



Application of C-arm CBV Measurement for Evaluation before and Immediately after Neuroendovascular Treatment

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Objective: To evaluate changes related to cerebral endovascular treatment, a C-arm cerebral blood volume (CBV) study was performed before and after treatment. Although conditions related to treatment-administered contrast medium of the pretreatment examination differs from that for post-treatment, no study has investigated the effect on the results. In this study, we examined differences in the results of the C-arm CBV examination before and after treatment in patients who underwent carotid artery stenting (CAS).

Subjects and Methods: Fifteen subjects were included in this study. The time interval until the volume of contrast medium reached a peak in points established at the proximal and distal sites of stenosis on a lateral view of a cervical common carotid artery angiogram before and after treatment was ≤ 0.5 seconds. For the C-arm CBV study, 25% diluted contrast medium was trans-arterially administered. The first C-arm CBV study was performed before angiography for preoperative assessment, and the second study was performed immediately after the completion of the CAS. The mean CBV value in each vascular territory was calculated, and the change in CBV after treatment was evaluated. In addition, the relative CBV ratio was calculated.

Results: For both the unaffected and affected sides, the CBVs measured in the post-treatment study were high. When evaluating the relative CBV ratio, there were no marked changes after treatment. The value was constant.

Conclusion: The results suggest that a C-arm CBV study is influenced by the contrast medium used during treatment. To apply a C-arm CBV study for pretreatment and post-treatment evaluation, relative evaluation parameters, such as the relative CBV ratio, should be used.

Keywords ▶ C-arm cerebral blood volume, relative cerebral blood volume value, contrast medium, carotid artery stenting

Introduction

Advances in flat-detector-equipped C-arm angiography systems and innovative software algorithms have facilitated the assessment of the cerebral blood volume (CBV), as a parameter of cerebral perfusion, in addition to an anatomical assessment with CT-like and 3D-DSA images. A C-arm

CBV study requires two rotational acquisitions: a non-contrasted “mask run” and a contrasted “fill run.” These acquisitions are used to generate a volumetric dataset, which provides both a CBV map and an anatomical image.¹⁻⁵ Recently, this method has also been applied in clinical practice. Several studies have reported applications for the initial diagnosis of acute ischemic stroke or an assessment after carotid artery stenting (CAS).⁶⁻¹⁰ The C-arm CBV study facilitates the acquisition of real-time information on circulation in the angiography suite. Therefore, utilizing this characteristic, the results of examination before and after thrombectomy or CAS can be compared. In this case, the pretreatment and post-treatment examinations differ. In particular, the post-treatment examination is performed after the use of contrast medium. No previous study has reported the effect of treatment-administered contrast medium on a C-arm CBV study. Furthermore, methods to evaluate the results of the examination before

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and after treatment have not been sufficiently assessed. In this study, we examined differences in the results of a C-arm CBV study before and after treatment and evaluated the effective analysis methods in patients who underwent two C-arm CBV studies, one before and one immediately after CAS.

Subjects and Methods

Prior to cerebral angiography and the C-arm CBV studies (*syngo* DynaPBV Neuro; Siemens AG, Forchheim, Germany), the purpose and protocols of this study were explained sufficiently to the patients and their families and informed consent was obtained. For angiography and C-arm CBV imaging, a biplane flat-detector C-arm angiography system (Artis zee BA; Siemens AG) was used, and imaging data were analyzed using a work station (*syngo* XWP VB 15D; Siemens AG). This study was approved by the ethics review board of our hospital.

Case selection

In our angiography system, an application to analyze angiographic images on the work station and to visualize a complete DSA run in a color-coded single image (*syngo* iFlow; Siemens AG) was installed. The time-to-contrast intensity curve was obtained by establishing arbitrary measurement points on the prepared color map.³⁾ Using this application, we established two points as measurement sites on a lateral view of the cervical common carotid artery on the angiography of the affected side. The first was in the common carotid artery at the fifth cervical vertebral level, corresponding to the proximal site of stenosis. The second was in the knee region of the internal carotid artery, corresponding to the distal site of stenosis. We measured the time interval until the volume of contrast medium reached a peak on the time-to-contrast intensity curves at the respective sites, and calculated the difference in the peak time between the two points. Patients, in which the difference in the peak times calculated before and after treatment was ≤ 0.5 seconds, were regarded as showing no marked changes in circulation after treatment and were enrolled as subjects. Cervical common carotid artery angiography was performed at an imaging frame count of 4 frames/sec before and after surgery. Contrast medium at a volume of 7 mL was administered using a power injector at an administration rate of 5 mL/sec. In all, 15 patients met the above conditions. They had unilateral lesions, and the degree of stenosis

was 70%–90%. Stenosis was present on the right side in eight patients and on the left side in seven patients. It was asymptomatic in five patients, whereas minor stroke was observed in 10 patients. In all patients, a C-arm CBV study was performed before and after surgery.

