Clinical Significance of the CSF Pulsation Flow Sign in the Foramen of Monro on FLAIR in Patients with Aneurysmal SAH -Preliminary Report-

Rie AOKI,[1] Masami SHIMODA,[1] Shinri ODA,[1] Masaaki IMAI,[1]
Hideaki SHIGEMATSU,[2] and Mitsunori MATSUMAE[2]

[1]Department of Neurosurgery, Tokai University Hachioji Hospital, Hachioji, Tokyo, Japan;
[2]Department of Neurosurgery, Tokai University School of Medicine, Isehara, Kanagawa, Japan

Abstract

It is known that the cerebrospinal fluid (CSF) pulsation flow sign in the lateral ventricles directly above the foramen of Monro (CPF-M) on axial fluid attenuated inversion recovery (FLAIR) is a normal physiological finding as an artifact of FLAIR. In this study, whether CPF-M can be used as a neuroradiological finding related to pathological conditions in patients with acute aneurysmal subarachnoid hemorrhage (aSAH) was investigated. CPF-M-related clinical features were retrospectively evaluated in 147 aSAH patients who underwent adequate serial MRI examinations without massive intraventricular hemorrhage (IVH) of the lateral ventricle within 48 h of ictus. The frequency of the CPF-M in the control group was 32% (57/178), 33% (40/123), and 38% (45/117) for the normal control, chronic cerebral infarction, and deep white matter lesion (WML) groups, respectively. In aSAH patients, the overall prevalence of the CPF-M was 57% (84/147), significantly higher than in the three control groups. Multivariate analysis showed that age <70 years, lower IVH Hijdra score of the fourth ventricle, absence of T_1-FLAIR mismatch, deep WMLs, old infarction, diffuse brain swelling, symptomatic delayed cerebral ischemia (DCI), shunt-dependent chronic hydrocephalus (SDCH), and favorable outcome were significantly associated with the CPF-M. Although limited to SAH patients without massive IVH of the lateral ventricles, one can conclude that, in acute aSAH, the presence of CPF-M on admission MRI suggests that the circulatory dynamics of the CSF from the basal cistern to the ventricles are approximately normal. Thus, this finding may appear to offer an indicator of a good outcome without DCI and SDCH.

Key words: chronic hydrocephalus, CSF pulsation flow sign, delayed cerebral ischemia, foramen of Monro, subarachnoid hemorrhage

Introduction

Fluid attenuated inversion recovery (FLAIR) is useful for detecting brain diseases, including aneurysmal subarachnoid hemorrhage (aSAH).[1] One of the characteristics of FLAIR is ventricular cerebrospinal fluid (CSF) pulsation artifact causing inflow of non-inverted CSF from superior or inferior areas.[2] CSF pulsation artifacts on axial FLAIR are prominent and common in the third, fourth, and lateral ventricles. In the lateral ventricles, the artifact is found directly above the foramen of Monro.[2] In the physiological state, it has been suggested that the ventricular CSF pulsation artifact is enhanced by the increasing size of the ventricle and the decreasing compliance of the periventricular tissue in the aging brain,[2,3] and this artifact appears multifactorial and has relatively little clinical significance.[2]

However, when there is decreased intracranial compliance due to elevated intracranial pressure (ICP) due to the exponential pressure–volume relationship,[4] the reduction in intracranial compliance leads to an increase in cerebral pulsatility.[4] In patients with acute aSAH, we hypothesized that elevated ICP due to early brain damage[5] with decreased intracranial compliance is likely to result in increased pressure pulsatility and enhancement of ventricular CSF pulsation flow in the foramen of Monro. In aSAH patients, but not in normal cases, we thought that this finding would be useful not as an artifact, but as one of the neuroradiological

signs of the presence of CSF pulsation, similar to the image obtained by the time-spatial labeling inversion pulse method[6] and phase-contrast MRI technique.[7] We call this artifact the CSF pulsation flow sign in the foramen of Monro on FLAIR (CPF-M), and we were interested in whether the presence of the CPF-M is an indicator of pathological conditions in patients with acute aSAH. First, the frequency of the CPF-M was compared in aSAH patients and normal controls. Then, whether the CPF-M is clinically significant in aSAH patients without massive intraventricular hemorrhage (IVH) was examined.

Materials and Methods

Control group

The frequency of the CPM-M was examined by dividing the control group into a normal control group, a patient control group with chronic cerebral infarction, and a patient control group with deep subcortical white matter lesions (deep WMLs), and they were compared with SAH patients.

The normal control group consisted of 178 patients who visited our hospital because of neurological conditions other than cerebrovascular disorders, brain tumor, demyelinating diseases, dementia, and metabolic diseases, and who underwent head magnetic resonance imaging (MRI) and were normal (male: 61, female: 117, mean age: 61 ± 16 years). In the control group, the frequency of the CPF-M was examined separately for the elderly group (aged ≥70 years) (67 cases, male: 25, female: 42, mean age: 76 ± 5 years, range 70–91 years) and the young group (<70 years old) (111 cases, male: 36, female: 75, mean age: 52 ± 12 years, range 13–68 years). Normal MRI findings were defined as no asymptomatic or symptomatic cerebral infarction, cerebral hemorrhage including microbleeds, or hydrocephalus. Regarding periventricular and deep WMLs, grades 0–1 of the Fazekas scale[8] were regarded as normal.

