Evaluation of Patients with Acute Ischemic Stroke Using Angiographic C-arm Cerebral Blood Volume (C-arm CBV) Measurements

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Objective: CT-like images and cerebral blood volume (CBV) measurements have become available due to technical improvements in the angiographic C-arm system and workstation. In this study, we evaluated the usefulness of C-arm CBV measurements in patients with acute ischemic stroke.

Methods: The study included 27 consecutive patients admitted for acute ischemic stroke due to major intracranial artery occlusion within 7 hours of onset. Cerebral angiography and C-arm CBV measurements were performed immediately after CT or MRI. The areas with reduced CBV in CBV color maps were classified into infarcted and non-infarcted areas according to CT/MRI images obtained 8–48 hours after onset, and their relationship with CBV was retrospectively evaluated.

Results: The mean CBV values and the relative CBV ratios (ipsilateral/contralateral side) were 1.29 ± 0.51 mL/100 g and 0.41 ± 0.17 in the infarcted area and 3.19 ± 0.17 mL/100 g and 0.8 ± 0.1 in the non-infarcted areas. The CBV values and relative CBV ratios in infarcted areas with hemorrhage (n = 5) were 0.95 ± 0.56 mL/100 g and 0.3 ± 0.17, and significantly lower than in infarcted areas without hemorrhage.

Conclusion: C-arm CBV measurements with an angiography system can be performed readily in a short time and may provide useful information for the treatment of acute ischemic stroke patients.

Keywords: C-arm, cerebral blood volume, ischemic, stroke, digital subtraction angiography

Introduction

With the recent development of the angiographic C-arm system and workstation, the application called DynaPBV Neuro (Siemens AG, Forchheim, Germany) using C-arm CT was developed, and the evaluation of cerebral blood volume (CBV) using an angiography system has also become possible.

In this study, we retrospectively investigated the relationship of C-arm CBV data at the onset of acute ischemic stroke with infarcted and non-infarcted areas determined by CT or MRI performed 8–48 hours after stroke onset.

Subjects and Methods

Cerebral angiography and C-arm CBV measurements were performed after approval by the institutional review board of our hospital and with sufficient informed consent from the patients and their families prior to the examinations.

Subjects

We evaluated 27 consecutive patients, who were emergently transported to the hospital within 7 hours after the onset of acute ischemic stroke due to occlusion of major intracranial arteries. All patients underwent cerebral angiography and C-arm CBV measurements between February 2011 and April 2014. Table 1 shows the characteristics of the subjects. They consisted of 23 males and 4 females, with a mean age of 68.8 ± 9.3 years. The occluded vessels identified by angiography were as follows: the internal carotid artery (ICA) in 6; middle cerebral artery (MCA)
in 19, which included the horizontal segment (M1) in 6, insular segment (M2) in 1 and opercular–terminal segments (M3–M4) in 12; and basilar artery (BA) in 2.

Methods
After arrival, acute ischemic stroke due to major intracranial artery occlusion was diagnosed by MRI or MRA, and intravenous thrombolysis with tissue plasminogen activator (t-PA) was initiated in patients with an indication for this treatment. Immediately after this, cerebral angiography was performed to determine the indication for acute-phase recanalization. Cerebral angiography was also performed immediately in patients who had no indication for intravenous t-PA to examine the indication for acute-phase recanalization.

If patients in the acute phase of major artery occlusion showed marked disturbance of consciousness and could not be sufficiently calmed by head fixation alone, diazepam was injected intravenously as necessary to maintain sedation.

Angiography procedure: Under local anesthesia, a 4F or 9F sheath was inserted into the femoral artery at the inguinal region; a diagnostic 4F catheter (CX catheter; Gade lius, Tokyo, Japan) was placed in the ascending aorta immediately above the aortic valve, and C-arm CBV measurements were performed. Then, conventional angiography was carried out, and the intracranial blood vessels were examined. By evaluating the state of the intracranial vessels and changes in the general condition and neurologic findings together, the indication for acute recanalization was established. Table 1 shows the details of the treatment. To identify the infarcted area, CT or MRI was performed 8–48 hours after stroke onset.

C-arm CBV imaging procedure
C-arm CBV measurements were performed using a biplane flat-panel system (Artis zee BA; Siemens AG). The procedure was basically the same as that for transarterial contrast administration that we previously reported,5 but since the scan delay time was generally stable at 8.3 ± 1.5 seconds, it was set at 9 seconds by omitting test imaging to shorten the examination time and reduce the use of contrast medium.

C-arm CBV imaging was performed at a tube voltage of 70 kV, tube current of 460 mA, rotation angle of 200°, frame number of 397, and scanning time of 8 seconds. Mask images were obtained first, and then fill images were obtained on the 2nd C-arm CT with a 9-second scan delay after the beginning of contrast injection. The contrast medium consisted of 85 mL of a non-ionic iodine-based contrast medium (Iomeron 300; Eisai, Tokyo, Japan) diluted with physiologic saline to 300 mg I/mL and was continuously injected using a power injector at 5 mL/sec until the end of fill image acquisition. Although the contrast medium was initially diluted to 50%, dilution to 30% was used in 11 patients to reduce the dose of contrast medium because the image quality was not affected by dilution to 30%6).