C-arm CBV imaging methods

For the C-arm CBV study, a trans-arterial contrast injection procedure (aortic arch injection) with 25% diluted contrast medium was used.⁵⁾ The C-arm CBV imaging protocol is indicated in **Fig. 1**. A 4F diagnostic IA catheter (CX Catheter; Gadelius, Tokyo, Japan) was placed just above the aortic valve under fluoroscopic guidance and used as a route for administering the contrast medium. Initially, a mask run was performed. After back rotation to the starting position, 300 mgI/mL of non-ionic iodine contrast medium (Oypalomin, Fuji Pharma Co., Ltd., Toyama, Japan), which was diluted with saline to 25%, was continuously administered at a total volume of 77 mL (converted to non-diluted contrast medium: 19.3 mL) for 11 seconds at a speed of 7 mL/sec using a power injector. Then, a fill run was performed at 9 seconds after the start of the contrast medium administration for data collection. The data acquisition per run was performed using the following parameters: acquisition time, 6 seconds; 70 kV; 616×480 matrix; projection on a 30×40 cm flat panel; 200° total angle; 0.5° per frame; 400 frames total; and dose, 0.36 mGy per frame. The data obtained were transferred to the work station, and the C-arm CBV analysis was performed.

The first C-arm CBV study, as a preoperative assessment, was performed with cerebral angiography at 2–4 weeks prior to CAS treatment. After inserting a sheath, a catheter was inserted into the ascending aorta, and this study was conducted before the use of the contrast medium for the diagnostic angiography. Furthermore, the second C-arm CBV study, as a postoperative assessment, was carried out immediately after the completion of CAS.

For CAS, a distal protection method using a Filterwire EZ (Boston Scientific, Natick, MA, USA) was used in all patients under general anesthesia. Using a balloon measuring 3–3.5 mm in diameter, predilation was performed, and a Carotid Wallstent measuring 10×24 mm or 10×31 mm (Boston Scientific) was inserted. Subsequently, postdilation was additionally conducted using a balloon measuring 4–4.5 mm in diameter. After the completion of this procedure, the guiding catheter was removed, and a 4-6F coaxial catheter (CX catheter; Gadelius), which was used as a coaxial device at the time of the guiding catheter insertion,

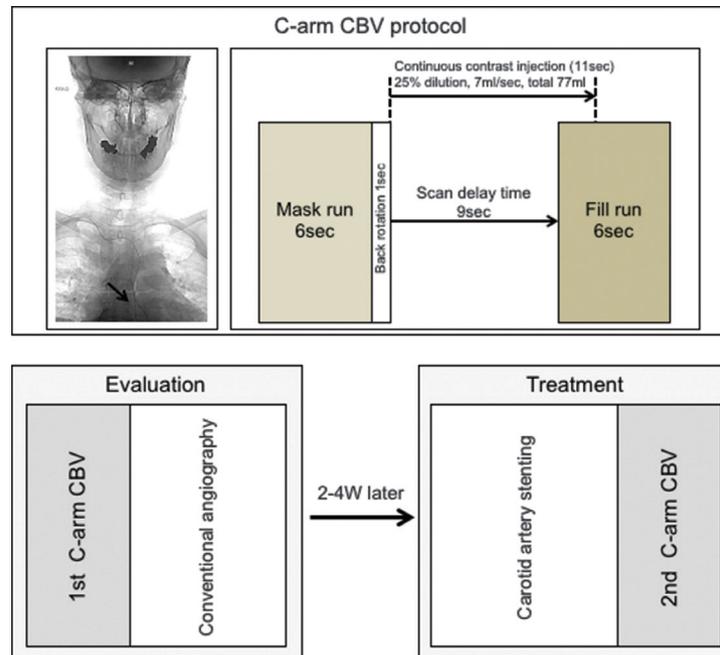


Fig. 1 Upper row: A schematic illustration of the acquisition protocol for the aortic arch injection of contrast medium. A C-arm CBV study requires two rotational acquisitions, the first without a contrast injection, and the second with a delay after the start of the contrast injection (arrow: site of catheter insertion). Lower row: The examination schedule before and after carotid artery stenting. CBV: cerebral blood volume

was inserted into the ascending aorta. The postoperative C-arm CBV study was performed as described for preoperative assessment.

