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Monitoring Posterior Cerebral Perfusion Changes With Dynamic Susceptibility Contrast-Enhanced Perfusion MRI After Anterior Revascularization Surgery in Pediatric Moyamoya Disease

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Objective: To determine whether dynamic susceptibility contrast-enhanced (DSC) perfusion magnetic resonance imaging (MRI) can be used to evaluate posterior cerebral circulation in pediatric patients with moyamoya disease (MMD) who underwent anterior revascularization.

Materials and Methods: This study retrospectively included 73 patients with MMD who underwent DSC perfusion MRI (age, 12.2 ± 6.1 years) between January 2016 and December 2020, owing to recent-onset clinical symptoms during the follow-up period after completion of anterior revascularization. DSC perfusion images were analyzed using a dedicated software package (NordicICE; Nordic NeuroLab) for the middle cerebral artery (MCA), posterior cerebral artery (PCA), and posterior border zone between the two regions (PCA-MCA). Patients were divided into two groups; the PCA stenosis group included 30 patients with newly confirmed PCA involvement, while the no PCA stenosis group included 43 patients without PCA involvement. The relationship between DSC perfusion parameters and PCA stenosis, as well as the performance of the parameters in discriminating between groups, were analyzed.

Results: In the PCA stenosis group, the mean follow-up duration was 5.3 years after anterior revascularization, and visual disturbances were a common symptom. Normalized cerebral blood volume was increased, and both the normalized time-to-peak (nTTP) and mean transit time values were significantly delayed in the PCA stenosis group compared with those in the no PCA stenosis group in the PCA and PCA-MCA border zones. TTP_{PCA} (odds ratio [OR] = 6.745; 95% confidence interval [CI] = 2.665–17.074; $P < 0.001$) and $CBV_{PCA\text{-}MCA}$ (OR = 1.567; 95% CI = 1.021–2.406; $P = 0.040$) were independently associated with PCA stenosis. TTP_{PCA} showed the highest receiver operating characteristic curve area in discriminating for PCA stenosis (0.895; 95% CI = 0.803–0.986).

Conclusion: nTTP can be used to effectively diagnose PCA stenosis. Therefore, DSC perfusion MRI may be a valuable tool for monitoring PCA stenosis in patients with MMD.

Keywords: Children; Posterior cerebral artery; Hemodynamics; Moyamoya disease; Magnetic resonance imaging

INTRODUCTION

Moyamoya disease (MMD) is a chronic cerebrovascular disease characterized by idiopathic progressive steno-occlusive changes of the circle of Willis, accompanied by collateral vessel development [1,2]. Cerebral blood flow (CBF)

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insufficiency to the anterior cerebral artery and middle cerebral artery (MCA) territories is complemented through leptomeningeal collaterals from the posterior cerebral artery (PCA) [3,4]. Progressive steno-occlusive changes occur in the PCA during the follow-up period after anterior revascularization, even in the absence of initial PCA stenosis [5,6].

Dynamic susceptibility contrast-enhanced (DSC) perfusion magnetic resonance (MR) is a noninvasive method for assessing cerebral hemodynamics [7-9]. DSC perfusion magnetic resonance imaging (MRI) provides quantitative perfusion parameters such as cerebral blood volume (CBV), CBF, time-to-peak (TTP), and mean transit time (MTT). Among these, both TTP and MTT have been reported to correlate well with clinical outcomes, such as successful revascularization surgery of anterior circulation [10-14]. Recent studies emphasize that patients with MMD undergoing PCA stenosis are more likely to have a worse prognosis than patients with preserved posterior circulation; therefore, the hemodynamics of MMD with PCA steno-occlusive changes must be accurately assessed and understood [6,15,16]. Thus, cerebral perfusion changes in posterior circulation should be carefully monitored because posterior revascularization is needed in cases of progressive PCA stenosis.

However, no studies have reported quantitative perfusion monitoring to assess posterior circulation impairment, except for those reporting risk factors such as advanced Suzuki staging or PCA–basilar artery angle [17,18]. Therefore, this study aimed to determine whether DSC perfusion MRI can be used to quantitatively evaluate perfusion changes in posterior cerebral circulation during the follow-up period.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB-No. 2210-166-1376). Due to the retrospective nature of the study, the requirement for informed consent was waived.

Patient Selection

To identify eligible patients, we retrospectively screened 432 patients with MMD who underwent DSC perfusion MRI and digital subtraction angiography (DSA) at the pediatric radiology department of the Seoul National University Children's Hospital between January 2016 and December 2020. Institutional indications for DSC perfusion MRI in patients with MMD were as follows: 1) DSC perfusion MRI and DSA within 1 month before anterior revascularization, and 2) DSC perfusion MRI without time-of-flight (TOF) MR angiography (MRA) 6 months after anterior revascularization surgery, followed by DSC perfusion with TOF-MRA annually thereafter. When new-onset symptoms appeared despite anterior revascularization, DSC perfusion MRI with or without TOF-MRA was performed to determine the need for posterior revascularization. Imaging follow-up protocol did not include contrast-enhanced MRA; therefore, we only used gadolinium-based contrast agent for DSC perfusion imaging. DSA was also performed during the posterior revascularization planning.