The image data were analyzed with the accompanying workstation (syngo XWP VB 15D; Siemens AG), and CBV color maps were prepared (matrix size = 512 × 512, voxel size = 0.47 mm, field of view = 240 mm). The C-arm CBV system could generate CBV color maps in any preferred cross section; however, axial cross sections were used in this study for analysis in a similar manner to images obtained by CT/MRI.

Evaluation methods
In this study, cerebral infarction was diagnosed 8–48 hours after stroke onset as low-density areas or high-density areas reflecting hemorrhagic infarction on CT, or hyperintense areas on diffusion-weighted MRI. The areas of newly developed infarction were regarded as infarcted areas, and brain tissues around the infarcted areas that did not develop infarction despite decreases in CBV were regarded as non-infarcted areas. Regions of interest (ROIs) were determined in the infarcted and non-infarcted areas in the CBV color maps, and the mean CBV was calculated in these ROIs as well as the relative CBV ratios (ipsilateral ischemic/contralateral non-ischemic side). The state of brain ischemia estimated from the relative CBV ratios and changes in 19, which included the horizontal segment (M1) in 6, insular segment (M2) in 1 and opercular–terminal segments (M3–M4) in 12; and basilar artery (BA) in 2.

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in the brain parenchyma 8–48 hours after stroke onset (in the infarcted and non-infarcted areas) were retrospectively evaluated.

Results

No complications due to any of examinations were observed in any patient, and satisfactory C-arm CBV data were collected in all patients. The CBV values and relative CBV ratios in the infarcted and non-infarcted areas based on the CBV color maps of the 27 patients are shown in Fig. 1. The mean CBV values and relative CBV ratios were 1.36 ± 0.45 mL/100 g and 0.44 ± 0.15 in the infarcted areas and 3.19 ± 0.17 mL/100 g and 0.8 ± 0.1 in the non-infarcted areas. A significant difference was observed in the relative CBV ratio between the infarcted and non-infarcted areas (P < 0.001). Furthermore, when the relative CBV ratios in the non-infarcted and infarcted areas were compared between the right and left sides, the ratios in the infarcted areas were 0.39 ± 0.15 on the left and 0.48 ± 0.15 on the right (P = 0.17), and those in the non-infarcted areas were 0.81 ± 0.1 on the left and 0.79 ± 0.11 on the right. The lack of any major differences between the left and right sides (P = 0.78) indicates that there was no significant asymmetry.

According to the present results, the lower limit of the relative CBV ratio in the non-infarcted area was 0.63. In the five patients who showed hemorrhagic changes, the mean CBV in the hemorrhagic areas was 0.95 ± 0.56 mL/100 g, and the relative CBV ratio was 0.3 ± 0.17; these values were lower than those in infarcted areas without hemorrhagic changes (P <0.001).

Representative cases are presented

Case 1: A 70-year-old woman exhibited right hemiplegia and aphasia and was transported to our hospital 7 hours after onset. Based on MRI, a diagnosis of acute ischemic stroke due to left ICA occlusion was made (Fig. 2A), and the patient was admitted to the cerebral angiography laboratory 7.5 hours after onset. First, the C-arm CBV examination using a 50% dilution of contrast medium showed that the relative CBV ratio was lowest (0.5) from the left putamen to the caudate nucleus, and that in the MCA cortical region in the left cerebral hemisphere was 0.78–0.91 (mean: 0.86) (Fig. 2C). On cerebral angiography performed immediately after C-arm CBV measurement, left common carotid angiography revealed occlusion of the left C3 portion (Fig. 2D). Right common carotid angiography showed collateral flow via the leptomeningeal artery to the left cerebral hemisphere (Fig. 2E). Although some time had elapsed from onset, no clear hyperintense areas were noted on diffusion-weighted MRI, and the National Institute of Health Stroke Scale (NIHSS) score was 16. Therefore, we performed mechanical thrombectomy for the occluded left ICA and obtained adequate recanalization (thrombolysis in cerebral infarction grade 3) 8 hours after stroke onset (Fig. 2F).

Diffusion-weighted MRI performed 24 hours after stroke onset showed cerebral infarction from the left putamen to the caudate nucleus, and the CBV ratio was reduced in these areas (Fig. 2B).