In the control group of patients with chronic cerebral infarction, the total number of cases was 123 (63 male, 60 female; mean age: 76 ± 9 years). In the control group of patients with deep WMLs, the total number of cases was 117 (32 male, 85 female; mean age 71 ± 10 years). Patients with deep WMLs were defined as grade 2 or higher on the Fazekas scale.[8]

In the normal control group, the chronic cerebral infarction group and the deep WML group, cases with ventricular enlargement with a relative bicaudate index (BCI) of 1 or more were excluded.

Patient population

Subjects were selected from among the 259 patients in the non-traumatic aneurysmal acute-phase SAH database who were treated at our hospital between September 2002 and December 2017. Of these, 13 patients who received conservative therapy instead of surgery because of the absence of brainstem reflexes and 20 patients with SAH due to ruptured dissecting aneurysms were excluded. The remaining 226 patients underwent acute-stage aneurysmal surgery by craniotomy or an interventional procedure within 72 h of aSAH onset, and the number of severe cases of World Federation of Neurological Societies (WFNS) grades[9] 3–5 was 72 (32% of 226 cases). Of the 226 cases, two could not undergo MRI because of a pacemaker. In addition, 53 of these 226 patients were excluded because adequate MRI could not be performed in patients with a poor neurological condition or restlessness. Furthermore, six patients admitted 49–72 h after SAH were excluded. Thus, 165 patients who were admitted within 48 h of aSAH onset and who underwent adequate MRI [including diffusion-weighted imaging (DWI), FLAIR imaging, and T_1-weighted imaging (T_1WI)] and computed tomography (CT) on admission were identified. Of these 165 patients, 18 patients with massive IVH of the lateral ventricle (Hijdra IVH score[10] of the lateral ventricle ≥2 points) diagnosed by CT and T_2*-weighted imaging were excluded from this study. Therefore, a total of 147 cases were examined.

Clinical and imaging records were evaluated retrospectively.

Imaging protocol

For patients with aSAH, serial MRI was routinely performed on admission, within 2–7 days after surgery, and before discharge. At all-time points, serial MRI included axial conventional T_1WI, FLAIR images, DWI, and magnetic resonance angiography, which were performed using a 1.5-T superconducting magnet (Signa EXCITE or HDX; GE Medical Systems, Milwaukee, WI, USA) with a quadrature head coil. Pulse sequences were collected according to our previously reported parameters.[11]

Plain CT was performed for all patients in whom SAH was diagnosed by MRI on admission. CT slice thickness was 4 mm. All patients underwent 3D-CT angiography to identify ruptured aneurysms. MRI was performed only after obtaining informed consent from the patient and/or a relative. Initial MRI at the time of admission was performed before conventional angiographic, surgical, or endovascular procedures in all cases.

Definitions of variables

At the time of admission, all patients were graded according to the grading system defined by the WFNS.[9] Severity of aSAH was classified using CT findings according to Fisher's scale.[12] The amount of cisternal and intraventricular blood on initial CT was graded semi-quantitatively with the Hijdra score.[10] The CPF-M was defined as a hyperintense signal in the lateral ventricle just superior to the foramen of Monro that did not correspond to any normal structure (Fig. 1).

Ventricular enlargement was quantified by measuring the BCI and the width of the third ventricle on CT performed on admission. The BCI is calculated as the width of the frontal horns at the level of the caudate nuclei and the foramen of Monro divided by the corresponding diameter of the brain.[13] The relative BCI was obtained by dividing the patient's BCI by the normal upper limit (95th percentile) for their age.[13] Acute hydrocephalus was defined as a relative BCI > 1. The widest diameter of the third ventricle was measured in millimeters. Measurements of the BCI and the third ventricle were performed by investigators blinded to the occurrence of the CPF-M.

Diagnosis of intracerebral hemorrhage (ICH) was defined as an accumulation of blood with a diameter > 1 cm on CT. On the MRI study performed on admission, high-intensity lesions visible on DWI that showed low signal intensity in the lesion on apparent diffusion coefficient mapping were defined as DWI-detected early infarction at the time of aSAH onset.[14] In patients with T_1WI-detected bright hyperintense subarachnoid blood (BHSB), T_1-FLAIR mismatch as a neuroradiological diagnosis of a minor leak before a major SAH was defined as a T_1WI-detected clear BHSB accompanied by SAH blood on FLAIR images that was distributed over a larger area than BHSB on T_1WI.[11] Rebleeding after admission was defined as a definite increase in the volume of blood visible on CT compared with baseline MRI or CT findings on admission accompanied by sudden deterioration in the level of consciousness.

