CT angiography in the evaluation of acute stroke.

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http://www.ajnr.org/content/18/6/1011
CT Angiography in the Evaluation of Acute Stroke

David A. Shrier, Hisashi Tanaka, Yuji Numaguchi, Shoko Konno, Uresh Patel, and Dean Shibata

PURPOSE: To determine the worth of CT angiography of the circle of Willis as a supplement to routine CT in the examination of patients with symptoms of acute stroke in terms of its depiction of the number and distribution of arterial stenoses or occlusions. We also sought to compare the accuracy of CT angiography with MR angiography and/or digital subtraction angiography (DSA).

METHODS: One hundred forty-five patients with symptoms of acute stroke were examined with routine head CT and CT angiography of the circle of Willis. MR angiography was also performed in 27 patients and DSA in 28 patients. CT and MR angiograms and DSAs were reviewed for stenoses or occlusions involving the vessels about the circle of Willis. MR and CT angiograms were also evaluated for image quality, and the corresponding routine CT and MR studies were evaluated for the presence of arterial infarction. RESULTS: CT angiograms were rated good or excellent in 89% of cases whereas MR angiograms were rated good or excellent in 92% of cases. Arterial stenoses or occlusions were present on 43% of CT angiograms, 48% of MR angiograms, and 21% of DSAs. Findings were in agreement in 98% of the vessels analyzed by CT angiography and MR angiography. Similarly, there was overall agreement of findings in 99% of vessels analyzed by CT angiography and DSA. None of the patients had any immediate adverse reactions after administration of intravenous nonionic iodinated contrast material.

CONCLUSION: CT angiography is an accurate and safe method for evaluating arterial stenoses or occlusions in the vessels about the circle of Willis. CT angiography should be used in patients with symptoms of acute stroke for whom evaluation of the intracranial vasculature is desirable.

Index terms: Arteries, stenosis and occlusion; Brain, infarction; Computed tomography, three-dimensional; Computed tomography, comparative studies


Stroke is the third most common cause of death, the most common cause of morbidity, and the third most costly adult disease in the United States (1). Infarction stemming from vascular occlusive disease is the major causative factor. The majority of infarctions are caused by thromboembolism from underlying atherosclerotic disease (2). The majority of stroke patients are treated conservatively, and often they are left with some degree of permanent deficit (3, 4). Acute local intraarterial thrombolysis has recently shown promise of improving patient outcome (3–5). However, thrombosis must be identified and treated promptly for optimal results. Arteriography is the accepted standard of reference for evaluating vascular disease but carries with it considerable cost and invasiveness as well as measurable risk (6, 7). Magnetic resonance (MR) angiography is a noninvasive, reliable way to evaluate cerebral vascular disease but requires a highly cooperative patient (8) and cannot be performed in patients with pacemakers and aneurysm clips.

Computed tomographic (CT) angiography is a new method for evaluating vascular anatomy. Making use of slip-ring technology, it allows visualization of vascular anatomy after iiodinated contrast medium has been administered intravenously (9–12). Recently, CT angiography has been shown to be a reliable alternative to MR angiography in the detection of arterial
anatomy in the circle of Willis and it has shown promise in the evaluation of carotid bifurcation disease as well as for intracranial aneurysms and vascular malformations (13–18). For the diagnosis of middle cerebral artery (MCA) occlusive disease, CT angiography has shown good correlation with transcranial Doppler sonography but appears less reliable than MR angiography (19, 20). This study was undertaken to evaluate the quality of CT angiograms obtained as an adjunct to head CT in patients with symptoms of acute stroke and to determine what additional information CT angiography would provide. Furthermore, we sought to evaluate the accuracy, sensitivity, and specificity of CT angiography in comparison with MR angiography and/or digital subtraction angiography (DSA) in this patient population.

Patients and Methods

One hundred forty-five patients (78 female, 67 male; average age, 62 years) who presented with symptoms of acute stroke from December 1994 through December 1996 were examined with 146 routine cranial CT and CT angiographic studies (two studies were obtained in one patient). Cranial MR imaging and MR angiography were also performed in 27 patients, and cerebral DSA was performed in 28 patients.