Evaluation methods

To analyze the C-arm CBV images, the mean CBV value in each vascular territory was calculated. Two axial cross sections, which included the basal ganglia (BG) and body of the lateral ventricle, were used. Regions of interest (ROIs) that encompassed both gray and white matter were subsequently placed in each vascular territory, including the anterior cerebral artery (ACA), the middle cerebral artery (MCA), and the posterior cerebral artery (PCA) territories, as well as the BG (**Fig. 2**). In patients with a minor stroke, the infarcted area was confirmed by MRI and excluded from the ROIs. Using the mean CBV value in each vascular territory, the changes in the CBV after treatment in both the unaffected and affected sides were calculated. To compare the mean CBV value and the change between the unaffected and affected sides with the pretreatment value, the significance was estimated using a paired t-test. In addition, the relative CBV ratio (CBV value on the affected side/CBV value on the unaffected side) was calculated, and

the presence or absence of changes after treatment was similarly examined using a paired t-test.

Results

There were no adverse events, such as contrast medium allergy or contrast medium-related nephropathy, on any examination. The C-arm CBV study could be performed under a constant procedure. Furthermore, the mean volume of contrast medium used for CAS was 67.4 ± 15.3 mL. There were no perioperative complications.

Interval until the volume of contrast medium reached a peak on time-to-contrast intensity curves before and after surgery

The time interval until the volume of contrast medium reached a peak on time-to-contrast intensity curves between the two points in the common carotid artery on the affected side was 0.66 ± 0.14 seconds before surgery and 0.48 ± 0.11 seconds after surgery, indicating a 0.18 ± 0.13 -second decrease. Although there was a significant difference between the two values, the difference after treatment was ≤ 0.5 seconds.

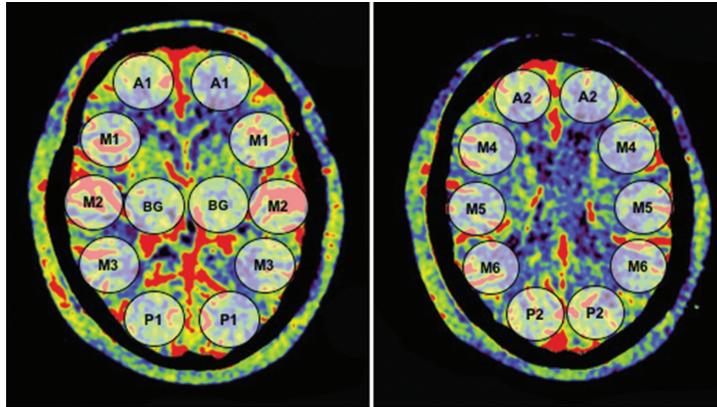


Fig. 2 Post-processing image analysis. Two axial cross sections, including the BG and body of the lateral ventricle, were used. ROIs that included gray and white matter were subsequently placed in each vascular territory; the ACA, the MCA, and the PCA territories, as well as the BG. ACA: anterior cerebral artery; BG: basal ganglia; MCA: middle cerebral artery; PCA: posterior cerebral artery; ROIs: regions of interest

Table 1 CBV values (mean \pm standard deviation) before and after carotid artery stenting

		C-arm CBV value (mL/100 g)	
		Before stenting	After stenting
ACA	Unaffected side	2.85 \pm 0.52	3.02 \pm 0.66
	Affected side	2.80 \pm 0.55	3.07 \pm 0.54
	p	p = 0.737	p = 0.567
MCA	Unaffected side	3.33 \pm 0.78	3.48 \pm 0.89
	Affected side	3.40 \pm 0.85	3.53 \pm 0.97
	p	p = 0.384	p = 0.601
PCA	Unaffected side	3.28 \pm 0.63	3.42 \pm 0.63
	Affected side	3.30 \pm 0.58	3.51 \pm 0.61
	p	p = 0.790	p = 0.440
BG	Unaffected side	3.19 \pm 0.56	3.31 \pm 0.72
	Affected side	3.22 \pm 0.59	3.53 \pm 0.61
	p	p = 0.822	p = 0.158