Delayed angiographic vasospasm was diagnosed based on findings from routine serial 3D angiography or conventional digital subtraction angiography performed on days 7 and 14. In principle, symptomatic delayed cerebral ischemia (sDCI) was defined as clinical deterioration with new infarction detected by DWI (serial DWI or DWI at the time of deterioration) according to previously reported protocols.[15]

Computed tomography and MRI findings were interpreted by at least three senior stroke neurosurgeons (MS, SO, and RA with 34, 29, and 14 years of experience, respectively). In cases of disagreement among raters, the diagnosis was determined by consensus of all three raters.

Surgical procedures and patient management were performed according to previously reported protocols.[14] Shunt-dependent chronic hydrocephalus (SDCH) was defined as hydrocephalus after aSAH requiring shunt diversion surgery. The indication for CSF diversion surgery in aSAH patients was based on the occurrence of a clinical constellation of decreased mental status, axial rigidity, and/or incontinence beyond the time of vasospasm and radiological evidence of enlarged ventricles.

Outcomes were assessed at 3 months using the modified Rankin Scale (mRS).[16] Patients were stratified into a favorable outcome (mRS score 0–2) or an unfavorable outcome (mRS score 3–6).
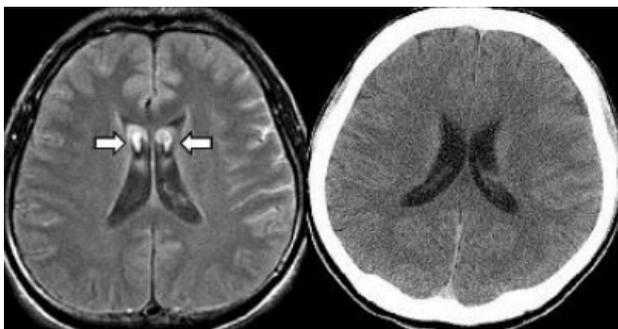
Statistical analysis

The significance of clinical factors potentially associated with the CPF-M was determined by Fisher's exact test for categorical variables and an independent sample, two-tailed Student's *t*-test for continuous variables (age, CT SAH score). All clinical factors with a significance level of $P < 0.05$ on univariate analysis were subjected to multivariate logistic regression analysis, with the occurrence of the CPF-M as the dependent variable. Statistical analyses were performed using commercially available software (SPSS for Windows version 22.0; IBM, Armonk, NY, USA).

Fig. 1   Images from a 43-year-old man with a ruptured left middle cerebral artery aneurysm without acute hydrocephalus. Axial FLAIR on admission shows lateral ventricular CSF pulsation flow signs bilaterally in the lateral ventricles just superior to the foramen of Monro (left) (*arrows*). CT performed at the same time shows no findings suggestive of intraventricular hemorrhage (right).

Results

Incidence of the CPF-M

In the normal control group, the overall prevalence of the CPF-M was 32% (57/178). On the other hand,

the prevalence of the CPF-M in elderly people was 30% (20/67), and that in younger people was 33% (37/111). There was no significant difference in the prevalence of the CPF-M in the two normal control groups (chi-squared test, *P* = 0.740). In addition, the prevalence of the CPF-M in males was 30% (18/61 cases), and the prevalence in females was 33% (39/117); there was no significant difference by sex (*P* = 0.735).

In the control group of patients with chronic cerebral infarction, the prevalence of the CPF-M was 33% (40/123). In the control group of patients with deep WMLs, the prevalence of the CPF-M was 38% (45/117). The frequencies of the CPF-M in the chronic cerebral infarction group (chi-squared test, *P* = 0.928) and the group of patients with deep WMLs (chi-squared test, *P* = 0.263) were not significantly different from that in the normal control group. In the 240 patients with chronic cerebral infarction (123 cases) and deep WMLs (117 cases), the frequency of the CPF-M in the 165 elderly people aged ≥70 years was 27% (44/165), and the frequency of the CPF-M in this elderly group was significantly lower than in the 75 young people (55%, 41/75, chi-squared test, *P* <0.001).

In the aSAH patients, the overall prevalence of the CPF-M was 57% (84/147) (Table 1). In this study, the percentage of male SAH patients <70 years old was very high (91%, 43/47 cases) compared with female SAH patients (57%, 57/100).

Values represent *n* (%) unless otherwise stated. The 'Number of patients' row shows the percentage of the total number of patients, whereas all other percentages in the 'Positive' and 'Negative' columns represent the percentages of positive and negative patients, respectively.

Comparing both the normal control group and SAH patients, the prevalence of the CPF-M was significantly higher in patients with SAH than in the overall (*P* <0.001), elderly (*P* <0.001), and younger normal control (*P* <0.001) groups.

In addition, the prevalence of the CPF-M was significantly higher in SAH patients than in the control group of chronic cerebral infarction (*P* <0.001) and the control group of deep WML patients (*P* = 0.003).

