Hemodynamic stress distribution reflects ischemic clinical symptoms of patients with moyamoya disease

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ABSTRACT

Objective: Currently, the probability of diagnosing asymptomatic moyamoya disease is increasing. In this study, we consider a less invasive method for predicting future ischemic symptoms in patients with moyamoya disease.

Methods: We reviewed cerebral blood flow (CBF)-related data obtained by xenon CT imaging (XeCT) in six patients with ischemic-type or asymptomatic moyamoya disease. The data were obtained as volume data using a 320-row CT, and applied to the automated region-of-interest-determining software (3DSRT) and converted to standardized images. Eight CBF-related parameters, including CBF value, cerebrovascular reserve capacity (CVRC), and hemodynamic distribution (hdSD), were compared between asymptomatic hemispheres and ischemic symptomatic hemispheres. A significant difference was determined by a two-sample t test. A difference with $p < 0.05$ was considered significant. When statistically significant differences between parameters of asymptomatic hemispheres and ischemic symptomatic hemispheres were identified, cut-off points were calculated with receiver operating characteristic (ROC) curves. Change in the parameters before and after bypass surgery was also assessed.

Results: Of the eight CBF-related parameters evaluated, statistically significant differences between the asymptomatic hemispheres and ischemic hemispheres were observed in the CBF value of the MCA region (CBF-MCA), both at rest and after acetazolamide loading, and in the hdSD, also both at rest and after acetazolamide loading. Of the four statistically significant parameters, ROC analysis revealed that the hdSD at rest and CBF-MCA after acetazolamide loading were the most sensitive and specific parameters (threshold 1.2, sensitivity 1, specificity 1 for hdSD at rest, and threshold 26.44 mL/100 g/min, sensitivity 1, specificity 1 for CBF-MCA after acetazolamide loading). From the CBF data obtained both before and after surgery from the three patients who had undergone direct bypass surgeries, the hdSD was higher than the threshold of 1.2 before surgery but decreased to lower than the threshold of 1.2 after surgery. Ischemic symptoms also resolved after surgery.

Conclusions: The data showed that hdSD at rest and CBF-MCA after acetazolamide loading reflects ischemic symptoms of patients with moyamoya disease. Thus, these parameters could be used as ischemic symptom markers for following patients with moyamoya disease. hdSD at rest is important because it is less invasive and can be performed without acetazolamide loading.

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1. Introduction

Moyamoya disease is a cerebrovascular disorder characterized by a progressive occlusion of the internal carotid artery (ICA)

terminus [1]. When this disease was first recognized, it was also called a "spontaneous occlusion of the circle of Willis [2]" by Kudo et al. However, the name "moyamoya disease" is now more frequently used. Moyamoya disease is characterized by a bilateral stenosis or occlusion of the ICA terminus or proximal part of its branch (i.e., A1 portion of anterior cerebral artery and M1 portion of middle cerebral artery) and abnormal vascular networks around the stenosis or occlusion [1]. This vascular change usually occurs bilaterally, and patients with unilateral lesions are diagnosed as

probable cases. The name "moyamoya" (a Japanese expression for something hazy like a puff of cigarette smoke drifting in the air) was named after the angiographical characteristics of these abnormal vascular networks [3]. Quasi-moyamoya diseases or moyamoya syndrome that have unknown underlying etiology cannot be fully excluded from diagnosis but should be eliminated.

Cerebrovascular reactivity in patients with moyamoya disease is known to be widely impaired in the ICA territory [4], and surgical treatments such as extracranial–intracranial bypass surgeries are performed to improve cerebral hemodynamics and reduce the risk of a subsequent stroke [5]. Based on this, an evaluation of cerebrovascular reactivity to acetazolamide has been the "gold standard" for evaluating cerebrovascular reserve capacity (CVRC) [1,5]. However, in June 2014, an emergent notification of life-threatening side effects of acetazolamide was announced by four major academic societies in Japan. In the notification, eight cases of heart failure and lung edema associated with acetazolamide during a 20-year period were reported. Therefore, an alternative method for the evaluation of cerebral hemodynamics in patients with moyamoya disease is needed.

