Transcranial Doppler Ultrasonography for Diagnosis of Cerebral Vasospasm After Aneurysmal Subarachnoid Hemorrhage: Mean Blood Flow Velocity Ratio of the Ipsilateral and Contralateral Middle Cerebral Arteries

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Received, August 28, 2010.
Accepted, March 31, 2011.
Published Online, May 6, 2011.

BACKGROUND: Transcranial Doppler (TCD) is widely accepted to monitor cerebral vasospasm after subarachnoid hemorrhage (SAH); however, its predictive value remains controversial.

OBJECTIVE: To investigate the predictive reliability of an increase in the mean blood flow velocity (mBFV) ratio of the ipsilateral to contralateral middle cerebral arteries (I/C mBFV) compared with the conventional absolute flow velocity.

METHODS: We retrospectively investigated the clinical and radiologic data of consecutive patients with SAH admitted from July 2003 to August 2009 who underwent TCD ultrasonography. The highest mBFV value in bilateral middle cerebral arteries was recorded, while delayed cerebral ischemia (DCI) was defined as neurological deficits or computed tomographic evidence of cerebral infarction caused by vasospasm. The ipsilateral side was defined as the side with higher mBFV value when evaluating the I/C mBFV. We thus elucidated the reliability of this rate in comparison with the conventional method for predicting DCI with receiver operating characteristic (ROC) analysis.

RESULTS: One hundred and forty-two patients were retrospectively analyzed with specific data from 1262 TCD studies. The ROC curve showed that the overall predictive value for DCI had an area under the curve of 0.86 (95% confidence interval: 0.76-0.96) when the I/C mBFV was used vs 0.80 (0.71-0.88) when the absolute flow velocity was used. The threshold value that best discriminated between patients with and without DCI was I/C mBFV of 1.5.

CONCLUSION: In patients with SAH, the I/C mBFV demonstrated a more significant correlation to vasospasm than the absolute mean flow velocity.

KEY WORDS: Blood flow velocity, Cerebral vasospasm, Delayed cerebral ischemia, Subarachnoid hemorrhage, Transcranial Doppler

Neurosurgery 69:876–883, 2011 DOI: 10.1227/NEU.0b013e318222dc4c www.neurosurgery-online.com

Cerebral vasospasm represents a major cause of morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (SAH).[1,2] Angiographic vasospasm occurs in approximately 70% of patients between days 3 and 14 after SAH,[3] and 20% to 40% of patients develop neurological deficits or infarction caused by delayed cerebral ischemia (DCI).[4-7] It is crucial to predict which patients are at risk of cerebral vasospasm, because the management influences significantly on the prognosis. Conventional angiography has been conceived as the most accurate and reliable modality of detecting vasospasm,[8-11] but it is sometimes invasive.[4,12]

ABBREVIATIONS: DCI, delayed cerebral ischemia; **I/C mBFV,** mean blood flow velocity rate of the ipsilateral to contralateral middle cerebral arteries; **IVH,** intraventricular hemorrhage; **mBFV,** mean blood flow velocity; **MCA,** middle cerebral artery; **ROC,** receiver operating characteristic; **SAH,** subarachnoid hemorrhage; **TCD,** transcranial Doppler

Induction of transcranial Doppler (TCD) ultrasonography in 1982 by Aaslid et al[13] allowed noninvasive detection of cerebral vasospasm, monitoring of the onset, and resolution of this condition.[14-17] Several studies have shown that the severity of cerebral vasospasm and the clinical onset of delayed ischemic deficits cannot be accurately detected only by measuring the absolute flow velocities with TCD. A mean blood flow velocity (mBFV) of more than 120 cm/s on TCD shows approximately 80% sensitivity and specificity for the presence of angiographic vasospasm in the proximal middle cerebral artery (MCA).[18] Meanwhile, TCD is usually not beneficial to detect spasm arising in the distal vessels. Previous studies have discussed the limited reliability of TCD to predict symptomatic vasospasm. An elevated TCD flow velocity induces only a small increase of the risk of DCI after SAH.[19] This is the case depending on which methodology, such as specific blood flow velocity thresholds,[11,20-22] the absolute increase of the mBFV,[23-25] or an increased Lindegaard ratio[21,26] (mBFV of the MCA divided by that of the cervical internal carotid artery) is employed to identify patients at risk.

TCD, however, remains the most widely examined imaging modality for diagnosing cerebral vasospasm. The sensitivity and predictive value of TCD are limited, and improved methods for identifying patients at high risk for DCI after SAH are still needed. The purpose of the present study was to improve the accuracy of TCD for diagnosis of cerebral vasospasm after SAH by elucidating the prognostic value of the mBFV of the ipsilateral to contralateral MCA (I/C mBFV). Additionally, we also analyzed clinical variables that could play critical roles in the onset of cerebral vasospasm.

