Three-dimensional computerized tomography angiography in patients with hyperacute intracerebral hemorrhage

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Object. The authors confirm the usefulness of extravasation detected on three-dimensional computerized tomography (3D-CT) angiography in the diagnosis of continued hemorrhage and establishment of its cause in patients with acute intracerebral hemorrhage (ICH).

Methods. Thirty-one patients with acute ICH in whom noncontrast and 3D-CT angiography had been performed within 12 hours of the onset of hemorrhage and in whom conventional cerebral angiographic studies were obtained during the chronic stage were prospectively studied. Noncontrast CT scanning was repeated within 24 hours of the onset of ICH to evaluate hematoma enlargement.

Findings indicating extravasation on 3D-CT angiography, including any abnormal area of high density on helical CT scanning, were observed in five patients; three of these demonstrated hematoma enlargement on follow-up CT studies. Thus, specificity was 60% (three correct predictions among five positives) and sensitivity was 100% (19 correct predictions among 19 negatives). Evidence of extravasation on 3D-CT angiography indicates that there is persistent hemorrhage and correlates with enlargement of the hematoma.

Regarding the cause of hemorrhage, five cerebral aneurysms were visualized in four patients, and two diagnoses of moyamoya disease and one of unilateral moyamoya phenomenon were made with the aid of 3D-CT angiography. Emergency surgery was performed without conventional angiography in one patient who had an aneurysm, and it was clipped successfully.

Conclusions. Overall, 3D-CT angiography was found to be valuable in the diagnosis of the cause of hemorrhage and in the detection of persistent hemorrhage in patients with acute ICH.

KEY WORDS • intracerebral hemorrhage • three-dimensional computerized tomography angiography • extravasation • cerebral aneurysm

Pontaneous intracerebral hemorrhage (ICH) is usually a monophasic event, ^{16,17} but bleeding can persist for up to 6 hours postictus; several authors have reported that in some patients with ICH the bleeding can continue even later during the treatment course. ^{1,8,22,23,26,27, 35,36} Continued bleeding associated with ICH may lead to enlargement of an existing hematoma, resulting in progressive neurological deterioration. ^{1–3,6,10,23}

We sought to determine whether evidence of extravasation on three-dimensional computerized tomography (3D-CT) angiography, and specifically leakage of contrast medium seen as a high-density area on helical CT images obtained at the site of the hemorrhage in the hyperacute stage, was useful in identifying active bleeding. As a corollary, we evaluated the reliability of the absence of extravasation as an indication of hemostasis that could be suitable for guiding decisions about surgery and intensive care.

In some cases of acute ICH, structural causes of hemorrhage may escape detection on routine CT scanning, including bleeding from a cerebral aneurysm and bleeding from a vascular malformation.⁴⁰ Recently, 3D-CT angiography has shown promise as a highly sensitive modality for determining the source of hemorrhage.^{7,12,13,21,29,31,32}

In this study, we assessed the effectiveness of 3D-CT angiography in detection of persistent bleeding in the acute stage of ICH and in identification of any anatomical causes of bleeding.

Clinical Material and Methods

Patient Population

Between November 1997 and December 1998, we prospectively assessed 31 consecutive patients in whom ICH had been diagnosed and who met the following inclusion criteria: 1) presence of ICH; 2) an initial CT scan performed within 12 hours after onset and a second CT scan performed within 24 hours of onset; 3) 3D-CT angiography performed within 12 hours after onset; and 4) cerebral angiography performed during the chronic stage. We excluded patients with a history of chronic renal failure and those with a history of an allergic reaction to iodine, as well as patients whose general medical condition was unstable. Of a total of 92 patients with ICH who were treated during the study period, 22 were admitted more than 12 hours postictus; 14 did not undergo a second CT scan to assess hematoma enlargement during the interval speci-

fied above because of emergency surgery or hemodynamic instability; and 25 did not undergo 3D-CT angiography and/or cerebral angiography because of emergency surgery, hemodynamic instability, inability to obtain consent, or other factors. The remaining 31 patients were studied; 17 (55%) of these were men. Patients included in the study ranged in age from 34 to 74 years (mean 56.4 years).

