

# Detection of symptomatic vasospasm after subarachnoid haemorrhage: initial findings from single time-point and serial measurements with arterial spin labelling

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## Abstract

**Objectives** To detect symptomatic hemispheres during the postoperative course of subarachnoid haemorrhage (SAH) using arterial spin labelling (ASL).

**Methods** Eighteen patients with aneurysmal SAH were included; four exhibited symptomatic vasospasm postoperatively. All patients underwent ASL on days 9–10 (single time-point ASL). Nine patients underwent serial measurements of ASL (serial ASL) on days 1–2, 9–10 and 13–21, and seven patients also underwent imaging on days 4–7. CBF in the posterior part of the MCA territory was measured, and the ipsilateral/contralateral ratio of CBF was calculated. Differences between symptomatic hemispheres and others underwent ROC analysis.

**Results** Single time-point ASL revealed that  $CBF_{day9-10}$  and  $CBF_{i/c\_day9-10}$  were significantly lower in symptomatic hemispheres than in asymptomatic hemispheres ( $P < 0.001$ ). Serial ASL was significantly decreased on  $CBF_{day4-7}$  compared with  $CBF_{day1-2}$  and on  $CBF_{day9-10}$  compared with  $CBF_{day4-7}$ , and significantly increased on  $CBF_{day13-21}$  compared with

$CBF_{day9-10}$ . ROC analysis of single time-point ASL revealed that AUC for  $CBF_{day9-10}$  was 0.95, significantly higher than  $CBF_{i/c\_day9-10}$  ( $P < 0.001$ ). ROC analysis of serial ASL showed that AUC for  $CBF_{day9-10}$  was 0.93 and significantly higher than  $CBF_{day9-10/day1-2}$  and  $CBF_{i/c\_day9-10}$  ( $P < 0.001$ ).

**Conclusions** Single time-point ASL revealed significant CBF reduction in symptomatic hemispheres compared with asymptomatic hemispheres. Serial ASL showed time-dependent CBF changes after SAH.

## Key Points

- MR arterial spin labelling (ASL) can non-invasively assess cerebral blood flow (CBF)
- ASL revealed significant CBF reduction in symptomatic hemispheres compared with asymptomatic hemispheres
- Serial ASL measurements enable observation of time-dependent CBF changes after SAH
- ASL is non-invasive and suitable for serial repeated examinations

**Keywords** Arterial spin labeling · Subarachnoid haemorrhage · Vasospasm · CBF · MRI

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## Introduction

Angiographic vasospasm occurs in 30–70 % of patients with aneurysmal subarachnoid haemorrhage (SAH), with a typical onset of 3–5 days after haemorrhage, maximal narrowing at 5–14 days, and gradual resolution over 2–4 weeks [1]. However, the risk of symptomatic vasospasm remains between 20–40 %, and vasospasm has been thought to be associated with delayed ischaemic neurological deficits. Approximately 15–20 % of patients suffer stroke or die of vasospasm during the postoperative course [2].

Imaging studies including diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) or magnetic resonance (MR) imaging [3, 4], single photon emission computed tomography [5], positron emission tomography (PET) [6], and computed tomography (CT) have been reported to be advantageous in guiding the management of the vasospasm [1]. However, diagnostic accuracy varies with time, and serial measurements are necessary. Transcranial Doppler ultrasound (TCD) can be performed repeatedly, but covers only the middle cerebral artery (MCA), and a meta-analysis found no evidence for TCD as a valid method for diagnosing vasospasm [7]. Many centres continue to rely on cerebral angiography for the diagnosis of vasospasm [1].

Arterial spin labelling (ASL) has been introduced as a non-invasive method capable of assessing cerebral blood flow (CBF) [8]. ASL can be performed without administration of contrast media or exposure to radiation, allowing repeated measurements. The purpose of this study was thus to evaluate CBF in patients with aneurysmal SAH during the postoperative course using ASL and to examine the capabilities of ASL for diagnosing vasospasm.

## Patients and methods

This study was approved by the local institutional review board, and written informed consent was obtained from all patients or their families. The group of participants comprised 18 patients with aneurysmal SAH treated in our hospital (4 men, 14 women; mean age,  $62.2 \pm 11.2$  years). Patient characteristics are provided in Table 1. Fourteen patients underwent surgical clipping and four underwent endovascular coiling. Treatment was conducted within 24 h of onset for all patients. Metallic materials were not applied in cranioplasty for surgical clipping as far as possible in order to avoid metallic artefact over cortices on ASL.

Symptomatic vasospasm was defined as any new neurological deficit presenting after onset of SAH, confirmed and explained by angiographic findings, and not explained by other causes of neurological deterioration (rebleeding, hydrocephalus, electrolyte disturbances, hypoxia, or seizure). Four symptomatic patients were examined with conventional cerebral angiography when symptoms became apparent. Angiography confirmed vasospasm in all four symptomatic patients at least at the posterior trunk of the ipsilateral MCA. The other 14 asymptomatic patients were not examined using conventional angiography. The laterality was determined by the location of the ruptured aneurysm. When the aneurysm was located in the midline, the side with more subarachnoid haemorrhage was termed as ipsilateral.

## Imaging protocol

Patients underwent MR imaging using a 3-T system (Magnetom Verio; Siemens, Erlangen, Germany) with a 32-channel phased array head coil. Day 0 was designated the day of SAH onset. All patients underwent ASL measurement on days 9–10 (single time-point ASL). Nine patients had three serial ASL measurements on days 1–2, 9–10 and 13–21 (serial ASL). Seven also had an ASL measurement on days 4–7. Several additional measurements of ASL were performed when necessary. ASL on days 1–2 was considered to represent baseline postoperative CBF. Restless and/or uncooperative patients were sedated as necessary.