In the present study, we retrospectively analyzed CBF data obtained by xenon CT imaging (XeCT) with and/or without acetazolamide loading from procedures performed before the emergent notification in June 2014 to identify a value or ratio which reflects the ischemic clinical status of patients with moyamoya disease. All of the data in this study were obtained as volume data using a 320-row CT. We applied the data to automated region-of-interest (ROI)-determining software (3DSRT) for a more objective evaluation.

2. Materials and methods

2.1. Patients' characteristics

We retrospectively analyzed six adult patients with moyamoya disease (five definitive cases and one probable case) at our institution (Institute of Brain and Blood Vessels, Mihara Memorial Hospital, Isesaki, Gunma, Japan) from 2012 to 2014. The patients comprised two males and four females. The mean age was 44.8 years (range, 34–62 years). All of the patients included in the current study underwent a XeCT at rest. Five of the six patients also underwent a XeCT after an intravenous infusion of acetazolamide prior to the emergent notification in June 2014. Complete medical, neurological and radiological examinations were performed. The patients' characteristics are summarized in Table 1.

2.2. Managements of moyamoya disease

The management principles at our institution are as follows.

Asymptomatic patients with moyamoya diseases are conservatively observed without bypass surgeries or oral anti-platelet agents. They are observed with annual MRI/MRA in combination with CBF study of XeCT. The risk factors of the patients are also managed and lifestyle guidance is provided as the recommendation of The Research Committee on Moyamoya Disease in Japan [6].

Moyamoya patients with ischemic symptoms are initially given oral antiplatelet agents, and bypass surgeries are also recommended. In patients with fresh cerebral infarction on diffusion-weighted MRI, bypass surgeries are postponed at least 1 month from the onset of stroke for fear for stroke progression. CBF studies including acetazolamide loading are recommended to all patients who undergo bypass surgery but to patients suffered from refractory TIAs.

Table 1
Patients' characteristics.

Case	Age, sex	Type of moyamoya disease	Hemisphere	Suzuki's class.	Symptom	Type of bypass surgery	XeCT at rest (mL/100 g/min)			XeCT with acetazolamide (mL/100 g/min)			CVRC (%)	XeCT after bypass (mL/100 g/min)		
							MCA	LN	hdSD	MCA	LN	hdSD	CVRC (MCA)	MCA	LN	hdSD
1	55, M	Definite	Rt	3	Asymptomatic	Lt STA-MCA	25.94	30.60	1.18	29.13	35.97	1.23	12.30	28.68	30.56	1.07
			Lt	5	Symptomatic		14.58	23.27	1.60	15.33	22.56	1.47	5.14	28.71	30.88	1.08
2	62, F	Definite	Rt	3	Symptomatic	Rt STA-MCA	31.77	38.00	1.20	26.44	45.19	1.71	−16.80	31.20	29.13	0.93
			Lt	1	Asymptomatic		35.48	38.31	1.08	42.32	47.82	1.13	7.53	32.08	32.35	1.01
3	34, F	Definite	Rt	4	Symptomatic	Rt STA-MCA	20.40	30.55	1.50	21.94	42.86	1.95	7.53	46.15	44.81	0.97
			Lt	3	Asymptomatic		37.28	36.89	0.99	35.19	47.50	1.35	−5.61	47.86	47.10	0.98
4	34, M	Definite	Rt	4	Completed Infarction	Lt EDAS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	34.44	33.10	0.96
			Lt	3	Symptomatic		24.35	34.14	1.40	N/A	N/A	N/A	N/A	25.15	34.55	1.37
5	50, F	Definite	Rt	1	Asymptomatic	None	47.59	55.83	1.17	50.23	62.60	1.25	5.53			
			Lt	3	Asymptomatic		42.66	50.97	1.19	36.19	54.34	1.50	−15.16			
6	34, F	Probable	Rt		Asymptomatic	None	36.75	39.47	1.07	33.44	36.54	1.09	−9.02			
			Lt	–	Asymptomatic		40.99	39.03	0.95	34.86	39.46	1.13	−14.95			

F, female; M, male; Rt, right; Lt, left; IC, internal carotid artery; Bil, bilateral; MCA, middle cerebral artery; hdSD, hemodynamic stress distribution.