CPF-M, clinical features, and neurological status

Table 1 summarizes the clinical features and neurological status as preoperative clinical factors that differed significantly between patients with and without the CPF-M on admission. Patients with the CPF-M were significantly younger, and the prevalence of the CPF-M was significantly lower in elderly aSAH patients (≥70 years old) (Table 1). However, there was no significant association between poor neurological grade and the appearance of the CPF-M.

CPF-M and neuroradiological features on admission

Table 2 summarize the neuroradiological features on admission that differed significantly between patients with and without the CPF-M on admission. Neuroradiological factors such as Fisher group 3, diameter of the third ventricle, BCI, relative BCI, ICH, acute hydrocephalus, fourth ventricle IVH, third ventricle IVH, minor lateral ventricle IVH, size of the aneurysm, timing of initial MRI after SAH onset, acute infarction on DWI, DWI-detected SAH on the basal cistern, and DWI-detected SAH on the convexity were not associated with the occurrence of the CPF-M. Prevalences of the CPF-M were

Table 1 Clinical features and neurological status of the patients on admission

| | Total | CSF pulsation flow sign in the foramen of Monro | | *P*-value |
		Positive	Negative	
Number of patients	147	84 (57)	63 (43)	
Mean (±SD) age (years)	61.0 ± 14.4	57.1 ± 13.7	66.2 ± 13.7	<0.001
Age range (years)	21–89	21–83	29–89	
Age group of patients				
≥70 years	47	18 (38)	29 (62)	0.002
Male sex	47	40 (85)	7 (15)	<0.001
Rebleeding after admission	26	11 (42)	15 (58)	0.126
WFNS grade on admission				
Grades 1 and 2	118	69 (58)	49 (42)	0.413
Grades 3–5	29	15 (52)	14 (48)	0.513

CSF: cerebrospinal fluid, SD: standard deviation, WFNS: World Federation of Neurological Surgeons.

Table 2 CT and MRI findings on admission

| | Total | CSF pulsation flow sign of the foramen of Monro | | *P*-value |
		Positive	Negative	
Number of patients	147	84 (57)	63 (43)	
CT findings				
Fisher group 3	102	56 (55)	46 (45)	0.365
Maximum diameter of third ventricle (mm)	8.4 ± 3.6	8.1 ± 3.4	8.7 ± 3.8	0.371
BCI (mean ± SD)	0.16 ± 0.05	0.16 ± 0.04	0.17 ± 0.05	0.133
Relative BCI (mean ± SD)	0.86 ± 0.24	0.84 ± 0.22	0.89 ± 0.27	0.249
Hijdra score on CT (mean ± SD)				
Total score (SAH + IVH)	18.0 ± 11.5	16.9 ± 11.2	19.5 ± 11.8	0.169
Total SAH score	16.5 ± 10.3	15.6 ± 10.0	17.7 ± 10.6	0.223
Total IVH score	1.50 ± 2.20	1.28 ± 2.17	1.79 ± 2.22	0.165
IVH score for the third ventricle	0.48 ± 0.77	0.43 ± 0.77	0.53 ± 0.76	0.445
IVH score for the fourth ventricle	0.54 ± 0.84	0.37 ± 0.73	0.77 ± 0.93	0.004
Intracerebral hemorrhage	26	14 (54)	12 (46)	0.666
Acute hydrocephalus	52	24 (46)	28 (54)	0.056
Fourth ventricle IVH	90	51 (57)	39 (43)	1.000
Third ventricle IVH	63	31 (49)	32 (51)	0.096
Minor lateral ventricle IVH	22	11 (50)	11 (50)	0.491
Aneurysm site				
Anterior communicating artery	45	25 (56)	20 (44)	
Anterior cerebral artery	8	6 (75)	2 (25)	
Internal carotid artery	48	28 (58)	20 (42)	
Middle cerebral artery	37	21 (57)	16 (43)	
Posterior circulation	9	5 (56)	4 (44)	1.000
Aneurysm size (mm)				
>5	79	47 (59)	32 (41)	0.617
>10	12	6 (50)	5 (50)	0.762
Mean ± SD (mm)	5.6 ± 2.7	5.6 ± 2.5	5.6 ± 2.9	0.938
MR findings				
Timing of initial MRI				
Mean interval between onset and initial MRI (mean ± SD) (h)	10.5 ± 17.0	10.9 ± 17.9	9.9 ± 15.9	0.540
<3 h after onset	82	45 (55)	37 (45)	0.615
<6 h after onset	105	60 (57)	45 (43)	1.000
<12 h after onset	117	68 (58)	49 (42)	0.682
<24 h after onset	133	75 (56)	58 (44)	0.778
T_1-FLAIR mismatch	54	24 (44)	30 (56)	0.024
Acute infarction on DWI	14	7 (50)	7 (50)	0.586
Periventricular WM lesion	39	14 (36)	25 (64)	0.002
Deep WM lesion	60	23 (38)	37 (62)	<0.001
Old infarction	24	6 (25)	18 (75)	0.001
DWI-detected SAH on the basal cistern	94	49 (52)	45 (48)	0.163