A neurological examination was performed in each patient on admission, and their vital signs were recorded. Intracranial hemorrhage was confirmed on CT scanning, and a calcium channel antagonist was administered to reduce the systolic blood pressure to 80% of the initial value or to keep it below 140 mm Hg for the first 6 hours postictus. The blood pressure was monitored continuously for 24 hours after the clinical onset of hemorrhage. Venous blood samples were used to determine white and red blood cell counts, platelet count, glutamate-oxaloacetate transaminase concentration, and glutamate-pyruvate transaminase concentration. Patients in whom the 3D-CT angiographic findings did not indicate a specific vascular abnormality were divided into groups of individuals with and without evidence of contrast material extravasation on 3D-CT angiography for comparison of blood test results and of systolic and diastolic blood pressures at admission and 6 hours after onset. Informed consent was obtained from all patients or their families.

Computerized Tomography Scanning

Hematoma volume on CT scans (in millimeters) was estimated based on an ellipsoid alpha model as: $\pi/6 \times 1000$ long diameter \times short diameter \times number of 1-cm-thick CT slices. When intraventricular hemorrhage was present, accurate measurement of parenchymal hemorrhage was considered impossible because of the spread of blood via cerebrospinal fluid pathways, and in these cases no hematoma volume calculation was performed. When the hematoma was irregular in shape, the volume of each portion was estimated separately. Initial CT scanning was performed 0.5 to 11.5 hours after onset (mean 6.2 hours). The second CT scan was obtained within 24 hours of onset to evaluate hematoma enlargement.

When expansion of the hematoma was detected on CT scans from changes in size or shape, an increase in volume of at least 15 ml was the parameter used to define significant enlargement. Initial 3D-CT angiographic images were assessed for abnormalities of vessels and identifiable contrast extravasation by a neuroradiologist (R.T.) and a neurosurgeon (Y.M.).

Computerized Tomography Angiography

Findings on 3D-CT angiography were classified as exhibiting one of three patterns. Type A, presence of extravasation without evidence of vascular abnormality as the source of hemorrhage (Fig. 1); Type B, absence of extravasation with no vascular abnormality as the source of hemorrhage (Fig. 2); or Type C, presence of a vascular abnormality as the source of hemorrhage (Fig. 3).

When ICH was detected on the initial CT scan, 3D-CT angiography was performed using a model W 3000 AD scanner (Hitachi Corp., Tokyo, Japan). A conventional examination was performed first, with 10-mm collimation

and 10-mm slice thickness, followed by helical CT studies with the following parameters: 120 kV, 175 mA, 1 second, 1-mm collimation, 1 mm/second table speed (1:1 pitch), 51-second acquisition time, and 21-cm field of view. Scanning began at the posterior margin of the hematoma and extended to the superior margin, including the middle cerebral artery and the circle of Willis, as visualized after an 100-ml intravenous bolus injection of nonionic contrast medium (Iomeprol, 350 mg iodine/ml) at 2 ml/second with a 25-second prescanning delay. Overlapping axial images were reconstructed at 1-mm intervals and stored as source images for further image processing.

The time required for patient positioning, noncontrast CT scanning, and helical CT data acquisition averaged 10 minutes per patient. Three-dimensional images were generated from the volumetric data in less than 10 minutes.

Reconstructions were performed in three dimensions at the console by using standard scanner software. The matrix size was 512 × 512 cm, and the field of view was adapted to the site and size of the lesions. Images for 3D-CT angiography were reconstructed using the voxel transmission method, ^{15,24,31} a volume-rendered technique. This method allows precise readings of the x-ray attenuation value for each voxel and permits generation of 3D-CT angiographic images reflecting x-ray attenuation within the threshold range. ¹⁵ For postprocessing, threshold values were set to a lower level (55–70 Hounsfield units [HU]). In all examinations, the 3D reconstruction procedure was completed by the same radiologist (R.T.), using the same technique.