The patient inclusion criteria were as follows: 1) diagnosed with MMD through DSA as a steno-occlusive change in the circle of Willis, accompanied by development of collateral vessels; 2) previously underwent uni- or bilateral anterior revascularization surgery; and 3) presented with neurological symptoms within the last 3 months during the postoperative follow-up period after anterior revascularization. We excluded 359 patients for the following reasons: planned DSA for anterior revascularization surgery (n = 247), PCA stenosis diagnosed at the time of anterior revascularization (n = 106), or inadequate image quality for DSC perfusion (n = 6). Two patients in this study overlapped with a previous report [8] because they had previously undergone anterior revascularization surgery between June 2016 and August 2017, and developed recurrent neurological symptoms until December 2020. Progressive PCA stenosis was defined when the presence of PCA narrowing progression (presence of PCA moyamoya vessels and with more than 30% narrowing compared with juxta proximal normal-looking PCA) on DSA was determined by pediatric radiologists (SBL, YJC, SL, and YHC with 7, 9, 10, and 17 years of experience, respectively), and matched to symptoms and perfusion abnormalities on perfusion MRI. Finally, 73 patients were included and classified into two groups according to the presence of PCA stenosis (Fig. 1). The PCA stenosis group included 30 patients with newly confirmed PCA involvement, and the no PCA stenosis group included 43 patients without PCA involvement.

Characteristics of Patients with Suspected Posterior Circulation Impairment

This study collected data on patients' age at initial diagnosis, completion of anterior revascularization for preceding symptoms, and onset of new symptoms. Age

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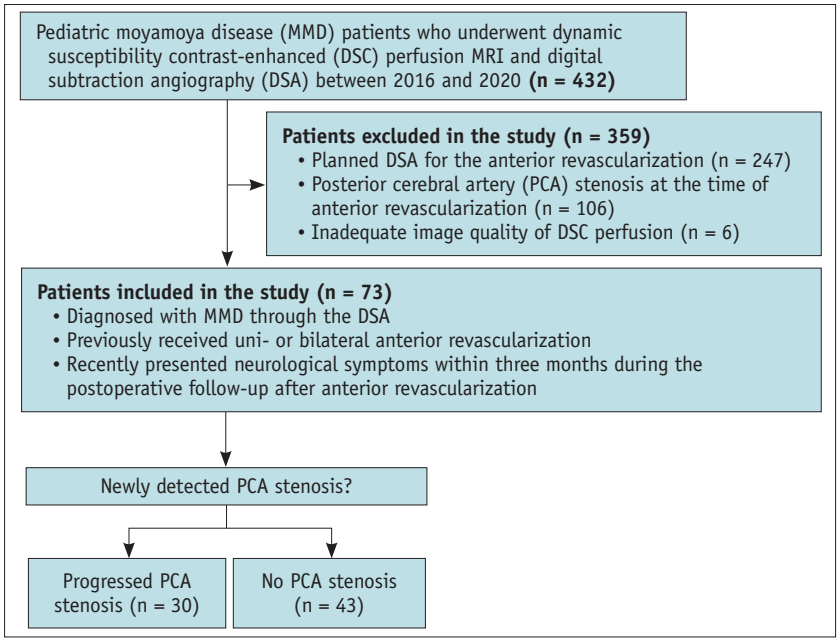

Fig. 1. Study diagram for patient selection. We retrospectively screened 432 patients with MMD. Finally, 73 patients were included and classified into two groups according to the presence of PCA stenosis. MRI = magnetic resonance imaging

at the initial diagnosis was defined as time of first DSA examination in each patient. Follow-up duration was defined as the period between the initial (done to perform anterior revascularization) and current DSA examinations. New-onset clinical symptoms were categorized as motor weakness, sensory abnormalities, headache, seizures, and visual disturbances. Clinical manifestations, information on familial MMD history, and clinical history of old infarction and hemorrhage were collected, and the initial Suzuki stages were evaluated using Suzuki staging on DSA examination [19].

Image Acquisition

DSC perfusion MRI was performed using a single-shot gradient-echo echo-planar imaging sequence with intravenous injection of a gadolinium-based contrast agent (Gadobutrol, Gadovist; Bayer AG) using the following parameters: repetition time/echo time, 1500/30 ms; flip angle, 60°; field of view, 24 x 24 cm; 17 sections; matrix, 128 x 128; thickness, 5 mm; intersection gap, 1.5 mm. Fifty images were captured at intervals equal to the number of repetitions per section. Gadolinium-based contrast agent dose was 0.1 mmol/kg with injection flow rate of 2 mL/s. DSA was performed with selective angiography at both the internal/external carotid and unilateral vertebral arteries (VAs) using an iodine contrast medium (Pamiray®250, Dongkook Pharm.), and was used for each biplane projection (Axiom Artis; Siemens Healthcare).

Image Analysis

DSC perfusion images were generated as relative CBV, CBF, TTP, and MTT maps using a dedicated software package (NordicICE; Nordic NeuroLab). Regions of interest (ROIs) were drawn at the vascular territory, including MCA, PCA, and the posterior border zone between these territories (defined as "PCA-MCA"), according to the Alberta Stroke Program Early CT score [7,8,12]. ROIs were drawn at the ganglionic and supraganglionic levels on axial images by two experienced pediatric radiologists (YSS and SL with 4 and 10 years of MRI experience, respectively) in consensus. Figure 2 illustrates the proposed method. DSA test results helped determine the affected side with PCA stenosis. If there was no PCA stenosis, the side associated with symptoms was selected; if the clinical symptoms were ambiguous, the side with severe TTP delay was selected. Perfusion parameters, such as normalized CBV (nCBV), CBF (nCBF), TTP (nTTP), and MTT (nMTT) were normalized to cerebellar perfusion status, which was defined as the average of the parameters for right and left cerebellar hemispheres [8]. Normalized values were defined using the following equations: $nTTP\ (s) = TTP_{vascular\ territory} \times TTP_{cerebellum}$, $nMTT\ (s) = MTT_{vascular\ territory} \times MTT_{cerebellum}$, $nCBV = CBV_{vascular\ territory}/CBV_{cerebellum}$, and $nCBF = CBF_{vascular\ territory}/CBF_{cerebellum}$.