Table 2   CT and MRI findings on admission—Continued

| | Total | CSF pulsation flow sign of the foramen of Monro | | *P*-value |
		Positive	Negative	
DWI-detected SAH on convexity	51	24 (47)	27 (53)	0.114
DBS on FLAIR	42	15 (36)	27 (64)	0.002

The 'Number of patients' row shows the percentage of the total number of patients, whereas all other percentages in the 'Positive' and 'Negative' columns represent the percentages of positive and negative patients, respectively. BCI: bicaudate index, DBS: diffuse brain swelling, DWI: diffusion-weighted image, FLAIR: fluid attenuated inversion recovery, IVH: intraventricular hemorrhage, SAH: subarachnoid hemorrhage, SD: standard deviation, WM: white matter.

significantly lower among patients with T_1-FLAIR mismatch, periventricular WMLs, deep WMLs, old infarction, and diffuse brain swelling (DBS) on FLAIR (Table 3). The incidence of T_1-FLAIR mismatch was significantly higher in elderly patients (≥70 years old) (24 of 47 cases, 51%, *P* = 0.017) than in younger patients (<70 years old) (30 of 100 cases, 30%). In addition, the incidences of deep WMLs (29 of 47 cases, 62%, *P* <0.001) and old infarction (17 of 47 cases, 36%, *P* <0.001) were significantly higher in elderly patients than in younger patients, and T_1-FLAIR mismatch was significantly higher in patients with deep WMLs (29 of 66 cases, 64%, *P* = 0.021) and old infarctions (17 of 25 cases, 68%, *P* <0.001)

Regarding parameters of the Hijdra score on CT, total score (SAH + IVH), total SAH score, total IVH score, and IVH score for the third ventricle were not associated with the occurrence of the CPF-M. However, the IVH score for the fourth ventricle was significantly lower among patients with the CPF-M (Table 2).

CPF-M, surgery, and subsequent events

Table 3 summarizes surgery and subsequent events that differed significantly between patients with and without the CPF-M on admission. Rates of delayed angiographic vasospasm, sDCI, and SDCH were significantly lower among patients with the CPF-M than among patients without. The prevalence of the CPF-M was significantly higher in patients with a favorable outcome (mRS score at 3 months, 0–2) than in patients without a favorable outcome (Table 3).

Clinical factors associated with the CPF-M on multivariate analysis

In all subjects, multivariate stepwise logistic regression analysis showed that age ≥70 years was a preoperative clinical factor associated with the CPF-M; lower IVH score of the fourth ventricle (Hijdra score on CT), absence of T_1WI-FLAIR mismatch, deep WMLs, old infarction, and DBS on FLAIR were

neuroradiological findings on admission associated with the CPF-M; and absence of sDCI, SDCH, and favorable outcome were subsequent events that were significantly associated with the occurrence of the CPF-M (Table 4).

Discussion

CSF pulsatile flow

The bulk flow theory, known as the classic hypothesis of CSF dynamics, has been undermined by experimental results,[17] with recent MRI studies showing that the CSF pulsates and moves, but does not circulate.[6,7] The driving forces for such CSF pulsation are known to be heartbeat, respiration, and posture.[18] Systolic arterial pulse waves entering the cortical grey matter will lead to sudden cortical brain expansion and initiate a positive-pressure shockwave of interstitial fluid propelled by centripetal force toward the center and, thus, the ventricle. When the shockwave arrives at the ventricular system, ventricular compression produces a CSF pulse wave extruding CSF through outlets in the ventricular system such as the foramen of Monro and the fourth ventricle to the subarachnoid space surrounding the brain and spinal cord.[19] With such CSF outflow through the fourth ventricle to the basal cistern and venous outflow through the sinus, ICP is dampened even if arterial blood flows into the cranial cavity with each heartbeat. As these are repeated by the cardiac cycle, the brain tissue itself will pulsate, and the CSF will move accordingly. Pulsatile flow of CSF results, and we can visually observe this on modalities such as the time-spatial labeling inversion pulse method[6] or phase-contrast MRI,[7] and as a CSF pulsation flow sign on FLAIR.[2] Needless to say, CSF pulsatile flow is a normal physiological phenomenon, and its presence or absence usually has no clinical significance.[2]

In general, intracranial compliance is assumed to decrease with increased ICP due to the exponential

Table 3 Details of surgery and subsequent events

| | Total | CSF pulsation flow sign of the foramen of Monro | | *P*-value |
		Positive	Negative	
Number of patients	147	84 (57)	63 (43)	
Aneurysm surgery				
Craniotomy	118	71 (60)	47 (40)	0.148
Coiling	29	13 (45)	16 (55)	
Delayed angiographic vasospasm	43	19 (44)	24 (56)	0.044
Symptomatic DCI	31	9 (29)	22 (71)	<0.001
Shunt-dependent chronic hydrocephalus*	54	19 (35)	35 (65)	<0.001
mRS score 0–2 at 3 months	100	68 (68)	32 (32)	<0.001

*Incidence of shunt-dependent chronic hydrocephalus was calculated for the surviving patients (138 cases). The 'Number of patients' row shows the percentage of the total number of patients, whereas all other percentages in the 'Positive' and 'Negative' columns represent the percentages of positive and negative patients, respectively. DCI: delayed cerebral ischemia, mRS: modified Rankin Scale.