Cerebral Angiography

Conventional cerebral angiographic studies were performed during the chronic stage in patients in whom 3D-CT angiography had not demonstrated a vascular abnormality, so that causes of hemorrhage such as vascular anomalies, cerebral aneurysms, moyamoya disease, and brain tumors could be ruled out. Conventional angiographic studies were performed in the acute stage in patients in whom 3D-CT angiography demonstrated a vascular abnormality. Although conventional angiography is not performed routinely in all patients with ICH at our institution,³⁹ we performed conventional angiography in all patients in this study to confirm the accuracy of 3D-CT angiography in identifying causes of hemorrhage. In line with relative clinical urgency, angiographic studies were performed in the acute stage only in patients with Type C findings on 3D-CT angiography.

Using the standard Seldinger technique, the right common femoral artery was punctured, and one- or two-vessel angiography was performed using a cut-film technique. Findings on conventional angiography were correlated with the various patterns seen on 3D-CT angiographic studies.

Choice of Treatment

Surgery for putaminal hemorrhage was indicated when the hematoma volume exceeded 30 ml or impairment of consciousness was present,¹¹ provided that the patient seemed able to tolerate an operation. We treated patients with pontine or caudate nuclear hemorrhage conservatively. Patients with thalamic, cerebellar, or subcortical hem-

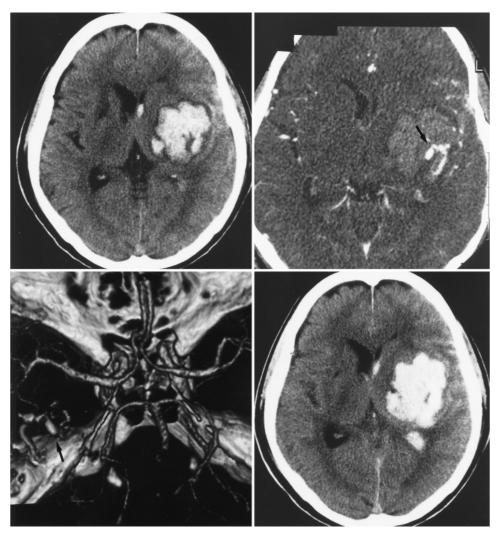


Fig. 1. Computerized tomography and 3D-CT angiographic studies obtained in a patient with ICH demonstrating a Type A pattern (extravasation). *Upper Left:* The initial CT study displaying a high-density area in the left putamen. *Upper Right:* A CT angiogram with a 2D image revealing areas of contrast enhancement (*arrow*) within the hematoma. *Lower Left:* A 3D reconstruction image demonstrating contrast extravasation (*arrow*) and no vascular abnormality. In this patient, a left carotid artery angiogram obtained during the chronic stage revealed no vascular abnormality. *Lower Right:* Follow-up CT scan demonstrating enlargement of the hematoma.

orrhage underwent surgery if we observed impairment of consciousness, again provided that they were able to tolerate the operation. In patients with concomitant massive intraventricular hemorrhage, ventricular drainage was also performed. Patients underwent craniotomy if their hematomas were too large or too irregular in shape for stereotactically guided aspiration. We did not use 3D-CT angiographic findings as an indication for operation.

Statistical Analysis

Data are expressed as the mean \pm standard deviation (SD). Comparisons between groups were analyzed using the Fisher test. To compare cases with Type A and B patterns of 3D-CT angiography contrast enhancement with respect to frequency of hematoma expansion, Student's ttest was used.