Perfusion parameter analysis of each vascular territory was performed using DSC perfusion MRI, at the time of suspected PCA stenosis after anterior revascularization

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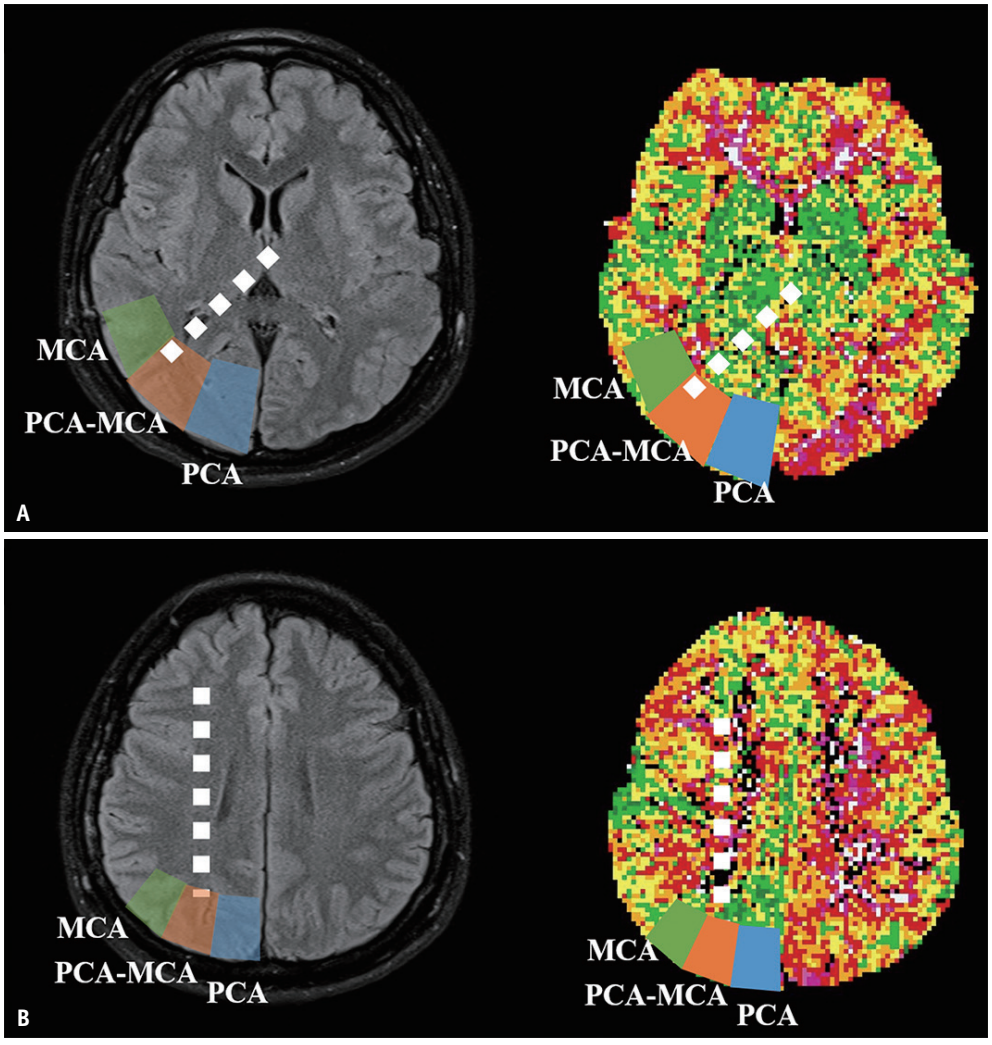

Fig. 2. Perfusion parameter analysis method in magnetic resonance imaging. **A:** Regions of interest at the ganglionic level. Based on the lateral ventricle (dotted line), the border zone (orange area) between the posterior cerebral artery (PCA) and the middle cerebral artery (MCA) was drawn. The MCA territory (green area) was drawn on the parietal side, while the PCA territory (blue area) was drawn on the occipital side. **B:** Regions of interest at the supraganglionic level. Based on the lateral ventricle roof (dotted line), the PCA-MCA border zone (orange area) is drawn. The remaining samples were prepared as described above. PCA-MCA = posterior border zone between PCA and MCA

surgery. To assess temporal hemodynamic changes in patients with progressive PCA stenosis, the previous MRI (defined as perfusion MRI just before time of suspected PCA stenosis) was also analyzed.

Statistical Analysis

Patient characteristics were compared using the chi-square test for categorical variables and the independent *t*-test for continuous variables. Average values of supraganglionic and ganglionic levels were used as perfusion parameters of the progressive and no-PCA stenosis groups and compared at each vascular territory using an unpaired *t*-test. Temporal perfusion changes between previous and current MRI scans in the progressive PCA group were compared using a paired *t*-test.

Factors associated with PCA stenosis were assessed using univariable logistic regression analysis, which additionally determined the categories used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). For continuous variables, an increase of 1 was used to calculate ORs and 95% CIs. As CBV has a small standard deviation compared with other variables, an increase of 10^{-1} was considered to calculate ORs and 95% CIs. Multivariable logistic regression analysis was performed for variables with $P < 0.015$ in univariable analysis, and likelihood ratio test was used to infer the logistic regression coefficient. Performance of each perfusion parameter with normalization for discriminating

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between the two groups was determined using receiver operating characteristic (ROC) analysis and area under the curve (AUC). By maximizing the Youden index, the optimal cutoff value was determined. All statistical analyses were conducted using SPSS Statistics for Windows (version 25.0; IBM Corp.), and statistical significance was set at $P < 0.05$.