METHODS

Patients' Eligibility

We reviewed the clinical and radiological information of all patients admitted to the Department of Emergency and Critical Care Medicine at Nippon Medical School (Tokyo, Japan) with spontaneous SAH from July 2003 to August 2009. An informed consent for this study was obtained from the patient or a surrogate, and it was approved by the local institutional review board. The diagnosis of SAH was established from the findings on admission computed tomography (CT) scans or magnetic resonance images, or by xanthochromia of the cerebrospinal fluid while CT was nondiagnostic.

Patients eligible in the present study were treated by microsurgical clipping or endovascular coiling. Their first TCD examinations were performed on or before day 3 (day 0 indicates the calendar day of the bleeding event). Exclusion criteria included nonaneurysmal SAH (eg, due to trauma, ruptured arteriovenous malformation, ruptured mycotic aneurysm, vasculitis, or cryptogenic causes), cardiopulmonary arrest before or on arrival at hospital, death by day 14, treatment by trapping and/or bypass, $\leq$7 TCD studies up to SAH day 14, lack of adequate cranial TCD windows, and incomplete medical or radiological records. Finally, of 397 patients with aneurysmal SAH who were managed from July 2003 to August 2009, 54 were excluded because of cardiopulmonary arrest on or before arrival at hospital, 83 were excluded because of death by day 14, and 5 were excluded because they received trapping and/or bypass. Subsequently, 82 were eliminated because initial TCD was performed after SAH day 3 and/or TCD was done $<$8 times up to SAH day 14, and 21 were excluded because of inadequate windows. We excluded 10 by incomplete medical or radiological records. One hundred forty-two patients were included: 57 men (40.1%) and 85 women (59.9%) with a mean age of 62.1 $\pm$ 12.2 years. Aneurysms were treated by surgical clipping, except in 5 patients who underwent embolization with coils. All of the available medical or radiological records were reviewed and information was exclusively collected about factors that are known or thought to be important key factors in vasospasm, the age, sex, history of hypertension, smoking status, admission Glasgow Coma Scale score,[27] Hunt and Hess grade,[28] systolic and diastolic blood pressures on admission, and body temperature. The initial laboratory workup was performed in all patients after admission, integrating blood cell count, hemoglobin, hematocrit, sodium, potassium, blood glucose, and arterial blood gases. Admission head CT scans were independently evaluated by study neurointensivists, and the amount of blood clot in the subarachnoid space was classified according to the modified Fisher scale.[29] They also determined the SAH sum score[30] based on the amount and location of subarachnoid blood, the intraventricular hemorrhage (IVH) sum score[30] based on the amount and location of intraventricular blood, the presence of intracerebral hematoma, and the presence of hydrocephalus. The SAH sum score was calculated as the total of scores from 0 to 3 assigned for each of 10 cisterns or fissures. A score of 0 indicated no blood, 1 meant that blood was barely visible, 2 meant an intermediate amount of blood, and 3 was assigned when the cistern/fissure was completely filled with blood. Judgment was based on the extent and intensity of density changes. The 10 cisterns/fissures investigated were the frontal interhemispheric fissure, the quadrigeminal cistern, both suprasellar cisterns, both ambient cisterns, both basal Sylvian fissures, and both lateral Sylvian fissures. The IVH sum score was calculated as the total of the separate scores for each of the 4 ventricles, ie, both lateral ventricles, the third ventricle, and the fourth ventricle. Scores were assigned as: 0, no blood; 1, sedimentation of erythrocytes in the posterior part; 2, ventricle partly filled with blood; and 3, ventricle completely filled with blood. Angiography or 3-dimensional CT angiography was performed on admission to locate the aneurysm. We recorded the location and size of each aneurysm, as well as the treatment (microsurgical clipping or endovascular coiling). Clinical evaluation was done serially throughout the day (at least every 2 hours) by the staff of the intensive care unit. Additional CT or MRI was performed more than once a week and for every major event. Patient outcome was scored according to Glasgow Outcome Scale score[31] at the end of their admission.