Results

A significant difference (p < 0.01) was noted in the time from symptom onset to performance of the initial 3D-CT studies between patients with and without evidence of extravasation (Types A and B; Table 1). The interval between noncontrast CT and 3D-CT angiographic studies ranged from 6.2 to 12.7 minutes (mean 10.2 minutes). The time interval between the first and second CT scan was shorter for Type A than for Type B cases (p < 0.01). In eight patients (four each with a Type A or Type B pattern), 3D-CT angiography was performed within 6 hours of the ictus; scans were obtained after more than 6 hours for the other 16 hematomas (one with the Type A pattern, 15 with Type B). Extravasation was evident on 3D-CT angiographic studies in five patients. Enlargement of the hematoma on follow-up CT scans was detected in three patients (Table 1), demonstrating a statistically significant correla-

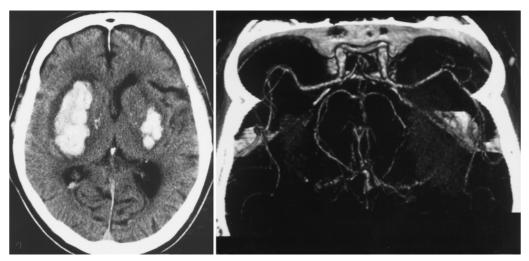


Fig. 2. Computerized tomography and 3D angiographic studies demonstrating a Type B pattern (no extravasation). *Left:* The initial CT scan demonstrating high-density areas in both putamina. *Right:* A 3D reconstruction image in which no vascular abnormality and no contrast extravasation are seen. In this patient, a follow-up CT scan revealed no enlargement of the hematoma. A left carotid artery angiogram obtained with compression of the right carotid artery demonstrated no vascular abnormality.

tion with 3D-CT angiographic evidence of extravasation (p < 0.01). Nineteen patients with no evidence of extravasation on 3D-CT angiographic studies were found to have no enlargement of the hematoma. All enhancing (extravasating; Type A) hematomas except two increased in volume, whereas all nonenhancing hematomas (nonextravasating; Type B) remained the same size. The resulting prediction rate for enlargement was 22 (91.6%) of 24 patients, with two false-positive predictions and no false negatives. Thus, specificity was 60% (three correct predictions among five positives) and sensitivity was 100% (correct predictions among all 19 negatives).

Two vascular abnormalities were detected incidentally on 3D-CT angiography and cerebral angiography in association with Type A or B patterns. One was a cerebral aneurysm of the distal portion of the anterior cerebral artery, and the other was a dural arteriovenous malformation (AVM) in the posterior cranial fossa. Type C (vascular abnormality) 3D-CT angiographic findings included five cerebral aneurysms in four patients; bilateral moyamoya disease in two patients; and a unilateral moyamoya phenomenon in one patient. In patients with the Type C pattern, conventional angiography was performed in the acute stage. Subarachnoid hemorrhage was also evident in all four patients with ruptured cerebral aneurysms, in two patients with bilateral moyamoya disease, and in one patient with unilateral moyamoya. Contrast material extravasation was detected on 3D-CT angiographic studies only in the patient with Type C findings due to unilateral moyamoya involvement (Fig. 3). Additionally, among Type C cases enlargement of the hematoma was evident only in this patient. These findings correlated completely with those from conventional cerebral angiography.

Among the 24 patients with Type A or B patterns, nine underwent surgery. The time between the onset of ICH and surgical intervention ranged from 26.5 to 52 hours (mean 28.2 hours). Craniotomy was performed in three of these patients, whereas five underwent ventricular drain-

age only. The remaining patient underwent stereotactically guided aspiration only. There was no postoperative enlargement of the hematoma in any patient. Patients who underwent craniotomy included two with a Type A pattern and one with Type B. We encountered no active bleeding in any patient during surgery.

Correlations of 3D-CT angiographic findings with blood pressure are summarized in Table 2. No significant differences were seen with respect to hemostatic parameters and blood pressure between patient groups with and without evidence of contrast extravasation on 3D-CT angiographic studies.

Discussion

Based on our results, including a prediction rate of 91.3%, 3D-CT angiography is a promising method for prediction of hematoma enlargement. In this study, we were able to predict the enlargement of all hematomas correctly, except in two cases in which "positive" imaging but with no subsequent enlargement was observed. All hematomas with no findings of enhancement remained unchanged in volume.

