows) due to lack of collaterals in the source image.

Figure 2. M2 segment occlusion (see arrows) in 3-D reconstruction with good collateral circulation displayed in the source image.
TABLE 1. Outcome After Therapy Initiation Based on Clinical and Diagnostic Findings

<table>
<thead>
<tr>
<th>Therapy</th>
<th>n (n=40)</th>
<th>Improvement (NIHSS &gt;8)</th>
<th>Moderate Improvement (NIHSS 4–7)</th>
<th>Good Complete Recovery (NIHSS &lt;4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombolytic therapy</td>
<td>20</td>
<td>4</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Intravenous heparin</td>
<td>20*</td>
<td>6</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

*1 patient died and 3 were lost to follow-up.

The analysis of the European multicenter study1 on systemic thrombolytic therapy identified the extent of collateral circulation as a strong predictor for outcome after therapy, with poor collaterals associated with a high risk of secondary hemorrhage and space-occupying infarction.1 Our data show that it is possible to determine the extent of leptomeningeal collateral circulation using CTA in patients with acute hemispheric ischemia. The highly significant correlation between the outcome after thrombolytic therapy and the extent of collateral circulation estimated by CTA in this study confirms the usefulness of this parameter in estimating outcome.

On the basis of the available clinical data on thrombolytic therapy, it is not yet clear whether systemic or local therapy will become state-of-the-art therapy. However, should systemic therapy yield the same results as local thrombolytic therapy, one may limit diagnostic DSA to those cases in which CTA is inconclusive. In our department CTA has been incorporated as part of the routine workup of patients with suspected acute cerebral ischemia. Furthermore, as a minimally invasive imaging modality, CTA can be repeated to monitor recanalization after thrombolytic therapy and to assess follow-up.

In a subset of patients we compared vascular diagnosis obtained by CTA with results of standard modalities. Although this was not the primary purpose of this study, the numbers are still small, and the data are not fully comparable, the diagnostic accuracy of CTA in this emergency setting was high compared with the standard methods of DSA and US.18,19 CTA clearly detected all 6 occlusions found by DSA. Results were different in 1 patient in whom CTA showed an ICA occlusion not confirmed by DSA 1 hour later. This mismatch was most likely due to spontaneous lysis between the two studies. This view is supported by wall irregularities displayed in DSA at the site of the presumed previous occlusion. Agreement between CTA and US was 100%.

In conclusion, our data demonstrate that CTA is feasible in patients with acute hemispheric ischemia. The extent of leptomeningeal collateral circulation, which has been confirmed as a predictor for outcome after thrombolytic therapy in other studies, can be determined by CTA. Identification of patients with autolized thrombi or occlusion of the ICA bifurcation is feasible with the use of CTA. Such patients may have little potential for benefit from thrombolytic therapy.

References

TABLE 2. Nonparametric Correlation (Spearman) Between Extent of Leptomeningeal Collateral Circulation as Revealed by CTA and Clinical Outcome After Therapy

<table>
<thead>
<tr>
<th></th>
<th>All Patients n=40</th>
<th>Thrombolytic Therapy n=20</th>
<th>Heparin Therapy n=20</th>
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<tr>
<td>$\rho$</td>
<td>0.41</td>
<td>0.46</td>
<td>0.39</td>
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<tr>
<td>$\rho$</td>
<td>0.009</td>
<td>0.043</td>
<td>0.086</td>
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</table>
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