Asymmetric Cortical Vessel Sign Indicates Hemodynamic Deficits in Adult Patients with Moyamoya Disease

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■ BACKGOUND: **Asymmetric cortical vessel sign (ACVS) on susceptibility-weighted imaging (SWI) indicates elevated concentration of deoxyhemoglobin and elevated oxygen extraction fraction in patients with cerebral ischemia. This study aimed to clarify whether ACVS is associated with impaired hemodynamics and hyperperfusion syndrome in patients with moyamoya disease (MMD).**

■ METHODS: **Consecutive adult patients with MMD were enrolled. ACVS data on SWI and perfusion data using dynamic perfusion computed tomography were obtained and evaluated preoperatively and on postoperative days 2 and 180.**

■ RESULTS: **A total of 24 patients with MMD were enrolled. Of 11 (45.83%) patients showing positive ACVS before surgery, 8 turned negative on postoperative day 2 and 9 showed absence of ACVS 180 days after surgery. Regions of interest showing positive ACVS had lower cerebral blood flow (CBF, $P<0.001$), increased cerebral blood volume ($P = 0.021$), prolonged time to peak ($P<0.001$), and mean transit time ($P = 0.009$). No patients with hemorrhagic symptoms showed positive ACVS($P = 0.041$) and patients with positive ACVS showed more increase in CBF ($P<0.004$).**

■ CONCLUSIONS: **In patients with MMD, ACVS on SWI indicates severe impairment in hemodynamics and is associated with more increase in CBF after bypass surgery. Hence, ACVS on SWI might be considered as a neuroimaging marker for the evaluation of hemodynamics in patients with MMD.**

INTRODUCTION

Moyamoya disease (MMD), a progressive occlusive cerebrovascular disease with spontaneous stenosis leading to occlusion of terminal portions of bilateral internal carotid arteries, is characterized by the compensatory formation of abnormal vascular networks that provides collateral circulation.[1] Adult patients with MMD may clinically present with ischemic and/or hemorrhagic symptoms due to the unique pathologic progress of this disease.[2] Revascularization surgery is recommended for patients with symptomatic MMD or patients with asymptomatic MMD but with impaired hemodynamics. Hence, evaluation of hemodynamics is critical for the management of patients with MMD.

Asymmetric cortical vessel sign (ACVS), asymmetric signal loss of dilated vessel, has been reported to be an indicator for penumbra that diminishes when hypoperfusion is ameliorated in patients with acute ischemic stroke.[3] ACVS is believed to be caused by high concentration of deoxyhemoglobin following an increased oxygen extraction fraction (OEF) in focal areas with severely impaired hemodynamics.[4] Accumulation of deoxyhemoglobin in cortical

Key words
- Asymmetric cortical vessel sign
- CT perfusion
- Hypoperfusion
- Moyamoya disease
- Susceptibility-weighted imaging

Abbreviations and Acronyms
ACVS: Asymmetric cortical vessel sign
BOLD: Blood oxygen level dependent
CBF: Cerebral blood flow
CBV: Cerebral blood volume
CTP: Computed tomography perfusion
GRE: Gradient echo
HPS: hyperperfusion syndrome
MMD: Moyamoya disease
MTT: Mean transit time
OEF: Oxygen extraction fraction
ROI: Region of interest
SWI: Susceptibility weighted imaging
TTP: Time to peak

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and subcortical veins can be detected in gradient echo (GRE) T2* weighted imaging and susceptibility-weighted imaging (SWI) due to blood oxygen level–dependent (BOLD) effect.[5] However, ACVS on SWI has been reported scarcely in patients with MMD so far. This study aimed to clarify whether ACVS can reflect the severity of hemodynamic impairment and whether ACVS has an association with hyperperfusion syndrome.

MATERIALS AND METHODS

Patients

Beginning from June 2016, consecutive patients treated at the Department of Neurosurgery at West China Hospital of Sichuan University were prospectively enrolled. A total of 24 adult patients who underwent intra-arterial angiography and were diagnosed with MMD according to consensus criteria and guideline for MMD proposed by the Research Committee on Spontaneous Occlusion of the Circle of Willis were enrolled.[6] All patients underwent superficial temporal artery–middle cerebral artery anastomosis in combination with encephalo-myo-synangiosis by the same experienced neurosurgeon. If superficial temporal artery was not available for bypass surgery, encephalo-myo-synangiosis alone was performed. Magnetic resonance imaging scan, including SWI and computed tomography perfusion (CTP), were performed within 3 days before surgery and at 2 and 180 days after surgery. Ethical approval by the institutional review board was obtained for this retrospective study, and the requirement for informed consent was waived.