RESULTS

Characteristics of Patients with Suspected Posterior Circulation Impairment

Demographic factors and clinical status of the patients are summarized in Table 1. All patients (age, 12.2 ± 6.1 years) underwent anterior revascularization surgery at a mean age of 9.2 years and the mean follow-up duration was 4.3 years. No differences between the two groups were found in terms of age at initial diagnosis, completion of anterior revascularization for preceding symptoms, or onset of new symptoms.

Visual disturbances were more common in the progressive PCA stenosis group ($P = 0.001$), but other symptoms did not differ between the two groups. The most common clinical manifestation was transient ischemic attack (TIA), appearing more frequently in the no PCA stenosis group ($P = 0.028$) with only four patients having ischemic stroke and no intracranial hemorrhage. Family

Table 1. Characteristics of patients with suspected posterior circulation impairment

Characteristics	PCA stenosis (n = 30)	No PCA stenosis (n = 43)	*P*
Sex, boy	12 (40.0)	23 (53.5)	0.256
Age, yr			
Initial diagnosis	7.1 ± 5.6	8.4 ± 3.7	0.266
Completion of anterior revascularization for preceding symptom	8.1 ± 6.5	10.0 ± 4.3	0.129
New onset symptom during follow-up	12.5 ± 7.2	11.9 ± 5.2	0.714
Follow-up duration, yr	5.3 ± 4.7	3.6 ± 4.2	0.096
Anterior revascularization			
Bilateral EDAS or EMAS*	8 (26.7)	15 (34.9)	-
Bilateral EDAS with frontal EGPS	22 (73.3)	28 (65.1)	-
Unilateral EDAS	5 (16.7)	8 (18.6)	-
Symptoms			
Motor weakness	14 (46.7)	25 (58.1)	0.233
Sensory abnormality	5 (16.7)	13 (30.2)	0.147
Headache	20 (66.7)	22 (51.2)	0.187
Seizure	4 (13.3)	4 (9.3)	0.588
Visual disturbance	10 (33.3)	2 (4.6)	0.001
Clinical manifestations			
Transient ischemic attack	14 (46.7)	31 (72.1)	0.028
Ischemic stroke	2 (6.7)	2 (4.7)	0.546
Intracranial hemorrhage	0 (0.0)	0 (0.0)	-
Family history of MMD	6 (20.0)	7 (16.2)	0.683
History of old infarct	8 (26.7)	6 (14.0)	0.175
History of old hemorrhage	3 (10.0)	3 (7.0)	0.479
Initial Suzuki staging			0.002
1	3	3	
2	2	22	
3	16	14	
4	8	4	
5	1	0	
6	0	0	

Values are presented as mean ± standard deviation or n (%) unless otherwise indicated.
*Only one patient underwent EMAS, and all others underwent EDAS surgery on the bilateral side.
PCA = posterior cerebral artery, EDAS = encephaloduroarteriosynangiosis, EMAS = encephalomyoarteriosynangiosis, EGPS = encephalogale operiostealsynangiosis, MMD = moyamoya disease

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history and history of old infarcts did not differ between groups; however, the progressive PCA stenosis group showed more advanced staging on DSA examination (P = 0.002). Median time interval between current perfusion MRI and posterior revascularization surgery, such as encephaloduroarteriosynangiosis through an occipital artery (n = 7) or occipital encephalogaleoperiostealsy nangiosis (n = 23) was 25 days [range: 0–322 days] in the progressive PCA stenosis group. Five patients did not undergo surgery within 3 months of perfusion MRI because of mild headache (n = 4) or loss to follow-up (n = 1).

Quantitative Perfusion Parameters at the Time of Suspected PCA Stenosis

A comparison of quantitative perfusion parameters between the progressive PCA stenosis and no PCA stenosis groups is presented in Table 2. nCBV of the progressive PCA group was significantly increased in PCA and PCA-MCA territories; however, nCBF values in each vascular region did not vary significantly. nTTP and nMTT values of the progressive PCA stenosis group were significantly delayed compared with those of the no PCA stenosis group in the PCA and PCA-MCA territories, but not in the MCA territory.

Table 3 summarizes temporal hemodynamic changes in the posterior hemisphere at the time of suspected stenosis in the PCA stenosis group. nCBV value of the current MRI showed a significant increase in PCA and PCA-MCA territories compared with previous perfusion parameters in the progressive PCA stenosis group. nTTP and nMTT values of the current MRI were significantly delayed in the PCA and PCA-MCA territories; however, nTTP and nMTT did not significantly vary between previous and current MRI scans in the MCA territory.