Table 4 Results of multivariate logistic regression analysis for the presence of the CSF pulsation flow sign in the foramen of Monro on admission FLAIR

	Odds ratio	95% CI	*P*-value
Preoperative clinical factors			
Age ≥70 years	0.320	0.160–0.660	0.002
Associated neuroradiological findings on admission			
Fourth ventricle IVH score on CT	0.538	0.348–0.838	0.006
T_1-FLAIR mismatch	0.444	0.392–0.910	0.022
Deep WM lesion	0.338	0.158–0.723	0.005
Old infarction	0.280	0.096–0.821	0.020
Diffuse brain swelling on FLAIR	0.310	0.146–0.659	0.002
Postoperative factors			
Symptomatic DCI	0.208	0.068–0.634	0.006
Shunt-dependent chronic hydrocephalus	0.296	0.135–0.651	0.002
mRS score 0–2	3.984	1.905–8.333	<0.001

CI: confidence interval, DCI: delayed cerebral ischemia, FLAIR: fluid attenuated inversion recovery, IVH: intraventricular hemorrhage, mRS: modified Rankin Scale, WM: white matter.

pressure–volume relationship,[4] and the reduction in intracranial compliance leads to a dramatic increase in the pulse wave.[4] Therefore, in patients with acute aSAH, elevated ICP due to early brain damage[5] with decreased intracranial compliance is likely to result in increased pressure pulsatility. We thereby expected that the rate of the CPF-M would be increased in aSAH patients. Actually, in this study, the prevalence of the CPF-M in patients with aSAH was significantly higher than in the three control groups, the normal, the chronic cerebral infarction, and the deep WML control group.

However, the pulsations out of the cranium transfer through either venous or CSF outflow pathways.[20] If blockage of the subarachnoid space and ventricle and cerebral venous circulation disturbances due to early brain damage[5] are serious, intracranial pulsatility may be restricted, and the CPF-M is less likely to occur on FLAIR in aSAH patients. In fact, the occurrence of the CPF-M showed a significant inverse association with clinical factors associated with IVH of the fourth ventricle (from direct ventricular perforation due to aneurysm rupture and/or reflux of the clot from the basal cistern).

Correlations between the CPF-M and old infarction/deep WMLs/old age/DBS

In this study, in aSAH patients, it was surprising that the prevalence of the CPF-M was significantly lower in patients with old cerebral infarction, deep WMLs, old age, and DBS, which are pathologies with low brain compliance. Therefore, as a control group, the frequencies of the CPF-M in the control group of patients with chronic cerebral infarction and in the control group of patients with deep WMLs were additionally verified. It was found that the frequency of the CPF-M in the control group of chronic cerebral infarction and deep WML without ventriculomegaly was not so different from that in normal controls. Furthermore, in the control group of chronic infarction and deep WML, the frequency of the CPF-M was significantly lower in elderly patients than in younger patients. Furthermore, it was also confirmed that the frequency of the CPF-M was significantly lower in the control groups than in SAH cases.

It is known that overall intracranial compliance comprises of four main components: actual brain tissue compliance, arterial compliance, venous compliance, and compliance of the spinal thecal sac that communicates with the brain through the cerebrospinal fluid spaces.[20] Of these components, the effect of actual brain tissue compliance is thought to be small.[20] The enhancement of ventricular CSF pulsation artifact due to reduced compliance of periventricular tissues with aging that was suggested by Sherman et al.[3] and Bakshi et al.[2] is not supported by clinical data. From the results of this study, the CPF-M does not occur frequently in pathological conditions where the compliance of brain tissue is simply decreased, such as the control group of chronic cerebral infarction, deep WMLs, and elderly patients without ventriculomegaly. Namely, to increase pulsatility, it is most important to have decreased compliance accompanied by increased ICP.[20] In addition, the CPF-M may occur more frequently with multiple factors (such as ventriculomegaly, block of the CSF pathway in the subarachnoid space, and brain atrophy) interfering with each other. For further clarification, further research is needed.

On the other hand, in this study, unexpectedly, DBS, a disease condition accompanied by both decreased brain compliance and increased ICP, was inversely correlated with the occurrence of the CPF-M. The cause is that diagnosis of the CPF-M is difficult because the lateral ventricle of SAH patients with DBS is slit-like.