Imaging Protocol and Analysis

SWI data were acquired using a 3.0T MR scanner (Skyra; Siemens Medical Solutions, Erlangen, Germany) with following parameters used: repetition time, 27 milliseconds; echo time, 30 milliseconds; flip angle, 20°; field of view 20 cm; matrix, 256 × 207; section thickness 2 mm.

CTP was conducted on a 128-row dual-source computed tomography system (SOMATOM Definition FLASH, Siemens Healthcare, Forchheim, Germany), and dynamic images were acquired with the settings of 70 KV and 150 mAs. By using a power injector, 40–50 mL of Ultravist 370 was injected intravenously at a flow rate of 5 mL/s with a 5-second delay and followed by a saline flush of 20 mL at the same low rate. By using adaptive spiral scanning technique ("shuttle mode"), the scanning range covered the whole brain in z-axis above the skull base. A set of axial images was obtained with constant parameters for every patient (5-mm slice thickness, 512 × 512 matrix size, 0.28 rotation time and 32 × 1.2-mm collimation).[7]

CTP data were transferred to a workstation (Syngo MMWP [VE40A]; Siemens Healthcare) for data postprocessing. "Auto stroke MTT," a semiautomatic deconvolution algorithm, was used for perfusion analysis. Perfusion parameter maps of cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP), and mean transit time (MTT) were generated.

Blinded to the enrolled patients' clinical information and CTP parameter, 2 experienced neuroradiologists evaluated the presence of positive ACVS. According to previously mentioned definitions, patients were classified as positive ACVS if there were more and/or larger vessels with a greater signal loss compared with vessels on the opposite side. Those whose bilateral hemispheres showed no apparent difference were classified as ACVS negative.

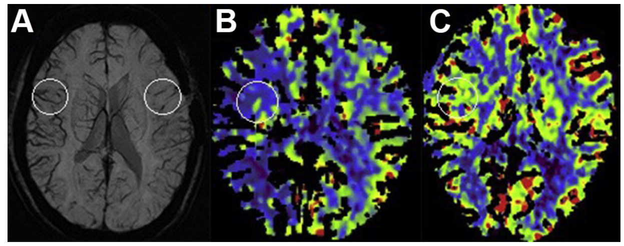

Figure 1. Regions of interest (ROIs). (**A**) Circular ROIs were placed in the areas showing positive asymmetric cortical vessel sign (ACVS) and its mirroring location. (**B** and **C**) ROIs were placed in areas with increased cerebral blood flow (CBF) postoperatively.

Round regions of interest (ROI) of 2 cm were placed manually within the area of positive ACVS and the mirroring area in patients with ACVS. ROIs were also placed in areas with increased CBF postoperatively (Figure 1). Both hemodynamic parameters and presence of ACVS were evaluated separately at 3 time points (preoperatively, days 2, and 180 days postoperatively).

Statistical Analysis

Data are presented as mean ± standard error of the mean and were analyzed by using SPSS, version 21.0 (IBM Corp., Armonk, New York, USA). The independent-sample t test and Fisher exact

Table 1. Baseline Characteristics of Patients with MMD

	Patients with MMD, $n = 24$
Age, years	34.5 ± 12.2
Female sex, *n* (%)	13 (54.2)
BMI	24.2 ± 2.82
Vascular risk factors, *n* (%)	
Dyslipidemia	4 (16.7)
Current smoker	5 (20.8)
Hypertension	6 (25.0)
Diabetes mellitus	0 (0)
Disease subtype	
Ischemic onset, *n* (%)	19 (79.2)
Hemorrhagic onset, *n* (%)	5 (20.8)
Suzuki grading	3.8 ±1.1
MRI findings, *n* (%)	
White matter lesions	14 (58.3)
CMB	6 (25.0)
Ivy sign	23 (95.8)
ACVS	11 (45.8)

MMD, Moyamoya disease; BMI, body mass index; MRI, magnetic resonance imaging; CMB, cerebral microbleeds; ACVS, asymmetric cortical vessel sign.

Table 2. Characteristics From Patients with and Without ACVS

	ACVS *n* = 11	No ACVS *n* = 13	*P* Value
Age, years	31.4 ± 7.2	37.2 ± 15.0	<0.001
Disease subtype, *n* (%)			
Ischemic onset	11 (100)	8 (61.5)	
Hemorrhagic onset	0 (0)	5 (38.5)	0.041
Suzuki grading	3.5 ± 1.0	4.2 ± 1.1	0.153
White matter lesions, *n* (%)	7 (63.6)	7 (53.9)	0.584
CBF, mL/100 g/min	37.0 ± 9.40	45.4 ± 6.7	0.017
CBV, 100 g/min	3.6 ± 0.6	3.5 ± 0.8	0.763
TTP, seconds	15.1 ± 3.1	12.1 ± 1.6	0.006
MTT, seconds	7.3 ± 3.0	5.8 ± 1.9	0.164
ΔCBF, mL/100 g/min	21.9 ± 7.2	13.4 ± 4.2	0.004

ACVS, asymmetric cortical vessel sign; CBF, cerebral blood flow; CBV, cerebral blood volume; TTP, time to peak; MTT, mean transit time.

test were performed to compare continuous and categorical characteristics. Paired-sample t test was used to identify difference between hemodynamic parameters of ROIs showing ACVS and without. Differences were defined as significant at a probability level of <0.05.