CT scans and CT angiograms were obtained on a GE High Speed Advantage helical CT scanner. Routine non-contrast head CT was initially performed from the skull base to the vertex with 10-mm-thick contiguous axial sections. Subsequently, 55 patients received 75 mL of iohexol (Omnipaque 240) for CT angiography at an injection rate of 2.5 mL/s for 20 seconds followed by 1.0 mL/s for 25 seconds. Scans were begun 15 seconds after the initiation of the contrast injection. Ninety-one scans were performed within 1 day. Of the 28 DSAs, 22 included both anterior and posterior circulations. Six studies were performed in 27 patients, and cerebral DSA was performed in 28 patients.

Filming was performed in a 12-on-1 format with a standard axial view and two sagittal views (one magnified 25%) in the top row. Magnified coronal projections were filmed in the two middle rows. Each coronal image was filmed at a 15° caudal angulation to the previous view. Finally, three magnified axial views were filmed in the bottom row with the outside images rotated 12° from the nonrotated center image. This technique allows for stereoscopic viewing.

MR angiography was performed on a 1.5-T system. Images were acquired with a 3-D time-of-flight pulse sequence using the following parameters: 48–54/3.3–6.0/1 (repetition time/echo time/excitations), 16 to 32-kHz bandwidth, 20 × 15-cm or 18 × 13-cm field of view, 512 × 192 or 256 matrix, 0.8- to 1.0-mm section thickness, and 60-section slab. A ramped pulse from the inferior to superior direction was used, centered at a flip angle of 25°. A magnetization transfer pulse was used to reduce background signal. Early MR angiograms were obtained with a 256 × 128 matrix. All 27 MR angiograms were obtained within 3 days of CT angiography and 16 of these scans were obtained within 1 day.

DSA was performed on a combined biplane system using a 512 × 512 matrix with 12-bit integration. One DSA study was obtained at an outside institution. Standard doses of nonionic contrast material (Omnipaque 300) were used. Indications for DSA included carotid artery disease (four patients), intracranial occlusive disease (five patients), and aneurysm/arteriovenous malformation workup (19 patients). All 28 DSA studies were obtained within 3 days of CT angiography and 22 of these were obtained within 1 day. Of the 28 DSAs, 22 included both posterior and anterior circulations. Six studies were performed exclusively for evaluating the anterior circulation.

Images were rated by three neuroradiologists in consensus fashion. CT angiograms, MR angiograms, and DSAs were reviewed independently and at separate times.
and all radiologists were blinded to the clinical information. Overall image quality for CT and MR angiograms was rated from excellent to poor according to the following scale: excellent = M2 branches of both MCAs clearly seen, good = M2 branches of both MCAs faintly seen, fair = both M1 branches clearly seen, poor = M1 branches of both MCAs faintly seen.

Individual vessels evaluated included the MCA, the anterior cerebral artery (ACA), the posterior cerebral artery (PCA), the distal internal carotid artery (ICA), and the distal basilar arteries. A value was assigned to each vessel according to the following arbitrary three-point scoring system: 0 = normal vessel, 1 = stenosis, 2 = occlusion. A stenosis was considered present when there was evidence of any abnormal narrowing. The degree of stenosis was not measured. Only first- or second-order branches of the intracranial vessels were evaluated.

Percentage of agreement was measured between CT angiographic, DSA, and MR angiographic data. Statistical analysis included the intrarater $k$ statistic and sensitivity-specificity outcomes.

Routine head CT and MR studies were evaluated for significant vascular lesions (infarcts) concurrent with respective CT angiographic or MR angiographic analysis. An infarct (bland or hemorrhagic) was considered significant if it involved the cortex or involved deep gray nuclei or white matter and was greater than 1 cm in diameter. Vascular lesions were classified according to which vascular territory was involved (MCA, ACA, PCA, ICA, or basilar distributions). Hematomas and small lacunar infarcts (<1 cm) were excluded because of the low likelihood of correlating with a major arterial branch occlusion.

One-millimeter-thick axial CT source images were reviewed in all patients in conjunction with angiographic reconstructions and routine axial images.