Association between DSC Perfusion Parameters and PCA Stenosis

The results of logistic regression analysis are presented in Table 4. In univariable logistic regression analysis, the Suzuki stage and perfusion parameters such as nTTP, nMTT, and nCBV in the vascular territories were significantly

Table 2. Quantitative perfusion parameters at the time of suspected PCA stenosis

Parameters	Territory	PCA stenosis	No PCA stenosis	P
nCBV	PCA	1.22 ± 0.25	0.99 ± 0.11	< 0.001
	PCA-MCA	1.16 ± 0.23	1.01 ± 0.13	0.002
	MCA	1.07 ± 0.21	1.03 ± 0.21	0.408
nCBF	PCA	0.98 ± 0.14	1.01 ± 0.07	0.395
	PCA-MCA	0.95 ± 0.15	0.97 ± 0.09	0.488
	MCA	0.97 ± 0.14	1.00 ± 0.13	0.344
nTTP (s)	PCA	2.36 ± 2.73	-0.37 ± 0.68	< 0.001
	PCA-MCA	2.38 ± 2.50	0.68 ± 0.86	< 0.001
	MCA	0.07 ± 1.07	0.33 ± 0.90	0.269
nMTT (s)	PCA	1.62 ± 3.09	-0.21 ± 0.87	0.003
	PCA-MCA	2.30 ± 3.70	0.69 ± 1.28	0.029
	MCA	-0.13 ± 1.59	0.33 ± 1.43	0.198

Values are presented as mean ± standard deviation.
PCA = posterior cerebral artery, nCBV = normalized cerebral blood volume, PCA-MCA = posterior border zone between PCA and MCA, MCA = middle cerebral artery, nCBF = normalized cerebral blood flow, nTTP = normalized time-to-peak, nMTT = normalized mean transit time

Table 3. Hemodynamic changes with the 30 patients in the PCA stenosis group at the time of suspected PCA stenosis

Parameters	Territory	Previous	Current	Difference	P
nCBV	PCA	0.99 ± 0.32	1.22 ± 0.25	0.22 ± 0.29	< 0.001
	PCA-MCA	1.00 ± 0.28	1.16 ± 0.23	0.16 ± 0.32	0.010
	MCA	1.03 ± 0.30	1.07 ± 0.21	0.04 ± 0.28	0.497
nCBF	PCA	0.96 ± 0.16	0.98 ± 0.14	0.02 ± 0.20	0.599
	PCA-MCA	0.97 ± 0.17	0.95 ± 0.15	-0.02 ± 0.26	0.695
	MCA	1.00 ± 0.17	0.97 ± 0.14	-0.03 ± 0.20	0.426
nTTP (s)	PCA	-1.06 ± 1.45	2.36 ± 2.73	3.43 ± 2.60	< 0.001
	PCA-MCA	-0.39 ± 1.44	2.38 ± 2.50	2.77 ± 2.81	< 0.001
	MCA	-0.47 ± 1.24	-0.46 ± 2.02	0.01 ± 1.84	0.981
nMTT (s)	PCA	-1.08 ± 2.03	1.62 ± 3.09	2.70 ± 2.85	< 0.001
	PCA-MCA	-0.49 ± 1.77	2.30 ± 3.70	2.80 ± 3.80	< 0.001
	MCA	-0.43 ± 1.80	-0.13 ± 1.59	0.30 ± 2.20	0.461

Values are presented as mean ± standard deviation.
PCA = posterior cerebral artery, nCBV = normalized cerebral blood volume, PCA-MCA = posterior border zone between PCA and MCA, MCA = middle cerebral artery, nCBF = normalized cerebral blood flow, nTTP = normalized time-to-peak, nMTT = normalized mean transit time

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Table 4. Logistic regression analyses of the association between DSC perfusion parameters and PCA stenosis

Parameters	Univariable		Multivariable	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Initial Suzuki stage				
Stage 1–4	Reference			
Stage 4–6	4.179 (1.148–15.21)	0.030	-	-
Perfusion parameters				
CBV_{PCA} (for increase by 10^{-1})	1.910 (1.374–2.655)	< 0.001	-	-
$CBV_{PCA-MCA}$ (for increase by 10^{-1})	1.623 (1.206–2.184)	0.001	1.567 (1.021–2.406)	0.040
TTP_{PCA} (for increase by 1)	6.697 (2.709–16.55)	< 0.001	6.745 (2.665–17.074)	< 0.001
$TTP_{PCA-MCA}$ (for increase by 1)	2.259 (1.365–3.740)	0.002	-	-
MTT_{PCA} (for increase by 1)	2.075 (1.311–3.284)	0.002	-	-
$MTT_{PCA-MCA}$ (for increase by 1)	1.377 (1.029–1.842)	0.031	-	-

The perfusion parameters are relative values.
DSC = dynamic susceptibility contrast-enhanced, PCA = posterior cerebral artery, OR = odds ratio, CI = confidence interval, CBV = cerebral blood volume, PCA-MCA = posterior border zone between PCA and middle cerebral artery, TTP = time-to-peak, MTT = mean transit time

Table 5. ROC curve analysis of perfusion parameters in discriminating PCA stenosis and no PCA stenosis groups

Parameters	Territory	AUC	95% CI	*P*
TTP	PCA	0.895	0.803–0.986	< 0.001
	PCA-MCA	0.736	0.612–0.861	0.001
	MCA	0.402	0.265–0.538	0.154
MTT	PCA	0.783	0.666–0.900	< 0.001
	PCA-MCA	0.696	0.561–0.831	0.005
	MCA	0.419	0.285–0.554	0.244
CBV	PCA	0.753	0.622–0.885	< 0.001
	PCA-MCA	0.747	0.615–0.878	< 0.001
	MCA	0.585	0.449–0.721	0.217
CBF	PCA	0.386	0.233–0.539	0.099
	PCA-MCA	0.451	0.310–0.592	0.480
	MCA	0.456	0.318–0.594	0.523

ROC = receiver operating characteristic, PCA = posterior cerebral artery, AUC = area under the curve, CI = confidence interval, TTP = time-to-peak, PCA-MCA = posterior border zone between PCA and MCA, MCA = middle cerebral artery, MTT = mean transit time, CBV = cerebral blood volume, CBF = cerebral blood flow

associated with progressive PCA stenosis. In the final multivariable analysis, TTP_{PCA} (OR = 6.745; 95% CI = 2.665–17.074; $P < 0.001$) and $CBV_{PCA-MCA}$ (OR = 1.567; 95% CI = 1.021–2.406; $P = 0.040$) were independently associated with PCA stenosis.