## Imaging parameters

Pulsed ASL was performed using the second version of the quantitative imaging of perfusion with thin-slice TI periodic saturation (Q2TIPS) [9]. Imaging parameters were as follows: repetition time, 3,000 ms; echo time, 14 ms; field of view,  $256 \times 256$  mm; matrix,  $64 \times 64$  pixels; slice thickness, 8 mm; interslice gap, 2 mm; 9 slices; partial Fourier acquisition rate, 7/8;  $TI_1$ , 700 ms;  $TI_{1s}$ , 1,600 ms;  $TI_2$ , 1,800 ms; 45 pairs of labelled and unlabelled images. For quantitation, the following values were used:  $\lambda$  (brain/blood partition coefficient of water), 0.9 g/ml;  $\alpha$  (inversion efficiency), 0.95;  $T_{1a}$  (longitudinal relaxation time of arterial blood), 1,496.19 ms. Other routine imaging sequences including DWI, T2-weighted imaging, and MR angiography were performed as needed.

## Image data analysis

The CBF images were created on the MR operating system. DICOM data of ASL images were transferred to an off-line workstation. ASL images were anatomically normalised using iNeurostat software (Nihon Medi-Physics, Tokyo, Japan). Region of interest (ROI) analysis was automatically performed for normalised CBF images based on vascular territories, and ROIs were placed on each slice; average CBF values for each ROI were calculated (Fig. 1) [10]. ROIs of the posterior parts of MCA territories were adopted and the number of ROIs was 26 for each hemisphere.

Box-and-whisker plots of CBF for all ROIs involving the posterior parts of MCA territories on days 9–10 ( $CBF_{day9-10}$ ) were calculated for each subject to evaluate single time-point ASL measurements, and three percentiles (25th, 50th and 75th) were determined. For serial ASL, plots of CBF for all ROIs in the posterior parts of MCA territories in nine patients were also created for days 1–2 ( $CBF_{day1-2}$ ), days 4–7 ( $CBF_{day4-7}$ ), days 9–10 ( $CBF_{day9-10}$ ), and day 13–21 ( $CBF_{day13-21}$ ). In two patients, no ASL imaging was conducted on days 4–7 and the values of seven patients were

**Table 1** Patient characteristics

Case	Sex	Age	Operation	Aneurysm	H&K	WFNS	Fisher	Symptomatic vasospasm	ASL measurement
1	F	37	Coiling	BA	IV	IV	III	No	Single time point
2	F	73	Clipping	Rt MCA	III	II	III	No	Single time point
3	F	55	Clipping	Lt. IC-PC	III	II	III	No	Single time point
4	F	70	Clipping	Lt. IC-PC	III	II	III	No	Single time point
5	F	62	Coiling	Acom	III	II	III	No	Single time point
6	M	51	Clipping	Acom	III	II	III	No	Single time point
7	F	78	Clipping	A2-3	III	IV	III	No	Single time point
8	F	62	Clipping	Rt. MCA	III	II	III	No	Single time point
9	F	58	Clipping	Acom	III	II	III	No	Single time point
10	M	68	Clipping	Rt. IC-PC	IV	IV	III	No	Serial
11	F	69	Coiling	BA	I	I	II	No	Serial
12	F	65	Coiling	BA	III	II	III	No	Serial
13	F	69	Clipping	Lt. IC-PC	III	II	II	No	Serial
14	F	54	Clipping	Lt. AChA	III	II	III	Yes	Serial
15	F	67	Clipping	Rt. IC-PC	III	II	III	Yes	Serial
16	M	39	Clipping	Acom	III	II	III	Yes	Serial
17	M	77	Clipping	Rt. IC-PC	III	II	III	Yes	Serial
18	F	66	Clipping	Rt. IC-PC	III	IV	III	No	Serial

AChA = Anterior choroidal artery, Acom = anterior communicating artery, BA = basilar artery, IC-PC = internal carotid-posterior communicating artery, MCA = middle cerebral artery

H&K = Hunt and Kosnik scale, WFNS = World Federation of Neurosurgeons grading system, Fisher = Fisher SAH CT grading scale

thus used. When ASL was performed multiple times during days 13–21, ASL of the latest day was adopted.

For  $CBF_{day9-10}$ , CBF ratios of ipsilateral to contralateral sides of ruptured aneurysms ( $CBF_{i/c\_day9-10}$ ) were derived for both single and serial ASL. Ratios of CBF

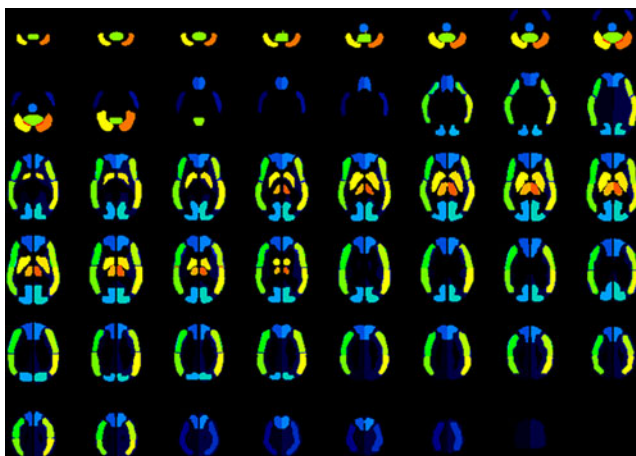
(days 9–10) against baseline ASL (days 1–2) were also calculated ( $CBF_{day9-10/day1-2}$ ) for serial ASL.