Our results indicate that evidence of contrast extravasation on 3D-CT angiographic studies correlated well with hematoma enlargement and that 3D-CT angiography was highly sensitive in diagnosing vascular abnormalities in patients with ICH. The finding of extravasation on 3D-CT angiographic studies indicated a persistent hemorrhagic process and predicted an increase in hematoma size. Awareness that a hematoma is likely to enlarge and accurate diagnosis of any underlying vascular abnormality during the acute phase are very important for management decisions. Thus, 3D-CT angiographic findings should be useful in determinations of the required level of blood pressure control, indications for surgery, and choice of craniotomy or stereotactically guided surgery. When hemostasis is confirmed on 3D-CT angiographic studies,

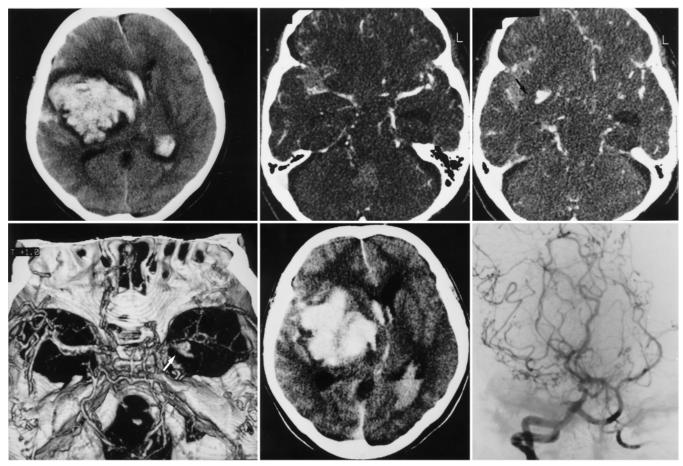


FIG. 3. Computerized tomography, 3D-CT angiographic, and angiographic studies demonstrating a Type C pattern (vascular abnormality). *Upper Left:* The initial CT scan revealing a high-density area in the right frontotemporal region. *Upper Center* and *Upper Right:* A CT angiogram with a 2D image demonstrating a stenotic change in the middle cerebral artery (*upper center*) and areas of contrast enhancement (*arrow*) within the hematoma (*upper right*). *Lower Left:* A 3D reconstruction image demonstrating occlusion of the right internal carotid artery, moyamoya vessels, and areas of contrast enhancement (*arrow*). *Lower Center:* Follow-up CT scan revealing enlargement of the hematoma. *Lower Right:* Right carotid artery angiogram demonstrating occlusion of the right internal carotid artery and moyamoya vessels.

CT-monitored, stereotactically guided aspiration of the hematoma would be possible, whereas evidence of continued bleeding on 3D-CT angiographic studies would contraindicate stereotactically guided aspiration because of the anticipated difficulty in controlling bleeding; craniotomy would be necessary. A hyperacute-stage hematoma has a density similar to that of the cerebral parenchyma on two-dimensional (2D) images before reconstruction of the 3D image, making extravasation of contrast material into an existing hematoma easy to visualize. Unlike angiography, 3D-CT angiography is noninvasive. 14,21,29,31,34

TABLE 1
Extravasation on 3-D CT angiography, timing of imaging, and hematoma enlargement in 24 patients with Type A or B ICH

Extravasation	Hours From Symptom Onset to Angiography (mean ± SD)	Enlargement of Hematoma
present in 5	2.2 ± 1.03	present in 3, absent in 2
absent in 19	6.1 ± 3.8	present in 0, absent in 19

However, not many institutions presently have the resources to perform emergency 3D-CT angiography at all times of the day.