RESULTS

Baseline Data

Between June 2016 and April 2018, 24 patients (age, 34.5 ± 12.2 years) diagnosed with MMD were enrolled, including 13 female patients and 8 male patients. Baseline data for patients enrolled are summarized in Table 1. There were 19 (79.2%) patients with ischemic onset, whereas 5 (20.8%) presented with hemorrhagic symptoms. Of all 24 patients, 11 (45.8%) showed positive ACVS.

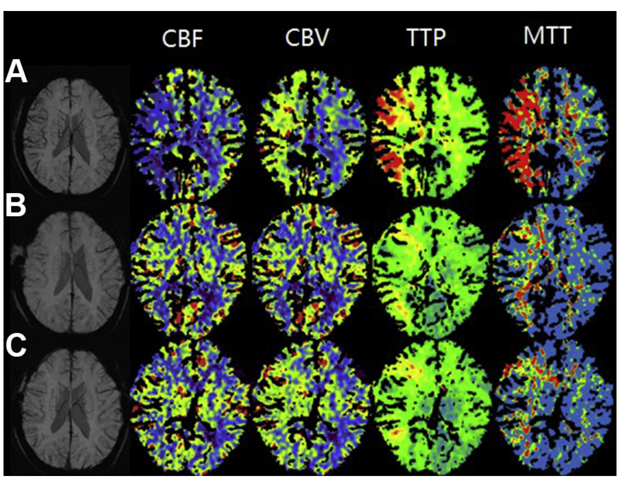

Figure 2. Representative case. Serial susceptibility-weighted imaging (SWI) and computed tomography perfusion studies (**A**) preoperatively and (**B**) at days 2 and (**C**) 180 postoperatively in a 30-year-old female patient with moyamoya disease. Asymmetric cortical vessel sign (ACVS) was obvious preoperatively with marked hemodynamic impairment in right hemisphere, which improved after surgery and during the follow-up.

Relationship of Hemodynamics and the Presence of ACVS

Table 2 shows data from patients with and without ACVS on SWI images at admission. No significant differences were observed in Suzuki grading, white matter lesions, CBV, and MTT. Age in the ACVS-positive group (31.4 ± 7.2 years) was younger ($P<0.001$) than the ACVS negative-group (37.2 ± 15.0). Disease subtype significantly differ between 2 groups ($P = 0.041$). Interestingly, 5 patients with hemorrhagic MMD all showed negative ACVS. There were significant differences in preoperative CBF and TTP between ROIs showing positive ACVS and their mirroring areas, which indicates that ACVS may reflect severe hemodynamic impairment. A representative case is shown in Figure 2. Furthermore, increases in CBF after bypass surgery in patients with ACVS were significantly greater than those of patients without ($P<0.001$), although no symptomatic hyperperfusion was seen in this study.

Hemodynamic parameters in ROIs showing positive ACVS and their mirroring ROIs are presented in Table 3. Differences in CBF, CBV, TTP, and MTT between ROIs and their mirroring ROIs were significant which indicated more severely impaired hemodynamics.

Figure 3 shows patient numbers showing ACVS at each time point. Of 11 patients with positive ACVS, 3 patients remained ACVS positive on postoperative day 2 and 2 remained ACVS positive 180 days after surgery, whereas no newly formed ACVS was observed in patients without preoperative ACVS. Hemodynamic improvement observed on CTP in these patients.

DISCUSSION

Elevated concentration of deoxyhemoglobin in ischemic brain tissue can be detected on GRE and SWI due to increased BOLD effects, which makes SWI and GRE techniques candidates for revealing increased OEF.[8] This phenomenon may appear as hypointensity of cortical vessels, deep white matter vessel (brush sign), and parenchyma (ischemic tissue sign).[9] Compared with GRE, SWI has greater sensitivity in revealing increased deoxyhemoglobin.[10] However, it is difficult to quantify ACVS on SWI.[11] Furthermore, SWI is less commonly used and requires extra scanning time in comparison with GRE.