#### Statistical analysis

$CBF_{day9-10}$  for single time-point ASL was compared between symptomatic and asymptomatic hemispheres using one-way analysis of variance in all 18 patients, followed by Tukey's *post-hoc* test. Distal MCA ROIs were selected, because vasospasm was confirmed at the posterior trunk of the ipsilateral MCA in all four symptomatic patients on conventional angiography. ROIs of both symptomatic as well as asymptomatic hemispheres were compared in the statistical analysis. ROIs at the ipsilateral hemisphere of symptomatic patients were assigned to symptomatic hemispheres. ROIs at the contralateral hemisphere of symptomatic patients and ROIs at both hemispheres of asymptomatic patients were assigned to asymptomatic hemispheres.

Concerning serial ASL, changes among  $CBF_{day1-2}$ ,  $CBF_{day4-7}$ ,  $CBF_{day9-10}$  and  $CBF_{day13-21}$  of both hemispheres were compared using the Games-Howell test for nine patients (7 patients for  $CBF_{day4-7}$ ).

Receiver-operating characteristic (ROC) curve analysis was conducted to detect CBF decreases in distal MCA areas for  $CBF_{day9-10}$  and  $CBF_{i/c\_day9-10}$  with single time-point ASL, and for  $CBF_{day9-10}$ ,  $CBF_{i/c\_day9-10}$  and  $CBF_{day9-10/day1-2}$  with



**Fig. 1** ROI analysis was automatically performed for the normalised CBF based on vascular territories; the results of all ROIs were then analysed. Diagrams show ROIs of ACA, MCA (M2 anterior, M2 posterior), PCA, basal ganglia, thalamus, cerebellar hemisphere, and brainstem on the ROI template

serial ASL. Areas under the curve (AUCs) for  $\text{CBF}_{\text{day}9-10}$ ,  $\text{CBF}_{\text{i/c\_day}9-10}$ , and  $\text{CBF}_{\text{day}9-10/\text{day}1-2}$  were analysed using a non-parametric approach [11]. The positive predictive value (PPV) and negative predictive value (NPV) for symptomatic vasospasm were derived from ROC analysis. Values of  $P < 0.05$  were considered indicative of a statistically significant difference. SPSS version 15 software (IBM Japan, Tokyo, Japan) was used for all statistical analyses.

## Results

Box-and-whisker plots of  $\text{CBF}_{\text{day}9-10}$  and  $\text{CBF}_{\text{i/c\_day}9-10}$  for single time-point ASL are shown in Fig. 2a and b. The three percentiles (25th, 50th and 75th) for  $\text{CBF}_{\text{day}9-10}$  were 19.34, 22.63, and 25.21 ml/100 g/min for symptomatic hemispheres and 30.13, 35.76, and 43.60 ml/100 g/min for asymptomatic hemispheres, respectively ( $P < 0.001$ ) (Fig. 2a). The three percentiles (25th, 50th, and 75th) for  $\text{CBF}_{\text{i/c\_day}9-10}$  were 0.55, 0.65, and 0.79 for symptomatic hemispheres and 0.87, 1.01, and 1.19 for asymptomatic hemispheres, respectively ( $P < 0.001$ ) (Fig. 2b). Box-and-whisker plots of CBF for serial ASL are shown in Fig. 3. The three percentiles (25th, 50th, and 75th) were 41.99, 49.42, and 55.90 ml/100 g/min for  $\text{CBF}_{\text{day}1-2}$ , 33.70, 41.13, and 48.75 ml/100 g/min for  $\text{CBF}_{\text{day}4-7}$ , 29.67, 36.26 and 45.79 ml/100 g/min for  $\text{CBF}_{\text{day}9-10}$ , and 37.87, 40.26, and 53.59 ml/100 g/min for  $\text{CBF}_{\text{day}13-21}$ , respectively (Fig. 3). All  $P$  values were less than 0.05 except for  $\text{CBF}_{\text{day}4-7}$  compared with  $\text{CBF}_{\text{day}13-21}$  ( $P = 0.849$ ) (Table 2).

The ROC analysis for single time-point ASL revealed that AUCs for  $\text{CBF}_{\text{day}9-10}$  and  $\text{CBF}_{\text{i/c\_day}9-10}$  were 0.95 and

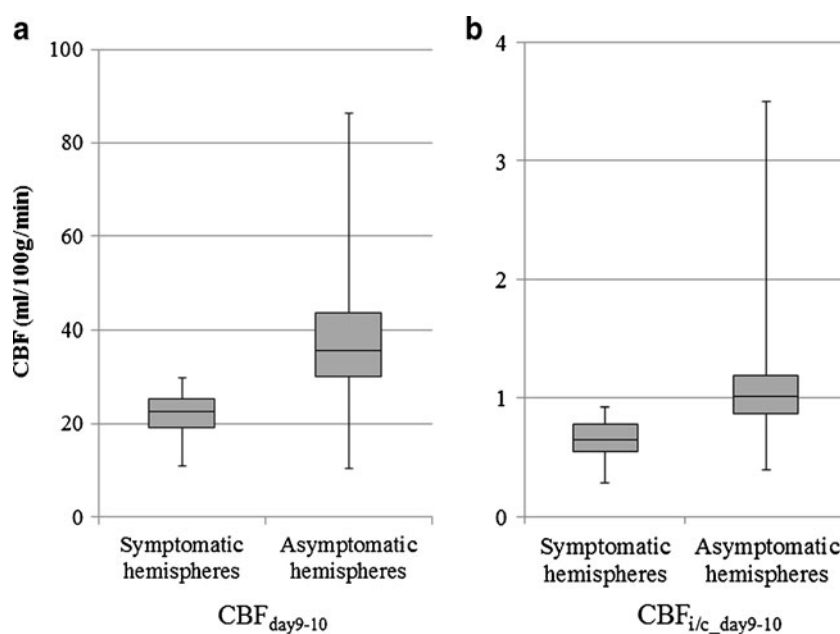
0.89 ( $P < 0.001$ ) (Fig. 4). The optimal cutoff for  $\text{CBF}_{\text{day}9-10}$  was 26.9 ml/100 g/min (sensitivity, 90.38 %; specificity, 93.89 %; PPV, 46.53 %; NPV, 99.40 %). ROC analysis of serial ASL measurements showed AUCs for  $\text{CBF}_{\text{day}9-10}$ ,  $\text{CBF}_{\text{day}9-10/\text{day}1-2}$ , and  $\text{CBF}_{\text{i/c\_day}9-10}$  of 0.93, 0.87, and 0.86, respectively (Fig. 5). The optimal cutoff for  $\text{CBF}_{\text{day}9-10}$  was 26.9 ml/100 g/min (sensitivity, 90.38 %; specificity, 92.31 %; PPV, 59.49 %; NPV, 98.71 %).  $P$  values from ROC analyses were as follows:  $\text{CBF}_{\text{day}9-10}$  vs.  $\text{CBF}_{\text{i/c\_day}9-10}$ ,  $P < 0.001$ ;  $\text{CBF}_{\text{day}9-10}$  vs.  $\text{CBF}_{\text{day}9-10/\text{day}1-2}$ ,  $P < 0.001$ ; and  $\text{CBF}_{\text{i/c\_day}9-10}$  vs.  $\text{CBF}_{\text{day}9-10/\text{day}1-2}$ ,  $P = 0.832$ .