ACA: anterior cerebral artery; BG: basal ganglia; CBV: cerebral blood volume; MCA: middle cerebral artery; PCA: posterior cerebral artery

C-arm CBV value and change before and immediately after treatment

The C-arm CBV values (mL/100 g) from the first session, as preoperative assessment, and that obtained in the second session, as postoperative assessment, are shown in **Table 1**. On both the unaffected and affected sides, the C-arm CBV values in the respective regions in the second C-arm CBV study after CAS were higher than those from the first study before the use of contrast medium. However, there was no significant difference in any region before and after treatment between the unaffected and affected sides.

Concerning the change in the C-arm CBV value after treatment, this value was increased from 3.8% to 6% on the unaffected side and by 3.8% to 9.6% on the affected side. There was a significant difference in the ACA region on the

affected side, but there were no significant differences in any other region (**Fig. 3**).

Relative CBV ratio before and after treatment

The relative CBV ratios in the ACA region before and after treatment were 1.01 \pm 0.25 and 1.04 \pm 0.18, respectively. Those found in the MCA region were 1.05 \pm 0.25 and 1.05 \pm 0.31, respectively. In the PCA region, the CBV ratios were 1.04 \pm 0.26 and 1.05 \pm 0.24, respectively and in the BG region they were 1.01 \pm 0.11 and 1.09 \pm 0.2, respectively. There was no marked difference between the affected and unaffected sides of the two C-arm CBV studies before and after treatment, resulting in a ratio of approximately 1.0. Furthermore, there were no significant differences between the pretreatment and post-treatment relative CBV ratios in any vascular territory (**Fig. 4**).

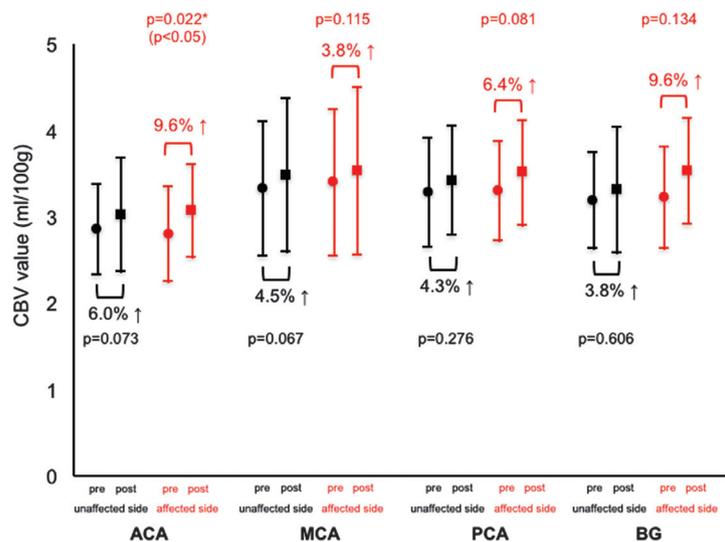


Fig. 3 Change in the C-arm CBV after carotid artery stenting. ACA: anterior cerebral artery; BG: basal ganglia; CBV: cerebral blood volume; MCA: middle cerebral artery; PCA: posterior cerebral artery

Illustrative Case

A 66-year-old female was taking medication for hypertension and hyperlipidemia. Carotid artery ultrasonography, which had been conducted in the Department of Internal Medicine, showed a progression of right cervical internal carotid artery stenosis, and she was referred to our department. Pretreatment angiography revealed 90% stenosis of the right cervical internal carotid artery. The time interval until the volume of contrast medium reached a peak between the two arterial points was 0.8 seconds. Under general anesthesia, CAS was performed with filter protection. Cerebral angiography after treatment confirmed a reduction of stenosis, and the time interval until the volume of contrast medium reached a peak was reduced to 0.53 seconds. Intracranial angiography showed an improvement in the visualization of the ACA. The relative CBV ratios of the preoperative and postoperative C-arm CBV values for the ACA region were 1.03 and 1.05, respectively. For the MCA region, they were 0.97 and 1.05, respectively. In the PCA region, they were 0.87 and 0.99, respectively, and in the BG region they were 0.95. Because we judged the relative CBV ratios were constant before and after CAS treatment, the patient was subjected to mild blood pressure control after waking from general anesthesia. There were no neurologic deficits during follow-up (**Fig. 5**).