Table 3. Preoperative Hemodynamic Parameters in the Selected Regions of Positive ACVS and Mirroring Locations

	ROI	Mirroring Area	*P* Value
CBF, mL/100 g/min	37.0 ± 9.4	54.1 ± 8.5	<0.001
CBV, 100 g/min	3.6 ± 0.6	3.1 ± 0.4	0.021
TTP, seconds	15.1 ± 3.1	11.1 ± 1.5	<0.001
MTT, seconds	7.3 ± 3.0	4.2 ± 0.7	0.009

ACVS, asymmetric cortical vessel sign; ROI, regions of interest; CBF, cerebral blood flow; CBV, cerebral blood volume; TTP, time to peak; MTT mean transit time.

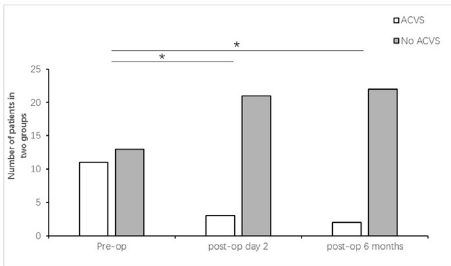

Figure 3. Patient numbers in the 2 groups divided by the presence of asymmetric cortical vessel sign (ACVS) preoperatively and at days 2 and 180 postoperatively. (*$P < 0.05$).

Hemodynamic impairment is commonly seen and considered as an important indication for bypass surgery in patients with MMD. In addition, an increase in OEF with decreased CBF is associated with an increased risk of infarction.[3] Recently, several studies indicated that ACVS may help evaluate extensive ischemia in patients with acute ischemic stroke on GRE and SWI.[9,12-14] Prominent ACVS on the affected side disappeared after full recanalization, which suggested that ACVS is transient and denotes real-time abnormality of cerebral perfusion. A recent study reported that ACVS might be a predictor for early neurologic deterioration and unfavorable prognosis in patients with middle cerebral artery territory infarction.[15] In our study, postoperative change in ACVS proved that ACVS denotes real-time impairment in hemodynamics. However, research focusing on this phenomenon in patients with MMD are quite limited.

In our study, we observed more severely impaired hemodynamics in ROIs showing ACVS. Along with postsurgical improvement in hemodynamics after bypass surgery, ACVS diminished after surgery and in postoperative follow-up, indicating that ACVS is a temporary sign that can reflect real-time hemodynamics of brain tissues. A recent study reported that cortical and subcortical vessel hypointensity on GRE correlates positively with regional cerebral blood flow which conflicts with our observation. This might be explained by different sensitivity of 2 magnetic resonance imaging sequences in detecting BOLD effect. Furthermore, they found that the number of cortical and subcortical vascular hypointensities decreased after bypass surgery, and this is similar to our findings.[11] Another study found that deep medullary veins on SWI, known as "brush sign," correlates negatively with hemodynamics and this is in accordance with our observation.[16] In addition, we found that all ACVS located in the areas had severely impaired perfusion, and this differs from brush sign, as the latter cannot give information about where hemodynamic impairment occurred. This might give a clue on where the anastomosis should locate. Moreover, CBF could be less affected in patients with hemorrhagic onset, which might explain why no ACVS was observed in patients with hemorrhagic MMD.[17]

ACVS was associated with more increase in CBF after bypass surgery in this study. One research reported that preoperatively elevated OEF as one risk factor for symptomatic hyperperfusion syndrome (HPS), which is characterized with more prominent increases in CBF postoperatively.[18] This is in accordance with our finding when considering ACVS reflects an elevation of OEF in cerebral ischemia. Another study in MMD reported a similar correlation between preoperative OEF and more increased CBF after bypass surgery.[19] ACVS was correlated with elevated CBV, which has been reported to be a risk factor for HPS in patients with MMD.[20] Considering Associations between preoperatively elevated CBV, OEF, and ACVS, ACVS might be a potential predictive imaging marker for HPS. However, no symptomatic HPS was observed in all the enrolled patients. A larger population of patients with positive results are warranted to verify whether ACVS is associated with hyperperfusion syndrome.

There are several limitations in our study. First, ACVS is quite subjective, and it is challenging to quantify ACVS on SWI. Further quantitative study about ACVS is needed. Second, the number of patients is limited in this study, and further research of larger population of MMD is required. Lastly, ACVS did not shift clinical decision-making, and further research about possible clinical use of ACVS is needed.

CONCLUSIONS

In this study, we found that ACVS on SWI helps evaluate which hemisphere and location is more affected with impaired hemodynamics and has an association with more increased CBF postoperatively in patients with MMD. Consequently, ACVS might potentially serve as a tool aiding in perioperative evaluation in patients with MMD.

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