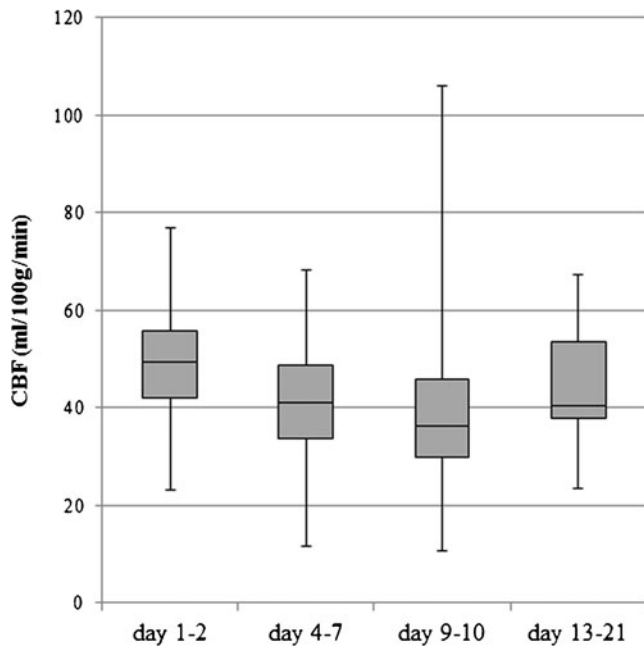
Representative cases of symptomatic patients (Figs. 6 and 7) and an asymptomatic patient (Fig. 8) are shown with serial CBF changes at multiple ROIs for the posterior parts of the MCA.

## Discussion

Single time-point ASL revealed a significant CBF reduction in the posterior parts of the MCA territory in symptomatic hemispheres compared with asymptomatic hemispheres on days 9–10. Decreased CBF associated with vasospasm will lead to cerebral infarction and delayed ischaemic neurological deficits (DIND). As the upper part of the pyramidal tract is fed by the long insular artery from the insular segment of the MCA and/or medullary arteries from the opercular and cortical segments of the MCA [12], a CBF decrease in the MCA territory due to vasospasm might cause motor weakness. As observed in the cases presented in Figs. 6 and 7, areas of decreased CBF were larger than the high-intensity areas on DWI for symptomatic patients, suggesting that

**Fig. 2** Box-and-whisker plot for  $\text{CBF}_{\text{day}9-10}$  and  $\text{CBF}_{\text{i/c\_day}9-10}$ . The three percentiles (25th, 50th, 75th) for ROIs of  $\text{CBF}_{\text{day}9-10}$  are 19.34, 22.63, and 25.21 ml/100 g/min for symptomatic hemispheres and 30.13, 35.76, and 43.60 ml/100 g/min for asymptomatic hemispheres, respectively ( $P < 0.001$ ) (a) The three percentiles (25th, 50th, and 75th) of  $\text{CBF}_{\text{i/c\_day}9-10}$  are 0.55, 0.6, and 0.79 for symptomatic hemispheres and 0.87, 1.01, and 1.19 for asymptomatic hemispheres, respectively ( $P < 0.001$ ) (b)





**Fig. 3** Box-and-whisker plot for CBF with serial ASL. The three percentiles (25th, 50th, 75th) for ROIs of CBF are 41.99, 49.42, and 55.90 ml/100 g/min for CBF<sub>day1-2</sub>, 33.70, 41.13, and 48.75 ml/100 g/min for CBF<sub>day4-7</sub>, 29.67, 36.26, and 45.79 ml/100 g/min for CBF<sub>day9-10</sub>, and 37.87, 40.26, and 53.59 ml/100 g/min for CBF<sub>day13-21</sub>. *P* values are less than 0.05 except between CBF<sub>day4-7</sub> and CBF<sub>day13-21</sub> (*P*=0.849). A gradual CBF reduction is observed from CBF<sub>day1-2</sub> to CBF<sub>day9-10</sub>, and recovery of CBF on CBF<sub>day13-21</sub> to nearly equal to CBF<sub>day4-7</sub> is observed

ASL reveals an ischaemic penumbra. However, additional study is necessary to confirm this possibility, given the relatively small number of symptomatic patients in this study.