Results

Of the 146 CT angiograms obtained during the study, 89% were rated good or excellent in quality (Table 1). Only 3% were considered of poor quality. Of the 16 CT angiograms rated fair or poor, 11 were obtained with a 75-mL dose of contrast material (including four of five of the poorly rated scans). Ninety-five percent of the CT angiograms obtained with 100-mL does of contrast agent were rated good or excellent, whereas only 80% of CT angiograms obtained with 75 mL of contrast material were rated good or excellent. Ninety-two percent of the MR angiograms were rated as either good or excellent (Table 2).
One hundred four vascular territories were involved on the 62 positive CT angiograms. Forty-five (43%) of these territories correlated with lesions on CT scans. Seventy-eight vascular territories were abnormal on the 57 positive CT scans. Most of the vascular lesions were in the MCA or PCA distributions (Table 2).

Twenty-four vascular territories were involved on the 13 positive MR angiograms. Nine (38%) of these territories correlated with lesions on MR images. Most of the lesions were also in the MCA or PCA distributions (Table 2).

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Table 3 gives a comparison of MR angiographic and CT angiographic data. Two hundred forty-two vessels were analyzed in 27 patients who underwent both CT angiography and MR angiography. There was agreement in vessel scoring in 236 of 242 vessels for an overall agreement between the techniques of 98% (Figs 1 and 2). This corresponds with a $\kappa$ value interrater reliability of .86 and a highly significant $P$ value ($P < .000001$). The outliers included two vessels scored as stenotic on CT angiograms but as normal on MR angiograms, and four vessels scored as stenotic on MR angiograms but as normal on CT angiograms. Assuming MR angiography as a standard of reference for comparison purposes, CT angiography had a sensitivity of 83% and a specificity of 99% for the detection of an arterial stenosis or occlusion about the circle of Willis (Table 4).

Table 5 gives a comparison of CT angiographic and DSA data. Two hundred twenty-seven vessels were analyzed in 28 patients who had CT angiography and DSA. There was agreement in vessel scoring in 225 of 227 vessels, for an overall agreement of 99% (Figs 1 and 3). This corresponds with a $\kappa$ value interrater reliability of .89 and a highly significant $P$ value ($P < .000001$). One MCA was misread as occluded on a CT angiogram because of signif-
A 74-year-old woman with a history of sudden onset of right upper extremity weakness and expressive aphasia.

A, Axial noncontrast CT scan shows subtle low density in the left periinsular region, consistent with early left MCA infarction.

B, Axial CT angiographic reconstruction shows high-grade stenosis of a left MCA M2 branch vessel (arrow).

C, Axial MR angiogram (48/6/1, 512 x 256 matrix) obtained 3 days after CT angiography confirms high-grade left MCA M2 branch stenosis (arrow).

D, Axial proton density–weighted MR image (2400/21/2) obtained at time of MR angiography confirms left periinsular MCA infarction.

TABLE 4: Results of CT angiography versus MR angiography and DSA for depicting stenosis or occlusion

<table>
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<tr>
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<th>Sensitivity of CT Angiography, %*</th>
<th>Specificity of CT, %*</th>
<th>Accuracy of CT, %*</th>
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<tr>
<td>MR angiography</td>
<td>83</td>
<td>99</td>
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<td>DSA</td>
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* Percent rounded to nearest whole number.
significant displacement by a large thrombosed MCA aneurysm. One angiographically evident occlusion of the left ICA was missed at CT angiography owing to retrograde flow from the opposite side (Fig 3). In comparison with DSA, CT angiography had a sensitivity of 89% and a specificity of 100% in detection of arterial stenoses or occlusions about the circle of Willis (Table 4). One-millimeter-thick axial source images