Significance of Contrast Extravasation on 3D-CT Angiography

Kandel and Peresedov²⁰ have observed recurrent hemorrhage in 16% of patients with hypertensive ICH, and Yamanaka and Sato³⁷ have reported a 4% rate of recurrent hemorrhage after aspiration surgery. Yamaguchi, et al.,³⁵ have found that contrast medium extravasation was demonstrated on angiographic studies in 42% of patients in whom the initial CT scan was obtained within 5 hours post-ICH. Brott, et al.,³ have reported that hematoma enlargement occurred in 38% of patients with ICH. In our study we observed hematoma enlargement on the second CT scan in 12.5% of patients whose first CT study was performed within 12 hours of the ictus. The mean time to the initial CT scan was 5.22 ± 12.73 hours.

Some investigators^{18,25,26,36} have reported that in patients with hypertensive ICH, the finding of contrast medium extravasation from ruptured blood vessels was common

when cerebral angiographic studies were performed in the hyperacute stage, within a few hours of onset. Intravenously administered contrast material cannot cross the normal blood-brain barrier (BBB), and contrast medium leakage seen on CT scans has been proven to originate from ruptured vessels or from vessels with ischemic changes in their walls caused by compression by the hematoma, resulting in increased vascular permeability.^{2,38}

In each patient in whom 3D-CT angiographic findings indicated contrast extravasation, such active hemorrhage into the preexisting hematoma could be potentially misconstrued as evidence of an AVM, a nearby developmental venous anomaly, or a portion of an aneurysm. However, orientation with respect to normal vascular structures, absence of distal connections to other vascular structures, and demonstration of contrast agent pooling within the preexisting hematoma effectively exclude such diagnoses.¹² Conventional cerebral angiographic and operative findings also corroborate diagnoses made using 3D-CT angiography. Additionally, whether contrast enhancement indicates an abnormal BBB or "contrast extravasation" cannot be determined with complete certainty. Our results indicate that evidence of contrast material extravasation on 3D-CT angiographic images correlated well with hematoma enlargement, and no hematoma enlarged without contrast extravasation. Furthermore, if an abnormal BBB were responsible for enhancement, our Type B cases, with no contrast enhancement within or surrounding the hematoma, probably would not have shown this pattern (Fig. 2). The reason why two "positive extravasation" hematomas did not enlarge subsequently is not clear. However, in these two cases the amount of extravasation was very small, and hematoma enlargement was too slight to meet our criteria for hematoma enlargement in this study.

The display threshold used for 3D-CT angiography (55-70 HU) excludes brain tissue (approximately 40 HU) and cerebrospinal fluid density (0 HU). The skull base, opacified vasculature, and extravasated opacified blood (all > 100 HU) are all displayed, although not all important details are known regarding opacity in areas with extravasation.

Vascular Abnormalities Seen on 3D-CT Angiography

Conventional angiography remains the gold standard for evaluation of vascular abnormalities such as intracranial aneurysms, AVMs, and moyamoya disease. Because this is an invasive procedure with a low but definite risk, the expected diagnostic yield and risk to the patient must be weighed. 13,21,39

One major task in patient management is to determine whether a hemorrhage is secondary to an underlying structural vascular abnormality, such as an AVM, a cerebral aneurysm, or moyamoya disease, so that appropriate treatment can be administered to prevent rebleeding. Computerized tomography angiography represents a non-invasive alternative for vascular abnormality assessment; 13,14,21,29,31,34 its strengths and limitations have been evaluated critically in recent years. 29,38 This modality has been demonstrated to be highly sensitive for detecting aneurysms larger than 3 mm. 13,21,29,32 The orientation of cerebral aneurysms can be difficult to determine on 3D-CT angiography when they cause only subarachnoid hemor-

TABLE 2

Blood pressure in patients with and without extravasation on 3-D

CT angiography*

Parameter (mm Hg)	Extravasation	No Extravasation
initial systolic BP	190.0 ± 40.1	212.4 ± 40.3
initial diastolic BP	105.0 ± 12.9	131.0 ± 35.1
systolic BP at 6 hrs	139.8 ± 8.3	153.0 ± 20.1
diastolic BP at 6 hrs	74.5 ± 5.5	82.9 ± 15.2

^{*} Values are expressed as the mean \pm SD. There was no significant difference between patients with and without extravasation. Abbreviation: BP = blood pressure.

rhage. Because a preexisting hematoma indicates the location of a vascular abnormality such as an aneurysm, the presence of ICH facilitates localization of a causative vascular anomaly, especially in patients with multiple cerebral aneurysms. Therefore, in patients with ICH, 3D-CT angiography is particularly useful in aiding diagnosis of vascular abnormalities.