Discussion

In this study, to evaluate the effect of pretreatment contrast on a C-arm CBV study, patients were selected so that

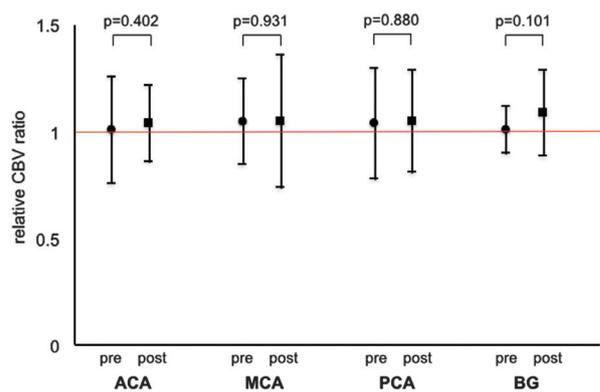


Fig. 4 Relative CBV ratio before and after carotid artery stenting. ACA: anterior cerebral artery; BG: basal ganglia; CBV: cerebral blood volume; MCA: middle cerebral artery; PCA: posterior cerebral artery

treatment-related changes in cerebral perfusion before and after CAS were minimized. In a previous study, the flow condition of contrast medium during CAS was evaluated by a qualitative method, such as slow-flow and normal-flow, based on the surgeons' subjective assessments. To our knowledge, as the only study using a quantitative assessment, Sorimachi et al.¹¹⁾ evaluated flow impairment of contrast medium on angiography performed before and after filter retrieval following CAS with distal filter protection. They conducted a quantitative analysis using a frame-by-frame evaluation procedure. Interestingly, they stated that when performing DSA at a rate of 3 frames/sec, the surgeon regarded a ≤ 4 -frame delay (corresponding to approximately 1.3 seconds) from the baseline image frame as normal flow. They reported that a delay in