Discrimination between PCA Stenosis and No PCA stenosis Groups Using DSC Perfusion Parameters

Table 5 presents the AUC values for each perfusion parameter. TTP_{PCA} showed the highest AUC for predicting PCA stenosis (AUC = 0.895; 95% CI = 0.803–0.986). The optimal cutoff value determined by maximizing the Youden index was 0.813, with corresponding sensitivity, specificity, positive predictive value, and negative predictive values of 0.833 (25/30), 0.977 (42/43), 0.962 (25/26), and 0.894 (42/47), respectively. Representative cases of progressive PCA stenosis are displayed in Figures 3 and 4.

DISCUSSION

The present study evaluated clinical and perfusion characteristics of progressive PCA stenosis with late-onset PCA insufficiency using DSC perfusion MRI in pediatric patients with MMD whose recent-onset symptoms appeared after anterior revascularization surgery. Our results demonstrated that quantitative perfusion parameters such as nTTP and nCBV could be used to evaluate posterior circulation involvement in progressive PCA stenosis. Delayed nTTP in the PCA territory and posterior border zone at both the supraganglionic and ganglionic levels could effectively indicate progression of PCA stenosis.

MMD is a non-atherosclerotic disease accompanying progressive steno-occlusive changes in intracranial vessels; therefore, progressive PCA stenosis may be explained by the primary disease process of MMD [20]. Mugikura et al. [20] postulated that increased blood flow through the PCA following anterior circulation impairment induces hemodynamic stress in the vascular endothelium of the PCA, causing progressive steno-occlusive changes. Additionally, progressive PCA stenosis can be explained by a reduction in leptomeningeal collateral flow after anterior revascularization, and a decrease in blood flow demand in the cerebral ischemic area [4]. These mechanisms are

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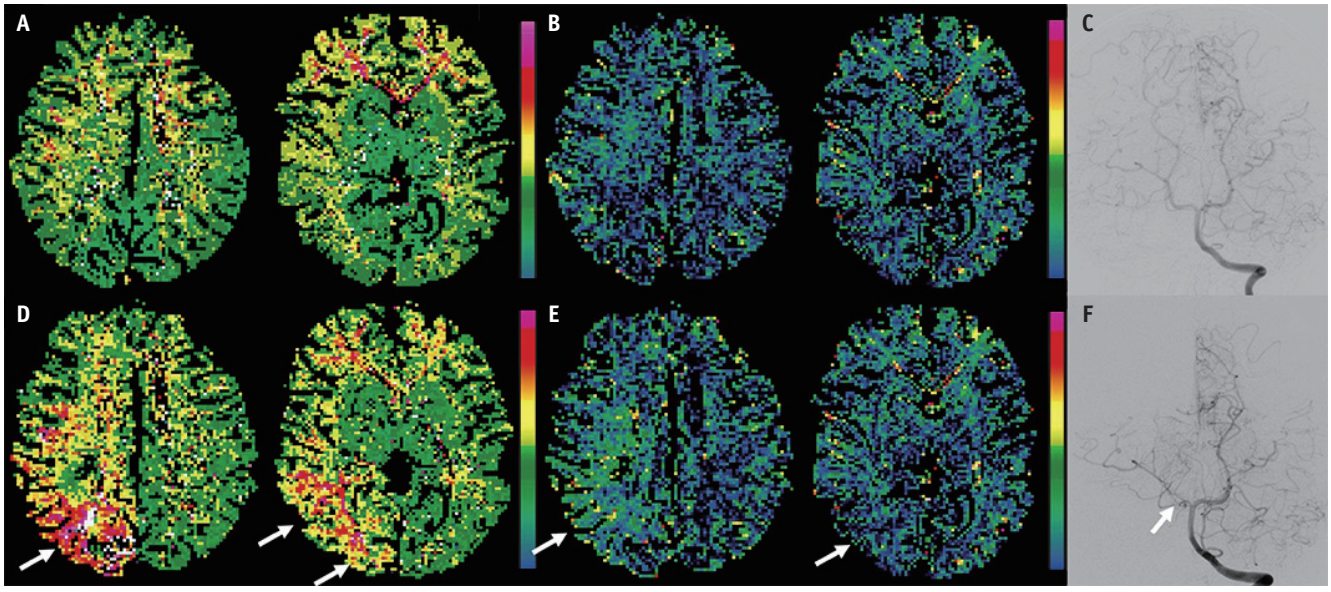

Fig. 3. Representative case with progressive posterior cerebral artery (PCA) stenosis. A 5-year-old boy with moyamoya disease developed bilateral encephaloduroarteriosynangiosis with frontal encephalogaleosynangiosis. At the 4-year follow-up, dynamic susceptibility contrast-enhanced perfusion magnetic resonance imaging (MRI) showed no time-to-peak (TTP) delay **(A)** or cerebral blood volume (CBV) increase **(B)** in PCA territory at the ganglionic and supraganglionic levels on axial images (PCA, PCA-MCA, and middle cerebral artery [MCA] territory; -1.87, -1.35, and 0.33 (s) for nTTP; 0.99, 1.07, and 1.54 for nCBV). **(C)** Digital subtraction angiography (DSA) performed for preoperative evaluation of anterior revascularization demonstrates intact bilateral PCA branches. **D, E:** However, headache and left-sided visual disturbance was seen at the 5-year follow-up. Perfusion MRI revealed TTP delay **(D)** and CBV increase **(E)** in the right PCA territory and posterior border zone area (arrows), and showed mild TTP delay and CBV increase at the right MCA territory supraganglionic level (PCA, PCA-MCA, and MCA territory; 7.57, 8.35, and 2.05 (s) for nTTP; 1.11, 1.49, and 1.50 for nCBV). **F:** A severe steno-occlusive change was noted in the right proximal PCA on DSA (arrow), and the patient underwent right-sided posterior revascularization surgery. PCA-MCA = posterior border zone between PCA and MCA, nTTP = normalized time-to-peak, nCBV = normalized cerebral blood volume