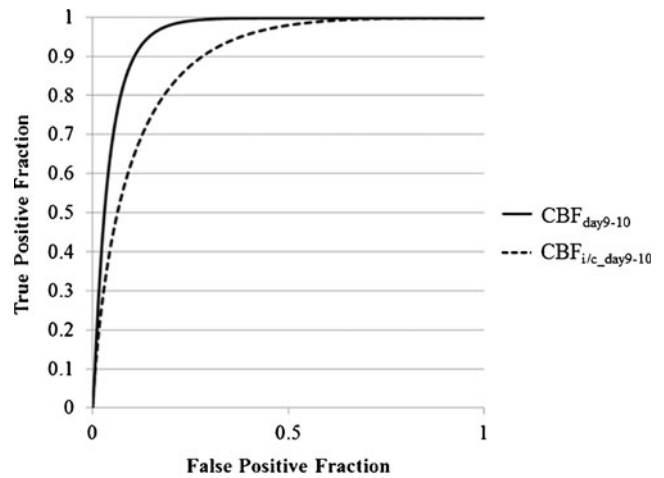
Our results showed that CBF<sub>day9-10</sub> can predict CBF reduction in the posterior part of the MCA territory better than CBF<sub>i/c\_day9-10</sub>. This suggests that CBF reduction on the contralateral side increased CBF<sub>i/c\_day9-10</sub>, which may indicate that weak vasospasm also occurred contralaterally [13].

Serial ASL revealed the value of CBF to be decreased to the order of CBF<sub>day1-2</sub>, CBF<sub>day4-7</sub>, and CBF<sub>day9-10</sub>, and

**Table 2** *P* values among CBF<sub>day1-2</sub>, CBF<sub>day4-7</sub>, CBF<sub>day9-10</sub>, and CBF<sub>day13-21</sub>

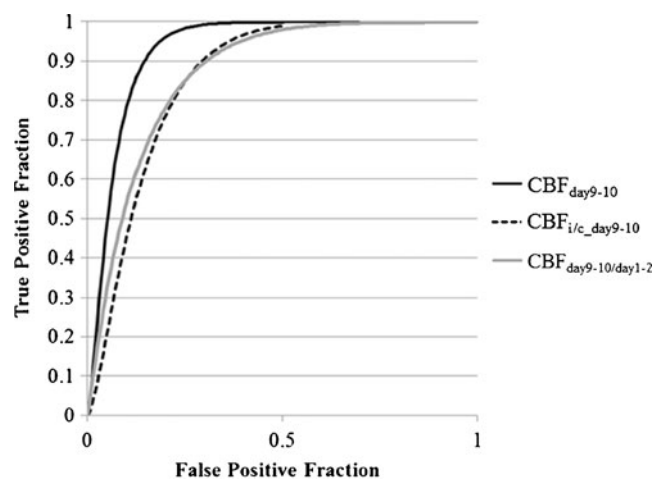
	CBF <sub>day1-2</sub>	CBF <sub>day 4-7</sub>	CBF <sub>day 9-10</sub>	CBF <sub>day 13-21</sub>
CBF <sub>day1-2</sub>				
CBF <sub>day 4-7</sub>	<0.001			
CBF <sub>day 9-10</sub>	<0.001	0.006		
CBF <sub>day 13-21</sub>	<0.001	0.849	<0.001	

*P* values among CBF<sub>day1-2</sub>, CBF<sub>day4-7</sub>, CBF<sub>day9-10</sub>, and CBF<sub>day13-21</sub> are shown. All *P* values were less than 0.05 except for CBF<sub>day4-7</sub> compared with CBF<sub>day13-21</sub>



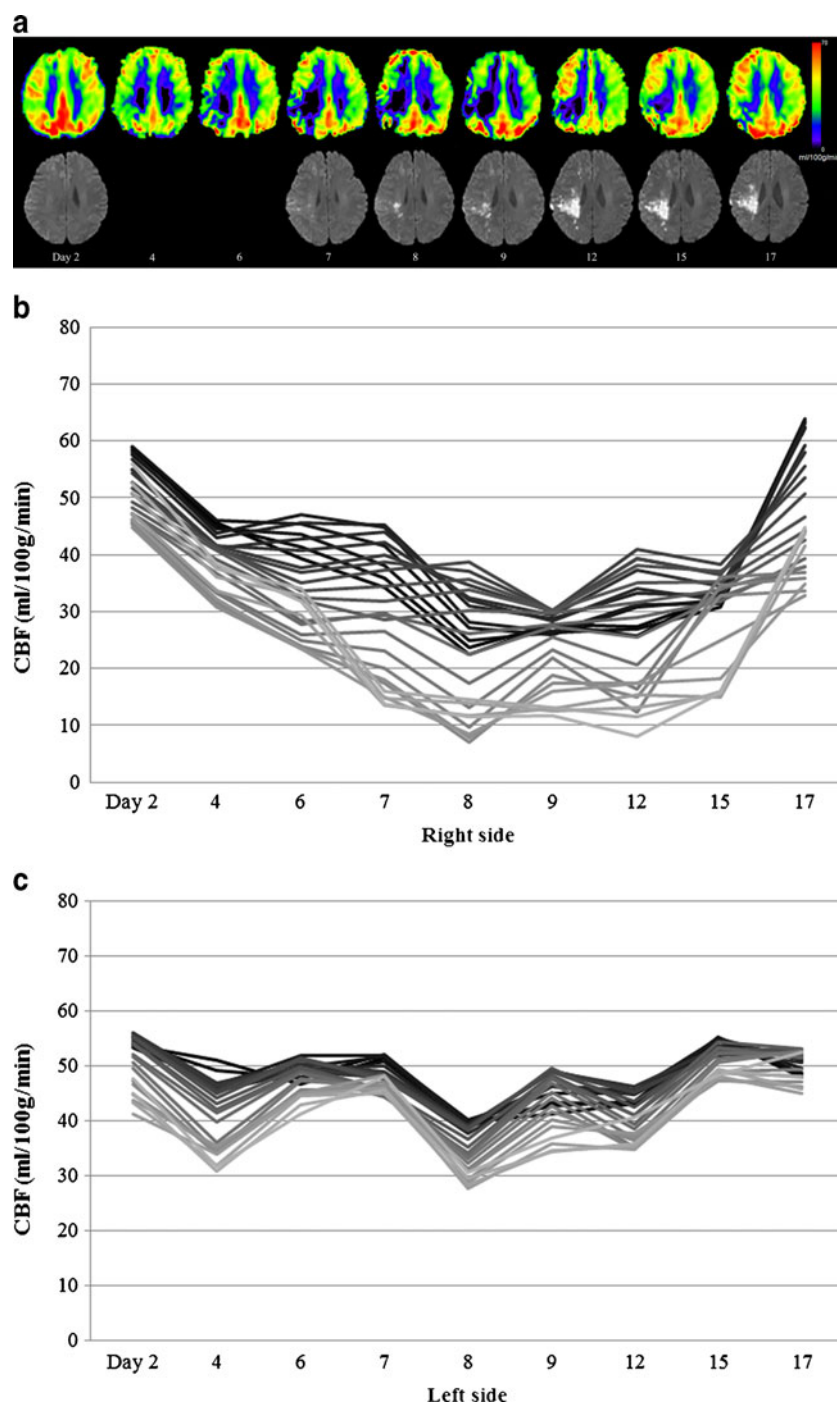
**Fig. 4** ROC analysis for single time-point ASL revealed that AUCs of CBF<sub>day9-10</sub> and CBF<sub>i/c\_day9-10</sub> are 0.95 and 0.89. This indicates that CBF<sub>day9-10</sub> is a better parameter for predicting CBF reduction than CBF<sub>i/c\_day9-10</sub>. The optimal cutoff for CBF<sub>day9-10</sub> is 26.9 ml/100 g/min (sensitivity, 90.38 %; specificity, 93.89 %; PPV, 46.53 %; NPV, 99.40 %)