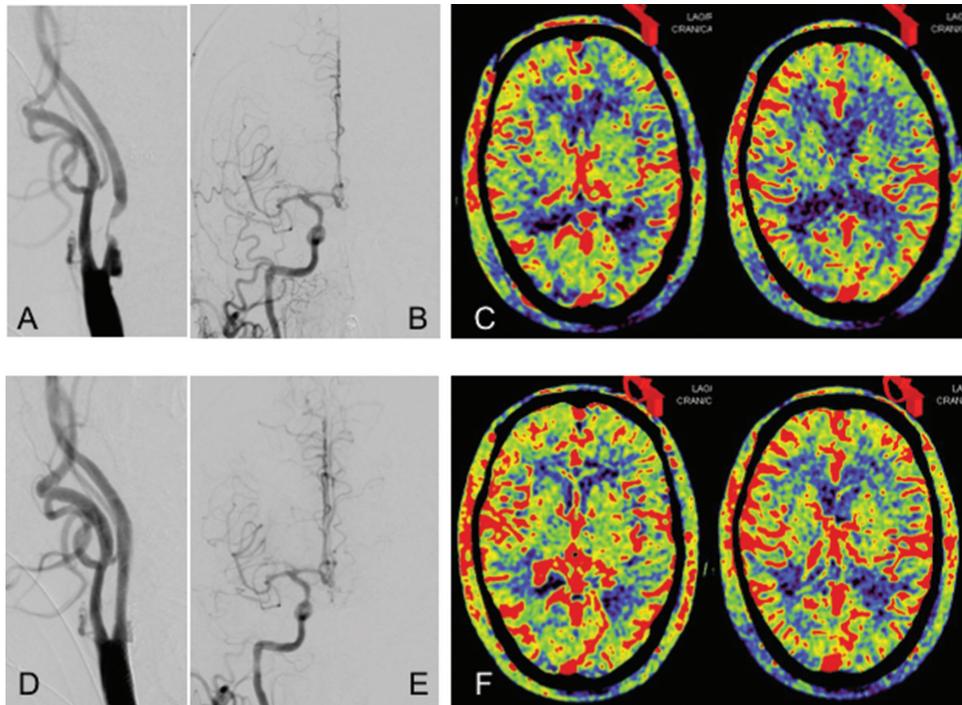


Fig. 5 A 66-year-old female. Carotid artery stenting for asymptomatic stenosis of the right cervical internal carotid artery (CAS) was performed. (A) A cervical lateral view of the preoperative right common carotid artery angiogram. At the bifurcation of the right cervical internal carotid artery, 90% stenosis was observed. (B) An antero-posterior view of the preoperative right common carotid artery angiogram. (C) A preoperative C-arm CBV image indicating no laterality. (D) The post-CAS angiogram shows a successfully dilated right cervical ICA. (E) An antero-posterior view of the postoperative right common carotid artery angiogram. Visualization of the anterior cerebral artery was improved. (F) A postoperative C-arm CBV image indicating no increase in the CBV on the affected side. CAS: carotid artery stenting; CBV: cerebral blood volume; ICA: internal carotid artery

blood flow was detected in four of five of patients with the quantitative analysis. However, it should be considered that there is a dissociation between such subjective expressions and a true quantitative assessment. In this study, patients were selected in reference to the procedure described by Sorimachi et al. However, the time-to-contrast intensity curve on the iFlow application was used as it facilitates quantitative assessment at established measurement sites. The time interval until the volume of contrast medium reached a peak on the time-to-contrast intensity curves in the two arterial measurement points was shortened by 0.18 ± 0.13 seconds after surgery, indicating a significant difference. However, this difference corresponded to a 1-frame difference on imaging at 4 frames/sec. We could only investigate this issue in patients without marked treatment-related changes in intracranial circulation.

The reason to measure CBV as a parameter of intracranial perfusion is to detect an infarcted focus of the brain as a CBV-decreased area reflecting cerebrovascular occlusion-related blood flow interruption in the acute

phase. In addition, it is possible to estimate the presence or absence of an increase in the tissue blood volume reflecting cerebrovascular dilation, which occurs in compensation to a reduction in the cerebral perfusion pressure in chronic cerebral ischemia. A C-arm CBV study can be performed without the need to transfer patients to another facility during cerebral angiography or cerebral endovascular treatment. Therefore, it is useful for evaluating acute ischemic changes in the brain. Previous studies reported the clinical application of a C-arm CBV study for the initial diagnosis of acute ischemic stroke. Struffert et al.⁶ and Fiorella et al.⁸ compared C-arm CBV images with Computed tomography perfusion (CTP)-CBV images in patients with cerebral infarction. They evaluated the accuracy or specificity of C-arm-CBV-based ischemia detection as satisfactory for the initial diagnosis of ischemic cerebrovascular disorder.^{6,8} Simultaneously, Fiorella et al.⁸ indicated the importance of keeping a steady state of contrast medium in the brain parenchyma during the acquisition of the fill run. According to their report, when a delayed

collateral pathway is present at a distal area of an occluded blood vessel, a sufficient distribution of contrast medium may not be obtained, and a reduction in the CBV may be overestimated in comparison with CTP-CBV. This finding differs from the purpose of our study, but applies C-arm CBV for the detection of ischemic complications related to endovascular treatment, including CAS. When delayed collateral circulation is present at the site of the distal embolism, a fill run may be performed without sufficient distribution of the contrast medium, even with an imaging delay time of 9 seconds, which was used in this present study. It must be considered that the area of decreased CBV may be overestimated.

In addition to such applications for the initial diagnosis, the C-arm CBV study is used to evaluate the therapeutic effects of neuroendovascular treatment. Terada et al.⁹⁾ and Fujimoto et al.¹⁰⁾ have reported efforts to detect hyperperfusion by comparing the results of a C-arm CBV study before and after CAS. When applying a C-arm CBV study as an auxiliary measure for the initial diagnosis, it is possible to evaluate its usefulness by comparing the images obtained on a single session of imaging with the results of other modalities, such as CT and MRI. However, when assessing the effect of neuroendovascular treatment, it is necessary to compare the results of examinations performed before and after treatment. In particular, it is important to evaluate the results of the postoperative examination while considering the influence of the contrast medium administered during treatment on the results. In clinical practice, it is difficult to perform pretreatment and post-treatment examinations under the same conditions. However, to assess the influence of the treatment-administered contrast medium on the postoperative examination, in this study subjects were selected so that the results of pretreatment and post-treatment examinations could be evaluated under similar conditions. As a result, the postoperative examination showed that the CBV value increased from 3.8% to 6% of the preoperative value on the unaffected side and by 3.8% to 9.6% on the affected side. On the unaffected side, there was also an increase in the CBV value similar to that on the affected side at the time of the post-treatment examination. Tokunaga et al.¹²⁾ reported previously the *in vivo* pharmacokinetics of non-ionic iodine contrast medium. They found that the plasma concentrations of iodine at 5 minutes, 30 minutes, and 4 hours after the intravenous injection of 370 mgI/mL iopamidol solution in 40 mL over approximately 30 seconds decreased with time to 1.9, 1, and 0.2 mgI/mL, respectively. Concerning