supported by the association between a higher initial Suzuki stage and PCA stenosis in our study. Patients with PCA stenosis are more likely to develop larger ischemic lesions, and have a worse prognosis, than patients with preserved posterior circulation [15,16]. PCA stenosis requires perfusion monitoring or an additional operation in the PCA territory for an average of 5 years, because progressive steno-occlusive changes in PCA can occur in patients with postoperative MMD despite the initial absence of stenosis [5,14].

Although progressive PCA stenosis in MMD after anterior circulation revascularization surgery is a common and expected process in many patients, its incidence and clinical features are diverse [4,14,21]. At the initial diagnosis of anterior circulation insufficiency, the patient's symptoms mainly present as TIAs; however, when posterior circulation insufficiency is suspected, PCA-specific symptoms are related to visual function in some, but not all, patients [17,21]. Lee et al. [17] reported that both presence of infarction and younger age at the time of diagnosis were significant clinical factors for PCA stenosis progression in pediatric patients with MMD. Our study also revealed new-onset symptoms at a mean duration of 5.3 years after anterior revascularization, advanced MMD at initial diagnosis, and more frequent visual disturbances in the progressive PCA stenosis group.

DSA is the gold standard for diagnosing MMD; however, it is an invasive procedure [22,23]. Several noninvasive imaging methods have been developed as alternatives, with TOF-MRA commonly being used for intracranial vessel evaluation. However, signal loss due to turbulent flow, as well as in-plane saturation artifacts, occur in horizontal sections, such as the proximal PCA vascular direction. Thus, TOF-MRA might overestimate the degree of steno-occlusive changes in intracranial vessels [24]. Another option, gadolinium contrast-enhanced MRA, has no disadvantages in terms of overestimating steno-occlusive changes. However, performing contrast-enhanced MRA and DSC perfusion MRI using a contrast agent twice is challenging. In addition, contrast-enhanced MRA cannot provide quantitative information regarding cerebral vascular territories using DSC perfusion MRI.

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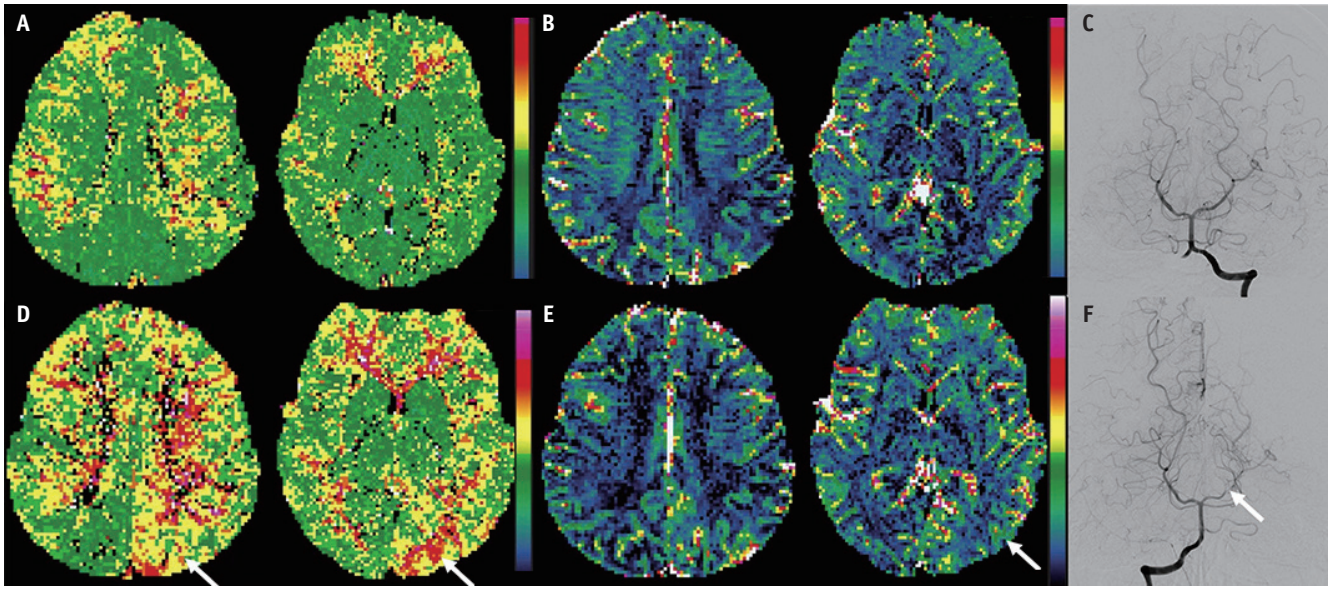