increased for CBF<sub>day13-21</sub>, confirming that serial ASL imaging is useful for monitoring vasospasm, although CBF<sub>day9-10/day1-2</sub> was less predictable than CBF<sub>day9-10</sub>. Vasospasm represents the most important cause of DIND, because early aneurysm surgery has been reported to decrease the risk of rebleeding [14]. Intensive prophylactic therapy for vasospasm such as hypervolaemia, hypertension, and haemodilution (triple-H) is preferable for impaired CBF [15]. A PET study showed a wide variation in CBF patterns for patients with vasospasm, ranging from reduced to normal to hyperaemic [6], because PET studies are usually performed only



**Fig. 5** ROC analysis for serial ASL measurements shows that AUCs of CBF<sub>day9-10</sub>, CBF<sub>day9-10/day1-2</sub>, and CBF<sub>i/c\_day9-10</sub> are 0.93, 0.87, and 0.86, respectively. Optimal cutoffs for CBF<sub>day9-10</sub> are 26.9 ml/100 g/min (sensitivity, 90.38 %; specificity, 92.31 %; PPV, 59.49 %; NPV, 98.71 %)

**Fig. 6** A 67-year-old woman with symptomatic vasospasm (case 15). Clipping for the right IC-PC aneurysm was performed on day 0. The patient had been conscious without motor weakness after surgery until day 6. Left-sided hemiplegia, sensory disturbance, and hemispatial neglect appeared on day 7. ASL immediately after the occurrence of these symptoms revealed decreased CBF in the right MCA territory, particularly in the distal slices (upper row) (a). Conventional angiography revealed vasospasm in the M1 segment of the right MCA. Repeated endovascular treatment was performed, and temporal improvement of MCA stenosis and paralysis was achieved, but left-sided hemiparalysis remained. Serial ASL measurements show gradual decreases in CBF even before the onset of symptoms and increasing hyperintensity on DWI (lower row) (a). A propensity towards a relative CBF decrease is seen in distal slices (b). Fluctuating CBF is shown on the left side, and a slight CBF decrease is shown in distal slices on day 8 (c). Note that DWI was not obtained for days 4 and 6. Proximal slices are displayed in black and distal slices in grey