FIG 3. A 74-year-old man with a history of global aphasia and right upper extremity weakness.
A, Axial noncontrast CT scan shows subtle low density in left basal ganglia and periinsular region, consistent with acute MCA infarction (arrows).
B, Increased vascular markings in the left periinsular region, consistent with vascular stasis (arrows). This confirms the early MCA infarction suspected on the noncontrast scan.
C, Coronal oblique CT angiographic reconstruction shows stenosis of the distal M1 branch of the left MCA (arrow) with decreased distal flow. Note apparent patency of the distal left ICA (arrowhead).
D, Arterial phase of a right common carotid arteriogram obtained on the same day as CT angiography confirms the stenosis of the M1 branch of the left MCA (arrow). Also note the poor distal left MCA flow and retrograde flow into the distal left ICA. A left common carotid arteriogram (not shown) revealed complete occlusion of the left ICA at its origin.
E, Capillary phase of a right common carotid arteriogram shows collateral flow to distal left MCA branches from the right ACA.

| TABLE 5: Comparison of CT angiography and DSA for classification of stenosis of intracranial vessels |
|---------------------------------|--------|--------|--------|
| CT Angiography                 | DSA    |        |        |
| Normal (0)                     | 217    | ...    | 1      |
| Stenosis (1)                   | ...    | 5      | ...    |
| Occlusion (2)                  | 1      | ...    | 3      |

Note.—Numbers in parentheses represent vessel scores.
proved useful in confirming subtle infarctions in 12% of CT angiographic studies (18 scans) (Fig 3).

Discussion

Many of the previous reports evaluating the usefulness of CT angiography in the brain have focused on aneurysms and vascular malformations (15–17, 21). A recent study by Katz et al (18) evaluated the sensitivity of CT angiography in the detection of arterial anatomy in the circle of Willis and found that CT angiography had a high sensitivity (88.5%) in the detection of vessels in the circle of Willis. These authors found no statistical difference between CT angiography and conventional angiography.

Diagnostic evaluation of the intracranial vasculature in patients with symptoms of acute stroke may provide valuable prognostic information and influence therapeutic interventions. Wong et al (19) found that CT angiography is feasible and potentially useful in the diagnosis of MCA occlusive disease. They found that CT angiography correlated well with transcranial Doppler sonography in 10 patients. Subsequently, the same group reported that MR angiography is more reliable than CT angiography in grading MCA stenosis (20).

In our study, CT angiographic data showed an excellent correlation with MR angiography and DSA. For purposes of comparing CT angiography and MR angiography, we took the liberty of using MR angiography as the standard of reference for arterial stenoses or occlusions. This construct was used only for statistical purposes, as it is well recognized that DSA remains the standard in this setting. However, the lack of a large number of DSA studies in this patient population restricts availability of data. Recent articles by Stock et al (8) and Korogi et al (22) have reported high sensitivity and specificity for MR angiography in detection of intracranial stenoocclusive lesions in comparison with DSA. In our patient population κ statistics and specificity-sensitivity data were similar for CT angiography in comparison with either MR angiography or DSA.

Our data suggest extremely high specificity of CT angiography for intracranial stenoocclusive lesions (Table 4). Our figures of 99% and 100% are close to those obtained by Korogi et al (22) and slightly higher than those reported by Stock et al (8) in comparing MR angiography with DSA. The sensitivity of CT angiography in comparison with MR angiography and DSA was 83% and 89%, respectively. These values are also comparable with those reported in the literature for MR angiography in comparison with DSA (8, 22).

Analysis of false-positive and false-negative CT angiographic findings shows some of the pitfalls inherent in CT and MR angiography. Of the two CT angiographic findings considered false positive in comparison with MR angiographic results, one may have been due to a sharp turn within the vessel. This applies particularly to turns occurring obliquely or orthogonally to the imaging plane and most likely are the result of partial volume artifacts. This problem could be ameliorated by imaging with thinner axial sections; however, this must be weighed against greater imaging noise and lesser scan coverage. The other false-positive CT angiographic finding points out a potential limitation of this study. An MR angiogram obtained 1 day after CT angiography failed to show a stenosis corresponding with infarction. This vessel may have recanalized or undergone distal clot propagation before the MR angiography. This type of problem could be minimized by performing CT angiography and MR angiography on the same day, but this is often not possible because of scheduling limitations and patient considerations.