Case 2: An 82-year-old man developed right hemiplegia and aphasia and was transported to our hospital 1.5 hours after stroke onset. On MRI, acute ischemic stroke due to left ICA occlusion was diagnosed (Fig. 3A). The NIHSS score was 23, and Alberta Stroke Program Early CT score-DWI was 8. Although the patient was elderly and was severely ill, he was transferred to the angiography laboratory 2.5 hours after stroke onset under intravenous thrombolysis with t-PA, as his family wished aggressive treatment. First, on C-arm CBV study using a 50% dilution of contrast medium, the relative CBV ratio was lowest (0.11) in the left basal ganglia, and it was 0.81±0.1 on the left and 0.79±0.11 on the right. The lack of any major differences between the left and right sides (P = 0.78) indicates that there was no significant asymmetry.

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Mean CBV values and CBV ratios for salvaged, ischemic, and hemorrhagic lesions. CBV: cerebral blood volume

Fig. 1
Head CT scans performed 8 hours after stroke onset showed extensive infarction of the left MCA territory and hemorrhagic infarction of the left basal ganglia (Fig. 3C).

**Discussion**

Information concerning the brain circulation obtained in the acute phase has been reported to be useful for the prognosis of brain parenchyma in an ischemic state. In the area with reduced perfusion not visualized as hyperintensity on diffusion-weighted MRI in the acute phase of cerebral ischemia (so-called diffusion-perfusion mismatch), it may be possible to estimate the final area of infarct core from the area of reduced perfusion. Therefore, CT perfusion, which is qualitative rather than quantitative, is performed at many institutions when an emergency brain perfusion study is required. CT perfusion is often evaluated because CBV, CBF, and mean transit time can be measured readily in a short time using contrast medium.

A C-arm CBV study consists of two sequential CT scans (i.e., mask run and fill run carried out with contrast administration), and CBV color maps are prepared by analyzing the differences in the concentration distribution of the contrast medium between the two images. CBV color maps have been reported to show a close correlation with CBV images derived from CT perfusion. We reported the effectiveness of C-arm CBV measurement by transarterial contrast administration in the ascending aorta immediately above the aortic valve, which facilitated the collection of CBV data during angiography. In this study, we performed a C-arm CBV study in patients with acute ischemic stroke and calculated the relative CBV ratio, which is the ratio of CBV on the ischemic ipsilateral side to CBV on the normal contralateral side. The results...
showed that the mean relative CBV ratio was 0.8 ± 0.1 in the areas that were later shown by CT or MRI to have been salvaged, but was 0.44 ± 0.15 in the areas that were infarcted, and hemorrhagic changes were more likely to occur when the relative CBV ratio was reduced even further. The lower limit of the relative CBV ratio in the areas that were not infarcted was 0.63. Murphy et al.\textsuperscript{15)} measured the blood flow in lesions of patients with acute cerebral ischemia using CT perfusion and reported that CBV was 1.12 ± 0.37 mL/100 g in the infarcted areas, but 1.78 ± 0.3 mL/100 g in the contralateral intact areas. The relative CBV ratio calculated from these values was similar to the mean relative CBV ratio in our study.

We previously reported the results of a C-arm CBV study that showed that CBV in normally perfused tissue was significantly lower on the left side in the anterior cerebral artery and MCA territories than on the right side.\textsuperscript{4)} However, in the present study, no asymmetry was observed in the relative CBV ratio in the non-infarcted or infarcted areas regardless of the severity of ischemia. This suggests that the mean interhemispheric difference in CBV is about 10% in the normal brain, but increases by 30%–91% due to ischemia. Furthermore, the evaluation of the relative CBV ratio obviates the need to consider interhemispheric differences in CBF in patients with acute ischemic stroke. Since a relationship was observed between the relative CBV ratio and the state of brain ischemia, and since correction for interhemispheric difference of the ischemic brain is unnecessary, the relative CBV ratio may be clinically useful in patients with acute ischemic stroke. In addition, as a C-arm CBV study provides CBV data easily and in a short time in patients undergoing angiography, further evaluation of its clinical application in patients with acute ischemic stroke is needed.

However, in a C-arm CBV study, acquisition of fill images may begin before the contrast medium reaches a stable state in ischemic brain tissues, where the circulation is markedly delayed. Caution is needed in this event because the area of delayed circulation may be estimated to be wider than it truly is. Further evaluation is necessary after accumulating more cases under different conditions.

Limitations of this study are that it was a single-center retrospective evaluation, and the number of subjects was
insufficient for statistical validation. Furthermore, there were differences in the sites of vascular occlusion, course of the disease, and therapeutic approach among patients. Accumulation of more cases is necessary for further evaluation.

**Conclusion**

C-arm CBV measurements, which can be performed readily using an angiography system, may be useful in patients in the acute phase of ischemic stroke. As it provides CBV data in a short time, it may shorten the time until the beginning of emergency recanalization.

With further evaluation, a C-arm CBV study is expected to become a routine examination of the brain circulation in the acute phase of cerebral infarction, as are the CBV images provided by CT and MRI. Moreover, C-arm CBV measurements may facilitate more precise evaluation of treatment indications in the acute phase of stroke.

**Disclosure Statement**

Neither the first author nor any of the coauthors have any conflicts of interest.

**References**