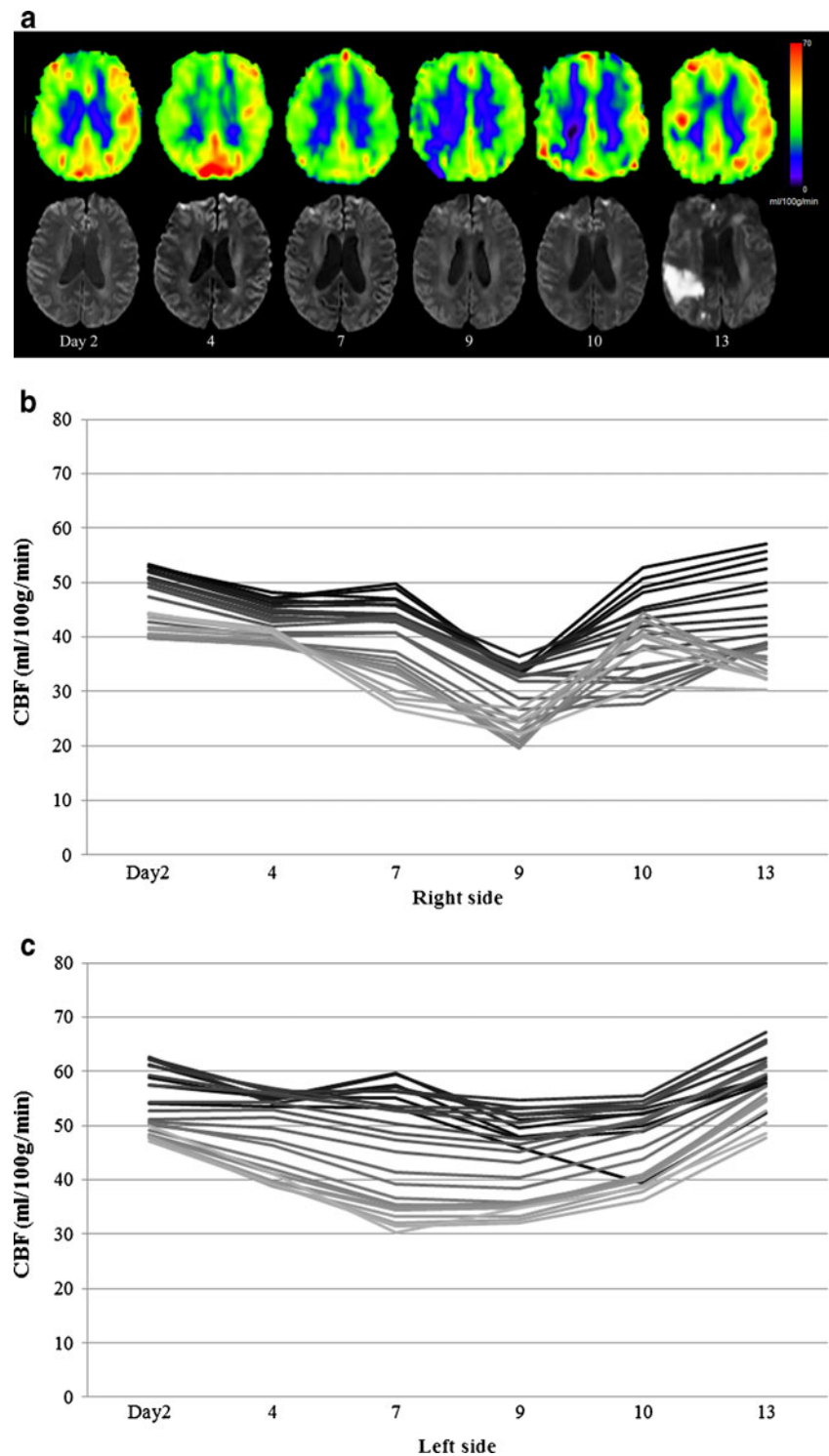


once during the postoperative course. Serial ASL imaging in the present study showed a gradual decrease in CBF before clinical symptoms or DWI abnormalities became evident, consistent with previous reports of DWI-PWI mismatch in vasospasm [4, 16]. Serial ASL may help us to understand temporal changes in vasospasm for each patient and to select the timing for the treatment of vasospasm, such as endovascular treatment and CSF drainage [17, 18]. ASL is less invasive than MR/CT perfusion and

suitable for repeated examinations, because ASL can measure CBF without any administration of contrast media or exposure to radiation.

Serial ASL also showed recovery from impaired CBF. Triple-H therapy has been widely performed, but the hypertension and hypervolaemia with such therapy may increase the risks of cardiac failure, electrolyte abnormality and cerebral oedema [1]. Hypertension and hypervolaemia therapy can be less intensive, if serial ASL shows improvement

**Fig. 7** A 77-year-old woman with symptomatic vasospasm (case 17). Clipping for right IC–PC aneurysm was performed on day 0. She had been well with no motor weakness except mild drowsiness until day 8. Left-sided hemiplegia and sensory disturbance occurred on day 9. ASL immediately after the occurrence of symptoms revealed decreased CBF in the right MCA territory, particularly in distal slices (upper row) (a). Conventional angiography revealed vasospasm in the M2 segment of the right MCA. Repeated endovascular treatment was performed, achieving a temporary improvement in paralysis. Unfortunately, left-sided hemiplegia deteriorated between days 10 and 13, and MR imaging was not performed during this interval. DWI (lower row) shows a hyperintense area in the posterior part of the right MCA territory on day 13 (a). Serial ASL measurements show gradual CBF decreases even before symptom onset and a propensity toward a relative CBF decrease in the distal slices (b). A slight CBF decrease is shown on the left side (c). Proximal slices are displayed in black and distal slices in grey