In comparison with DSA, there was only one false-positive CT angiographic finding. This involved an MCA falsely scored as occluded at CT angiography owing to displacement out of the imaging field of view by a large thrombosed MCA aneurysm. This points out potential problems with an imaging volume limited to 6 cm in craniocaudal dimension. Future improvements in tube cooling may resolve this limitation.

Superimposition of venous structures is a pitfall of CT angiography and accounted for two of four false-negative CT angiographic results in comparison with MR angiography. Both arteries and veins opacify with contrast material and, therefore, venous opacification cannot be eliminated from the reconstructions. This can be especially problematic in regard to the basal vein of Rosenthal and the PCA. Venous opacification may be limited by proper timing of the scans in relation to the contrast injection and careful postprocessing of the data.

One additional false-negative CT angiographic finding was due to retrograde flow into
the distal portion of a proximally occluded ICA. This points out a limitation of the CT angiographic technique in that direction of flow cannot be determined. This could be problematic in cases such as that presented in Figure 3, in which an anterior circulation intracranial arterial stenosis is present on the same side as a carotid occlusion. On the basis of CT angiographic findings, thrombolysis of the intracranial stenosis might be attempted without success owing to lack of arterial access. This is a disadvantage of CT angiography in comparison with MR angiography, which does provide information regarding flow directionality. However, the situation in which there is carotid occlusion combined with retrograde flow into the distal portion of that carotid and an ipsilateral intracranial arterial stenosis is relatively rare. In our series of 47 patients undergoing CT angiography and MR angiography or DSA, we identified five cases of carotid occlusion. In only one case was there retrograde flow mimicking carotid patency at CT angiography. Therefore, we recommend proceeding to conventional angiography in patients who may benefit from intraarterial thrombolytic therapy.

MR angiography is not without pitfalls (8, 15, 18). This technique depends on the properties of flowing blood to generate contrast; however, these same properties may be a source of significant artifacts. This may be especially problematic when there is decreased flow distal to a stenosis, leading to a false-positive diagnosis of occlusion or vascular irregularity. In one patient, a normal MCA distal to an ICA occlusion was scored as stenotic on the MR angiogram but as normal on the CT angiogram and the DSA study. This points out a limitation of assuming MR angiography as the standard of reference.

A similar percentage of CT and MR angiographic examinations had imaging findings of stenoocclusive lesions (43% and 48%, respectively). Only 21% of DSA studies had similar findings. This is most likely due to the preponderance of patients in our study undergoing DSA for suspected ruptured aneurysm (19 of 28 patients). These patients are less likely to have arterial stenoses or occlusions than are patients in whom stroke is the result of infarction.

Greater than 80% of arterial stenoocclusive lesions identified by CT, CT angiography, MR imaging, or MR angiography occurred in a PCA or MCA distribution. This is consistent with the known prevalence of atheroembolic disease. Only approximately 40% of MR or CT angiographic findings correlated with infarctions on corresponding MR images or CT scans (38 and 43%, respectively). Part of the discrepancy may be attributed to temporal factors. For example, in one patient, a left MCA stenosis on a CT angiogram corresponded with a normal CT scan; however, a follow-up CT scan showed a clinically expected left MCA infarction. Similarly, an old infarction noted on CT or MR studies may no longer show a corresponding vascular lesion (ie, recanalization or distal propagation of clot). Additional reasons for discordant findings may relate to lesion size or severity. A low-grade stenosis may not sufficiently reduce flow to cause infarction, or collateral flow may be sufficient. Alternatively, a small cortical lesion may only be consequent to distal branch occlusion/stenosis, which is beyond the resolution of CT angiography or MR angiography.

For this study we chose to standardize scan delay after injection rather than attempt a bolus timing procedure, as advocated by some investigators (9, 11, 18, 21). An optimum delay time of 20 seconds was achieved with a 100-mL dose of contrast material injected over 55 seconds. The advantage of this technique lies in its simplicity and reproducibility. Many of these patients are scanned during off hours when technical expertise and support staff are compromised. This technique reduces total table time for these acutely ill patients. Owing to safety concerns over the use of iodinated contrast media in patients with acute stroke, we initially experimented with a reduced dose (75 mL) to lessen potential toxicity. However, the higher dose of 100 mL used on later scans resulted in improved image quality (Table 1). Therefore, the safety of iodinated contrast material in this patient population warrants further discussion.