Magnetic Resonance Imaging, Conventional Angiography, and 3D-CT Angiography

We have previously described patients with spontaneous ICH in whom evidence of extravasation on magnetic resonance (MR) imaging indicated active bleeding.²⁸ We believe that postcontrast MR imaging is sometimes more accurate than 3D-CT angiography for detection of extravasation. On MR images obtained in the hyperacute stage, hematomas show a signal intensity essentially similar to that of cerebral parenchyma, so contrast medium extravasation can be visualized easily as a high-intensity area on T₁-weighted images.^{28,33} Gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA)-enhanced MR imaging reflects the extravasation component more selectively than enhancement from an iodinated contrast agent on CT scans because of the "flow void" phenomenon, which obscures Gd-DTPA in vessels with relatively high flow. Whereas 3D-CT angiography can be used to visualize areas of extravasation as well as the vasculature, Gd-DTPA-enhanced MR imaging would not display the vasculature because of the flow void phenomenon. Therefore, MR imaging is more useful for detection of extravasation but not for depicting the responsible vascular lesion. When intracranial tumors are the sources of hemorrhage, Gd-DTPA-enhanced MR imaging is more diagnostically sensitive than contrast-enhanced CT modalities. Other drawbacks of 3D-CT angiography relative to MR imaging include the need for patients to undergo intravenous injection of iodinated contrast medium and exposure to ionizing radiation.

Whereas 3D-CT angiography is essentially as accurate as conventional angiography in detection of vascular abnormalities, 13,32,34,39 pre- and postcontrast MR imaging is less useful in depicting these lesions than angiography, particularly in the case of cerebral aneurysms. Both 3D-CT angiography and MR angiography show a sensitivity approaching 90% for aneurysms larger than 3 mm in diameter according to conventional angiography. 13,32,34,39 Of importance, however, MR imaging and MR angiography require 30 to 60 minutes to obtain images, whereas 3D-

CT angiography can be performed more rapidly, which is an important advantage for patients who need immediate surgical or nonsurgical intervention. Also, MR imaging and MR angiography cannot be performed in patients who have pacemakers. Replacement of the alternate modality, digital subtraction angiography, with CT angiography in these cases should substantially reduce costs, although 3D-CT angiography cannot demonstrate collateral vessels, small perforating vessels, arteriosclerotic change, or vasospasm as clearly as digital subtraction angiography. In many cases, surgery may be based solely on 3D-CT angiography, a particularly important point for rapidly deteriorating patients with ruptured aneurysms. However, a negative result does not completely exclude the presence of a vascular lesion, and conventional cerebral angiography may be required. Because a hyperacute-stage hematoma has approximately the same density as cerebral parenchyma on two-dimensional CT scans, contrast extravasation into a preexisting hematoma was easy to visualize. For the same reason, vascular structural abnormalities were readily demonstrated on 3D-CT angiographic studies, even in patients with large intraparenchymal or thick subarachnoid clots.

Relationships to Clinical Parameters

In the hyperacute stage of hypertensive ICH, reported risk factors associated with hematoma expansion include liver dysfunction, 9.10 excessive alcohol consumption, 6.9.19.30 anticoagulant therapy, 5.10.19 thrombocytopenia, 30 poorly controlled hypertension, 4.5.19.23 and certain shapes of the hematoma on initial CT scans, 10 as well as extravasation on cerebral angiographic studies performed in the acute stage. 25.26 In our study, 3D-CT angiographic findings of extravasation showed no significant correlation with laboratory parameters and blood pressure levels.

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