Correlations between the CPF-M and T_1-FLAIR mismatch/DCI

We previously reported that neuroradiologically diagnosed minor leakage prior to major SAH using

T_1-FLAIR mismatch is significantly correlated with the occurrence of sDCI.[15] At the time of admission due to a major SAH episode, aSAH patients with a previous minor leak diagnosed by T_1-FLAIR mismatch corresponded to a clinical group in the subacute phase, and thus, initiation of prophylaxis for DCI is delayed in these patients. Previous minor leakage before a major SAH episode leads to more severe fibrous arachnoid adhesions and decreased clearance of the SAH, and, thus, blockage in the subarachnoid space becomes more severe.[15] Under such circumstances, DCI tends to occur,[21] and the CPF-M becomes difficult to see in patients with T_1-FLAIR mismatch.

On the other hand, we also reported that minor leakage diagnosed by T_1-FLAIR mismatch is significantly more frequent in elderly aSAH patients.[11] We think that symptoms due to minor leakage would be milder in elderly patients than in younger aSAH patients, because an increase in intracranial pressure may not occur even after aneurysmal rupture due to the age-associated enlargement of the subarachnoid space. Elderly aSAH patients tend to be transported to the hospital at the time of the subsequent major SAH, not at the time of the first episode due to minor leakage.[11,15] In this study, the frequency of T_1-FLAIR mismatch in elderly SAH patients was also significantly higher. Similarly, the frequency of old infarction and deep WMLs in elderly SAH patients was also significantly higher. Furthermore, T_1-FLAIR mismatch was significantly higher in patients with deep WMLs and old infarction. Therefore, in this study, T_1-FLAIR mismatch was strongly related with deep WMLs, old infarction, and older age, and all these factors seem to be inversely correlated with the expression of the CPF-M.

Risk factors for SDCH

According to a recent large meta-analysis and systematic review, risk factors for SDCH after aSAH included a high Fisher grade, acute hydrocephalus, in-hospital complications, presence of IVH, poor admission status, re-hemorrhage, location of the aneurysm in the posterior circulation, and age >60 years.[22] Development of SDCH after aSAH is often a result of: 1) clogging of CSF outflow and reduction of absorption through subarachnoid granules due to increased cell and protein content in the CSF; and 2) disturbances in CSF dynamics due to leptomeningeal fibrosis, arachnoid adhesions, and scarring in the basal cisterns.[23,24] SDCH thus has features of extraventricular obstructive hydrocephalus (hydrocephalus due to obstruction of the subarachnoid space). The presence of the CPF-M at the time of admission is a factor that directly

reflects the CSF circulatory dynamics in the acute phase covering the basal cistern from the ventricle. At the same time, because the CPF-M is associated with T_1-FLAIR mismatch, we think that this finding will also be a predictor of the presence of arachnoid adhesions in the future.

Limitations

As for the mechanism of the appearance of the CPF-M, there are still many unclear points. Even in cases where the CSF circulation dynamics are normal, why only about 30% do not appear cannot be considered in this study. In the future, it will be necessary to clarify this by detailed examinations of cerebrospinal fluid circulation dynamics by the time-spatial labeling inversion pulse method[6], phase-contrast MRI technique[7], etc.

One limitation of this study is that aSAH patients without massive IVH of the lateral ventricle were studied. In addition, adequate MRI could not be performed for aSAH patients with poor neurological conditions, so that the proportion of severe SAH in WFNS grades 3–5 in this study was low (only 29 of 147 cases, 20%). Therefore, because the true prevalence of the CPF-M in poor-grade aSAH patients could not be obtained in this study, the clinical significance of the CPF-M in poor-grade aSAH remains unclear.

In general, although CSF pulsation artifacts were common in the third and fourth ventricles, differentiating IVH using CT and T_2* imaging was difficult in aSAH patients. Thus, it was not possible to investigate CSF pulsation artifacts in the third and fourth ventricles.

The CPF-M is often absent in normal cases, and thus, negative findings cannot be considered abnormal. One cannot make conclusions about the clinical significance of absence of the CPF-M in patients with acute aSAH.

This was a retrospective study of a small group of patients, and prospective studies with a greater number of cases are warranted.

Conclusion

In aSAH patients, the overall prevalence of the CPF-M was 57% (84/147 patients), which was significantly higher than in the three control groups. Although limited to SAH patients without massive IVH of the lateral ventricles, one can conclude that, in acute aSAH, the presence of the CPF-M on admission MRI suggests that the circulatory dynamics of the CSF from the basal cistern to the ventricles are approximately normal. Thus, this finding may appear to offer an indicator of a good outcome without DCI

and SDCH. In aSAH patients, the CPF-M is useful as a neuroradiological finding and should not be discounted as a simple artifact of FLAIR.

Conflicts of Interest Disclosure

The authors declare that they have no conflict of interest.