It is well known that ionic contrast media have well-defined effects on the cerebral circulation and may result in blood-brain barrier disruption, producing leakage of contrast material and secondary neurologic complications (23–28). Previous researchers investigating the use of ionic contrast media in patients with acute stroke have drawn various conclusions (29–33). A 1987 study by Pfeiffer et al (33) concluded that intravenous administration of ionic contrast material is generally safe and can be used for patients with cerebrovascular dis-
eases but may induce further damage to affected neural tissues in some instances.

Nonionic low-osmolar contrast agents have lower neurotoxicity than ionic contrast media (25, 26, 34, 35). They have little or no effect on the blood-brain barrier and have lesser systemic hemodynamic effects (24, 25, 34, 36). Nonionic contrast agents have therefore been advocated for use in patients with known acute brain ischemia or infarction or any blood-brain barrier disrupting process (25, 28, 35). In our experience with 145 patients we did not encounter any significant immediate adverse events due to the contrast agent nor did we receive any reports of clinical deterioration linked to contrast administration. We consider the use of nonionic contrast media in the setting of acute stroke to be safe.

Recently, investigators have proposed using MR angiography and MR imaging with hemodynamic and diffusion-weighted pulse sequences in the work-up of patients with acute stroke (37, 38). Diffusion and perfusion images are highly sensitive to early infarction and can be coupled with detailed vascular information provided by MR angiography. There remain limitations to this technique, which may favor CT and CT angiography in the acute setting. Imaging times for CT and CT angiography are rapid, thus minimizing the possibility of artifacts from patient motion. Although our average reconstruction time for CT angiography was 30 minutes, it can be reduced to 15 minutes when performed by an experienced technologist. This limits total scan time with reconstruction to approximately 25 minutes. Sorensen et al (37) reported a total examination time of 30 to 35 minutes for diffusion-weighted and hemodynamically weighted echo-planar MR imaging and two-dimensional phase-contrast MR angiography. Although useful for flow directionality, 2-D phase-contrast MR angiography provides only limited morphologic detail of the intracranial vasculature. A 3-D time-of-flight pulse sequence would lengthen the acquisition time considerably. Furthermore, diffusion-weighted and hemodynamically weighted MR technology is not yet commercially available and optimal use of these pulse sequences requires echo-planar imaging. At present, availability of MR technology in the acute setting is markedly reduced compared with CT in the vast majority of institutions. No special life-support or monitoring equipment is necessary for CT scanning, and patients are easily seen when in the larger CT gantry. Patients with contraindications to MR angiography, such as those with pacemakers, aneurysm clips, or other metallic implants, may safely undergo CT angiography, and CT angiography is less expensive than MR angiography.

Compared with DSA, CT angiography is less invasive and entails less risk. Reconstructed 3-D CT angiographic data sets can be viewed at any angle whereas different DSA projections must be acquired separately. CT angiography is also less expensive than DSA.

Disadvantages of CT angiography include the need for iodinated contrast material and ionizing radiation. The amount of radiation is certainly greater than with conventional CT, but still significantly less than with DSA. The amount of ionizing radiation should not be a significant concern in this predominantly older patient population. As in any other situation, iodinated contrast agents must be used with caution in patients with significant risk factors, such as renal insufficiency, congestive heart failure, contrast hypersensitivity, and so forth.

In summary, we have shown that CT angiography is a safe, convenient, and accurate technique for the evaluation of vessel patency about the circle of Willis in patients with symptoms of acute stroke. CT angiography, when closely correlated with patients' clinical conditions, has the potential to become the screening method of choice for evaluating patients with significant vascular lesions amenable to acute intracranial transcatheater thrombolytic therapy.

Acknowledgments

We gratefully acknowledge the assistance of Alyce Norder and Sharon Shinners for secretarial support, Donna Hartley for statistical analysis, James Nichols and Soji Iwanaga for technical support, John Groves for medical photography, and Steven Meyers and Per-Lennart Westesson for critical review of the manuscript.

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