Fig. 4. A second representative case with progressive posterior cerebral artery (PCA) stenosis. An 18-year-old girl with moyamoya disease developed bilateral encephaloduroarteriosynangiosis and frontal encephalosynangiosis. At the 2-year follow-up, dynamic susceptibility contrast-enhanced perfusion magnetic resonance imaging (MRI) showed no time-to-peak (TTP) delay **(A)** or cerebral blood volume (CBV) increase **(B)** in the PCA territory at the ganglionic and supraganglionic levels on axial images (PCA, PCA-MCA, and middle cerebral artery [MCA] territory; -1.75, -0.67, and 0.08 (s) for nTTP; 1.32, 1.25, and 1.27 for nCBV). **(C)** Digital subtraction angiography (DSA) performed for preoperative evaluation of anterior revascularization demonstrates intact bilateral PCA branches. However, visual lightening, dimness, and headache developed on the 3-year follow-up, and perfusion MRI revealed TTP delay **(D)** and subtle CBV increase **(E)** in the left PCA territory and posterior border zone area (arrows) (PCA, PCA-MCA, and MCA territory; 2.47, 2.87, and -0.66 (s) for nTTP; 1.52, 1.23, and 1.02 for nCBV). **F:** A severe steno-occlusive change was noted in the left proximal PCA on DSA (arrow), and the patient underwent left-sided posterior revascularization surgery. PCA-MCA = posterior border zone between PCA and MCA, nTTP = normalized time-to-peak, nCBV = normalized cerebral blood volume

DSC perfusion MRI is helpful in predicting effects and risks of surgery by measuring hemodynamic changes in bypass surgery for MMD faster than other modalities [25,26]. Further, it has been widely used to evaluate hemodynamic changes after revascularization in patients with MMD [27,28]. A previous report showed that TTP reflects hemodynamic changes in the postoperative state of pediatric MMD patients [7]. Cerebral infarcts may involve anterior circulation territory at an early stage of MMD, and extend to the posterior border zone and PCA territory with disease progression by outpacing the compensatory blood collateral formation developing from the PCA [29]. This study explored whether perfusion parameters reflect posterior circulation impairment after anterior revascularization surgery, and validated the perfusion monitoring method currently used in pediatric patients with MMD. Delayed nTTP and nMTT with an increase in nCBV occurred in both the PCA territory and posterior border zones in the progressive PCA stenosis group. These perfusion changes can be interpreted as compensatory hemodynamic changes recompensing for the decrease in CBF and cerebral perfusion pressure through posterior circulation during the follow-up period.

These arterial transit time-related perfusion parameters (such as TTP or MTT), comprehensively represent the delay in arterial transit through collateral flow (such as leptomeningeal collaterals) during PCA stenosis progression. Arterial arrival delay in collateral vessels can cause overestimation of TTP delay and underestimation of CBF in pediatric patients with MMD [30]. When CBF compensation is possible, changes in CBV can be observed in the early stages of progressive PCA stenosis. However, no change in nCBF might be observed compared with the previous MRI in the progressive PCA group. The lack of difference in CBF may be explained by arteriolar vasodilation autoregulation [28]. Therefore, CBF is not an appropriate parameter for evaluating progressive PCA stenosis on DSC perfusion MRI.

Our study has several limitations. First, accurate ROI drawing of each vascular territory, such as the MCA, MCA-PCA, and PCA, was challenging; therefore, a potential bias might have existed owing to the inclusion of other portions. However, to minimize bias, we selected the same supraganglionic and ganglionic levels in the perfusion

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map using a coregistered axial conventional MR image. The second limitation concerns normalization of perfusion parameters in the cerebellar hemisphere. Although posterior circulation supplies the cerebellum, it is the most appropriate reference area because it is barely affected by revascularization surgery. The third limitation is the inability to quantitatively assess PCA stenosis using DSA. Quantification of PCA diameter to judge its progression is problematic owing to its small diameter. In addition, VA flow in MMD often increases to supply collateral flow to the anterior circulation, limiting PCA stenosis assessment due to washout by contralateral VA flow. However, these problems can be minimized by evaluating PCA stenosis and correlating it with the patient's symptoms and perfusion MRI findings. Finally, there may be bias due to the short follow-up duration. For this reason, even patients in the "no PCA stenosis" group can develop PCA stenosis after a prolonged period of time; thus, a sufficient follow-up duration is required in future studies. Furthermore, patients with MMD who undergo revascularization require sufficient follow-up duration of at least five years, considering previous studies [14].

In conclusion, this study showed that PCA stenosis progressing within 5 years of surgery could manifest with visual impairment in pediatric patients with MMD, even in the absence of initial PCA stenosis at the time of anterior revascularization. TTP perfusion parameters can sensitively depict the presence of PCA stenosis, which may be accompanied by an increase in CBV. Therefore, we demonstrated that changes in TTP values may be useful for monitoring posterior cerebral circulation in patients with PCA stenosis after anterior revascularization surgery.

Availability of Data and Material

All data generated or analyzed during the study are included in this published article.

Conflicts of Interest

Young Hun Choi and Jung-Eun Cheon, contributing editors of the *Korean Journal of Radiology*, were not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Seunghyun Lee. Data curation: Yun Seok Seo, Seunghyun Lee. Formal analysis: Yun Seok Seo, Seunghyun Lee. Investigation: Yun Seok Seo, Seunghyun Lee. Methodology: all authors. Project administration: Yun Seok Seo, Seunghyun Lee. Resources: Yun Seok Seo, Seunghyun Lee. Methodology: all authors. Software: Yun Seok Seo, Seunghyun Lee. Supervision: Seunghyun Lee. Validation: Yun Seok Seo, Seunghyun Lee. Methodology: all authors. Visualization: Yun Seok Seo, Seunghyun Lee. Writing—original draft: all authors. Writing—review & editing: all authors.

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