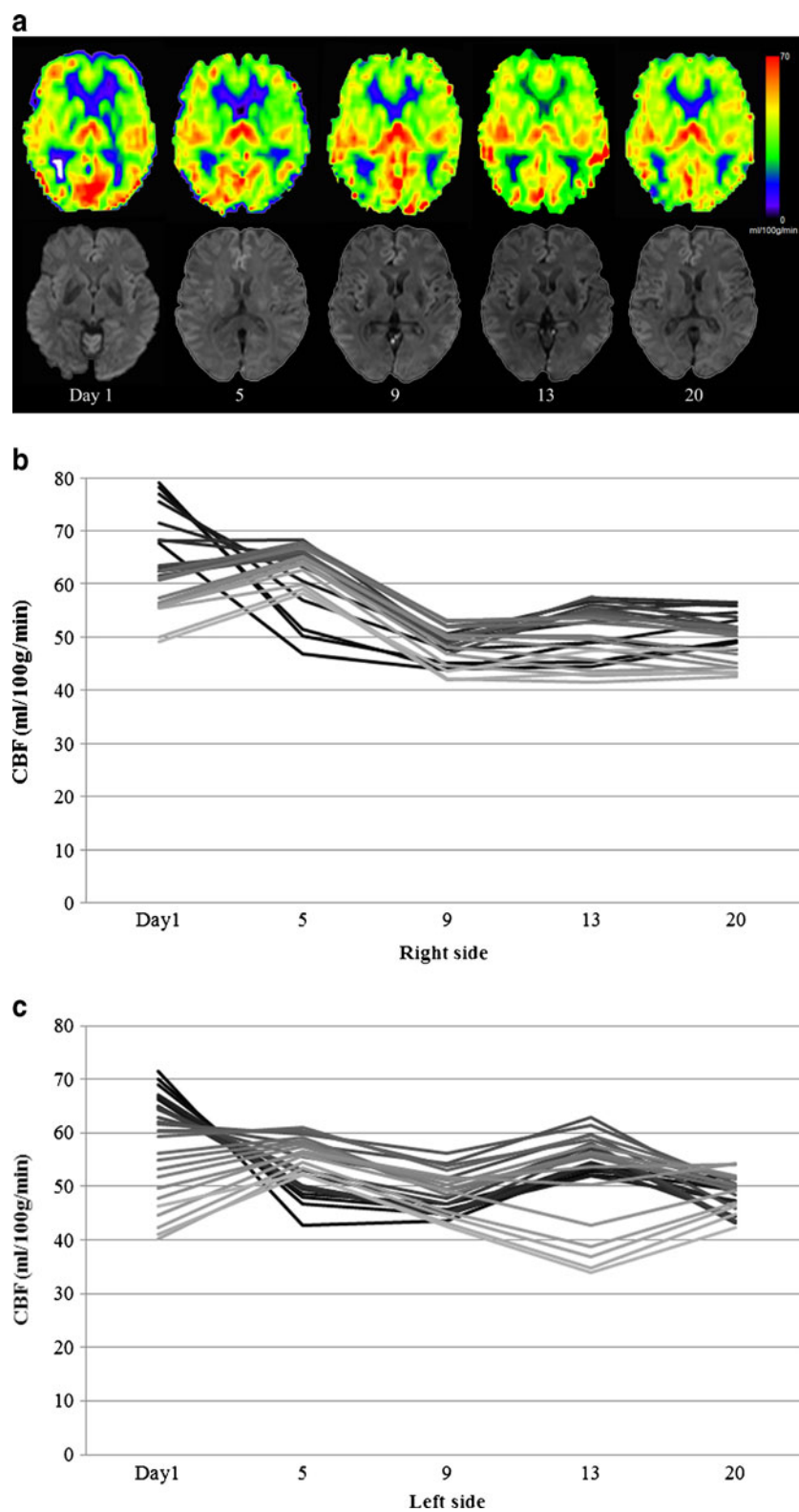


of CBF, although additional investigation is necessary to evaluate the therapeutic effects of serial ASL.

We focussed on ROIs for the posterior part of the MCA territory in this study. This was because metallic artefacts derived from aneurysm clips severely affected CBF values for ROIs placed at the anterior part of the

MCA territory. The purpose of this study was to diagnose vasospasm after SAH, so this selection was considered inevitable, and we chose a feasible imaging protocol and processing method. However, several limitations to this study must be considered when interpreting the results. Serpiginous high signal was sometimes

**Fig. 8** An asymptomatic 65-year-old woman (case 12). Emergency endovascular coiling for basilar aneurysm was performed on day 0. She had been under sedation with spinal drainage for SAH. After gradual recovery from drowsiness, no apparent neurological focal deficits were identified during the postoperative course. ASL shows no apparent decrease in CBF (upper row) and DWI (lower row) reveals no abnormalities (a). Serial ASL shows a mild CBF decrease around day 9, but to no less than 30 ml/100 g/min (b, c). Proximal slices are displayed in black and distal slices in grey



observed when labelled blood did not reach the capillary bed and remained in the artery, representing delayed artery transit artefacts [19]. Vasospasm occurs not only in the proximal artery segment, but also in the distal artery or even in intraparenchymal arterioles [20].

This increases the cerebral circulation time [21] and causes artery transit artefacts in ASL. In this context, CBF measured by ASL may not represent the true CBF, but serial ASL is still a useful tool for detecting vasospasm, because delayed artery transit indicates delayed artery circulation.



Another limitation is that symptoms might have developed around days 9–10. There has been no prospective study featuring vasospasm on ASL in the literature according to our knowledge. Therefore, we firstly focussed on the visualisation of cerebral ischaemia caused by vasospasm on ASL. It might have been helpful to have set the day for ASL imaging before day 9–10. However, the purpose of this study was to investigate visualisation of vasospasm, and early detection and prediction of vasospasm would be another study. Additional studies with more patients will be necessary to determine the lowest CBF and calculate the diagnostic performance of serial ASL for vasospasm.

Another limitation is that ASL images were not coregistered to three-dimensional (3D) anatomical images. Coregistration to 3D anatomical images is widely applied in image analysis [22], but 3D anatomical images were not obtainable because of the increased imaging time required conflicting with the need to minimise the time spent by ill patients in the MR unit. As we used ROI analysis, a small degree of misregistration may not have had a great effect on the results.

To increase the precision of perfusion quantification, the signal evolution after arterial labeling needs to be sampled at more than two points in time [23]. Multi-inversion time (TI) imaging could have been helpful for quantifying CBF; however, TI imaging requires longer imaging times for equivalent SNR [24]. Several reports demonstrated that single TI is sensitive to identification of abnormalities because of its high sensitivity to delay [25, 26]. Delayed arterial arrival time will lead to a decrease of CBF on ASL, which will add some advantage for the detection of vasospasm after aneurysmal SAH.

The last limitation is that the posterior part of MCA territory provides a very small window for evaluation of perfusion differences. Because conventional angiography confirmed vasospasm of at the posterior trunk of the MCA in all four symptomatic patients, we targeted posterior part of the MCA. Additional comparison studies are necessary to evaluate the entire brain perfusion after aneurysmal SAH.

In conclusion, single ASL revealed significant decreases in CBF for the posterior parts of the MCA territory in hemispheres with symptomatic vasospasm compared with asymptomatic hemispheres on days 9–10. Serial ASL detected a tendency towards CBF reduction related to vasospasm during the postoperative course of aneurysmal SAH.

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