References

1) Noguchi K, Ogawa T, Inugami A, et al.: Acute subarachnoid hemorrhage: MR imaging with fluid-attenuated inversion recovery pulse sequences. *Radiology* 196: 773–777, 1995

2) Bakshi R, Caruthers SD, Janardhan V, Wasay M: Intraventricular CSF pulsation artifact on fast fluid-attenuated inversion-recovery MR images: analysis of 100 consecutive normal studies. *AJNR Am J Neuroradiol* 21: 503–508, 2000

3) Sherman JL, Citrin CM, Gangarosa RE, Bowen BJ: The MR appearance of CSF flow in patients with ventriculomegaly. *AJR Am J Roentgenol* 148: 193–199, 1987

4) Marmarou A, Shulman K, LaMorgese J: Compartmental analysis of compliance and outflow resistance of the cerebrospinal fluid system. *J Neurosurg* 43: 523–534, 1975

5) Fujii M, Yan J, Rolland WB, Soejima Y, Caner B, Zhang JH: Early brain injury, an evolving frontier in subarachnoid hemorrhage research. *Transl Stroke Res* 4: 432–446, 2013

6) Yamada S, Tsuchiya K, Bradley WG, et al.: Current and emerging MR imaging techniques for the diagnosis and management of CSF flow disorders: a review of phase-contrast and time-spatial labeling inversion pulse. *AJNR Am J Neuroradiol* 36: 623–630, 2015

7) Matsumae M, Hirayama A, Atsumi H, Yatsushiro S, Kuroda K: Velocity and pressure gradients of cerebrospinal fluid assessed with magnetic resonance imaging. *J Neurosurg* 120: 218–227, 2014

8) Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA: MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *AJR Am J Roentgenol* 149: 351–356, 1987

9) Drake CG: Report of World Federation of Neurological Surgeons Committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg* 68: 985–986, 1988

10) Hijdra A, Brouwers PJ, Vermeulen M, van Gijn J: Grading the amount of blood on computed tomograms after subarachnoid hemorrhage. *Stroke* 21: 1156–1161, 1990

11) Oda S, Shimoda M, Hirayama A, et al.: Neuroradiologic diagnosis of minor leak prior to major SAH: diagnosis by T1-FLAIR mismatch. *AJNR Am J Neuroradiol* 36: 1616–1622, 2015

12) Fisher CM, Kistler JP, Davis JM: Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by

computerized tomographic scanning. *Neurosurgery* 6: 1–9, 1980

13) van Gijn J, Hijdra A, Wijdicks EF, Vermeulen M, van Crevel H: Acute hydrocephalus after aneurysmal subarachnoid hemorrhage. *J Neurosurg* 63: 355–362, 1985

14) Shimoda M, Hoshikawa K, Shiramizu H, et al.: Early infarction detected by diffusion-weighted imaging in patients with subarachnoid hemorrhage. *Acta Neurochir* (*Wien*) 152: 1197–1205, 2010

15) Oda S, Shimoda M, Hirayama A, et al.: Retrospective review of previous minor leak before major subarachnoid hemorrhage diagnosed by MRI as a predictor of occurrence of symptomatic delayed cerebral ischemia. *J Neurosurg* 128: 499–505, 2018

16) Shinohara Y, Minematsu K, Amano T, Ohashi Y: Modified Rankin scale with expanded guidance scheme and interview questionnaire: interrater agreement and reproducibility of assessment. *Cerebrovasc Dis* 21: 271–278, 2006

17) Orešković D, Klarica M: The formation of cerebrospinal fluid: nearly a hundred years of interpretations and misinterpretations. *Brain Res Rev* 64: 241–262, 2010

18) Takizawa K, Matsumae M, Sunohara S, Yatsushiro S, Kuroda K: Characterization of cardiac- and respiratory-driven cerebrospinal fluid motion based on asynchronous phase-contrast magnetic resonance imaging in volunteers. *Fluids Barriers CNS* 14: 25, 2017

19) Preuss M, Hoffmann KT, Reiss-Zimmermann M, et al.: Updated physiology and pathophysiology of CSF circulation—the pulsatile vector theory. *Childs Nerv Syst* 29: 1811–1825, 2013

20) Wagshul ME, Eide PK, Madsen JR: The pulsating brain: A review of experimental and clinical studies of intracranial pulsatility. *Fluids Barriers CNS* 8: 5, 2011

21) Reilly C, Amidei C, Tolentino J, Jahromi BS, Macdonald RL: Clot volume and clearance rate as independent predictors of vasospasm after aneurysmal subarachnoid hemorrhage. *J Neurosurg* 101: 255–261, 2004

22) Wilson CD, Safavi-Abbasi S, Sun H, et al.: Meta-analysis and systematic review of risk factors for shunt dependency after aneurysmal subarachnoid hemorrhage. *J Neurosurg* 126: 586–595, 2017

23) Børgesen SE, Gjerris F: The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus. *Brain* 105: 65–86, 1982

24) Daou B, Klinge P, Tjoumakaris S, Rosenwasser RH, Jabbour P: Revisiting secondary normal pressure hydrocephalus: does it exist? A review. *Neurosurg Focus* 41: E6, 2016

Address reprint requests to: Masami Shimoda, MD, Department of Neurosurgery, Tokai University Hachioji Hospital, 1838 Ishikawa-machi, Hachioji, Tokyo 192-0032, Japan.
e-mail: mashimoda-nsu@umin.ac.jp