excretion, they found that approximately 60% was excreted in the urine after 2 hours, and that the entire volume was excreted in the urine after 24 hours.¹²⁾ In this study, the postoperative C-arm CBV study was conducted within 15 minutes from the completion of CAS in all patients. Therefore, in the postoperative study, the plasma concentration of iodine was higher than on the preoperative study, which was performed prior to the administration of contrast medium. This may have contributed to the increase in the CBV value in the postoperative examination. Furthermore, the current C-arm CBV application was developed based on the idea that the CBV can be correctly calculated by differentiating mask images even when there is weak enhancement from residual contrast medium in the brain parenchyma. Although the details are not disclosed, the influence of the residual contrast medium on the study or a shortening of the contrast medium transfer time in the affected side, which may represent an improvement in stenosis after CAS on the CBV, is not considered when using this CBV-calculating formula (Kojima I, Siemens Healthcare Japan, June, 19, 2017). Therefore, as a factor that may increase the CBV value after the procedure, issues related to the calculation of the CBV in the application may be responsible. Considering the possibilities, when comparing the CBV values obtained before and after treatment using the current application, it must be considered that the postoperative CBV value may increase by approximately 10% from the preoperative value.

Alternatively, when evaluating the CBV value as a ratio, the relative CBV values obtained from preoperative and postoperative examinations were constant in this study. Briefly, the increase in the CBV value in the postoperative C-arm CBV study, which was performed after the administration of contrast, was similar between the affected and unaffected sides. Therefore, when evaluating the CBV value as a ratio, the increase in the postoperative study may be offset, facilitating the assessment of the results of preoperative and postoperative studies by applying the same scale. As indicated in the representative case, the relative CBV ratios before and after CAS treatment were approximately 1 in patients without marked changes in circulation after treatment. Alternatively, Fujimoto et al. evaluated patients with hemorrhage after CAS. In these subjects, the relative CBV ratio of the C-arm CBV study at the site of hemorrhage ranged from 1.59 to 2.1 after treatment, showing a marked increase.¹⁰⁾ Thus, a constant value may be obtained in patients without marked changes after treatment by evaluating the relative CBV ratio. If the treatment

induces changes, the influence can be more accurately evaluated based on this ratio than from the CBV value alone.

This study has several limitations. The number of subjects was small, and they were selected as those without marked changes in the state of circulation after treatment in accordance with our unique criteria. The subjects were not entirely without changes in intracranial circulatory kinetics. However, we could identify issues with the postoperative C-arm CBV study. In the future, patients with marked changes in circulation after treatment could also be investigated using similar methods although this was not the purpose of this present study. Furthermore, when using a trans-arterial contrast-medium injection, there may be laterality in the C-arm CBV images, as demonstrated in previous studies.^{3,5} Although this injection method was used in this study, no laterality was indicated in any of the subjects. However, when comparing the results before and after treatment in the same patient, the influence of laterality related to the examination protocol may be minimized by comparing the pretreatment and post-treatment CBV values on the affected side versus the unaffected side, or by evaluating the affected/unaffected side ratio as a relative value.

In the current C-arm CBV protocol, the data acquisition time of the mask or fill run for the C-arm CBV study was shortened from 8 to 6 seconds in comparison with initial reports, and the use of diluted contrast medium makes it possible to decrease the volume of contrast medium necessary for the examination. However, the C-arm CBV study should be indicated, considering that it is an auxiliary examination to be performed with cerebral angiography or cerebral endovascular treatment.

Conclusion

We report considerations to the application of a C-arm CBV study for assessment before and after neuroendovascular treatment. It was suggested that the C-arm CBV may be influenced by the contrast medium used during treatment, but treatment-related changes may be easily evaluated using the affected/unaffected side ratio as a relative value.

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Disclosure Statement

There are no conflicts of interest to be disclosed regarding this article.

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