Clinical Management

Patients received neurointensive care to stabilize and regulate their cardiopulmonary function, fluid balance, arterial blood pressure, intracranial pressure, serum glucose, and arterial blood gases. Before the aneurysm had been treated, the systolic blood pressure was maintained at $\leq$160 mm Hg in most cases. If necessary, the patient was sedated and ventilated. Triple-H therapy (hypertension, hypervolemia, and hemodilution therapy)[32] was routinely performed after treatment of the aneurysm, involving a target central venous pressure of more than 8 mm Hg, induction of hypertension with dopamine to maintain a systolic blood pressure of 140 to 160 mm Hg, and maintenance of the cardiac index at 3.5 L/min/m^2 or more by infusion of dopamine or dobutamine as needed. After April 2009, oral statin therapy (fluvastatin sodium: 30 mg/d) was routinely started within 72 hours of the event. Intracranial hypertension and acute symptomatic intracranial mass effect were treated

with repeated boluses of 10% glycerol (0.4-0.6 g/kg). Persistent fever (temperature exceeding 38.5°C) was treated with nonsteroidal anti-inflammatory drugs and surface cooling. To maintain the hemoglobin at ≥8 mg/dL we gave blood transfusions to such patients. Angiography was routinely performed in patients with DCI, and the location of angiographic vasospasm was recorded. Endovascular treatment of vasospasm entailed either intra-arterial fasudil hydrochloride hydrate or angioplasty. The treating consultants made decisions for each endovascular intervention.

Definition of DCI

DCI was defined as a new hypodensity on CT scans located in a vascular territory and/or associated symptoms, including a decrease of consciousness and focal deficits, due to cerebral vasospasm and not explained by other causes (eg, rebleeding, hydrocephalus, cardioembolic sources of emboli, hypoxia, electrolyte disturbances, or seizures). Patients who had cerebral infarction that was possibly related to complications of surgery or angiography were excluded.

TCD Studies

TCD ultrasonography of the left and right MCAs was performed daily or every other day between SAH days 1 and 14 by 2 experienced technicians. The mBFV was measured through transtemporal windows with a 2-MHz hand-held transducer (Intra-View; Rimed, Ltd, Park Raanana, Israel). The bilateral maximal mBFV and the ratio of the mBFV in the ipsilateral MCA to that in the contralateral MCA (I/C mBFV) were recorded for each TCD study. We defined the ipsilateral side as the side with a higher mBFV.

Statistical Analysis

Analysis of data was performed with standard statistical software (Version 16.0; SPSS, Inc, Chicago, Illinois). To determine whether there was a correlation between DCI and categorical variables, the χ^2 test or Fisher exact test was applied, whereas continuous variables were assessed with an independent two-tailed Student t test. For nonnormally distributed continuous variables, the Mann-Whitney U test was examined. Receiver operating characteristic (ROC) curves were drawn, and the area under the curve (C-statistic) was calculated to assess the overall predictive value for DCI of the I/C mBFV and the absolute flow velocity. To evaluate independent predictors of DCI, significant univariate variables ($P < .05$) were included in a multivariate analysis.

TABLE 1. Demographic, Clinical, and Laboratory Characteristics of Patients With or Without Delayed Cerebral Ischemia[a]

Characteristic	No DCI	DCI	P Value
Demographic data			
No. of patients	114	28	
Age, y	63.4 ± 12.4	57.0 ± 10.0	.012
Female, %	70 (61.4)	15 (53.6)	.45
History of hypertension, %	73 (64.0)	15 (53.6)	.31
Smoking status, %	42 (36.8)	11 (39.3)	.81
Clinical features			
Glasgow Coma Scale	9.8 ± 4.4	8.2 ± 4.1	.09
Eye component	2.5 ± 1.3	2.0 ± 1.2	.09
Verbal component	2.8 ± 1.7	2.3 ± 1.6	.22
Motor component	4.6 ± 1.8	3.9 ± 1.8	.016
Hunt and Hess grade			.44
1-2, %	25 (21.9)	4 (14.3)	
3-5, %	89 (78.1)	24 (85.7)	
Systolic blood pressure, mm Hg	171.8 ± 36.3	185.6 ± 44.5	.19
Diastolic blood pressure, mm Hg	96.6 ± 19.5	108.5 ± 18.1	.004
Body temperature, °C	35.8 ± 1.0	36.0 ± 1.1	.39
Laboratory findings			
WBC, $\times 10^9$/L	11.5 ± 4.2	11.3 ± 4.9	.85
Hb, mg/dL	12.9 ± 1.8	13.3 ± 1.4	.24
Ht, %	38.8 ± 5.0	40.0 ± 4.1	.27
Sodium, mEq/L	140.3 ± 3.2	139.3 ± 3.5	.14
Potassium, mEq/L	3.4 ± 0.5	3.2 ± 0.4	.10
Blood glucose, mg/dL	175.0 ± 55.1	187.8 ± 40.0	.08
Arterial blood gases			
pH	7.39 ± 0.06	7.38 ± 0.05	.15
pCO_2, mm Hg	40.2 ± 8.3	37.7 ± 6.6	.13
pO_2, mm Hg	270.5 ± 159.2	273.6 ± 142.9	.73
HCO_3^-, mmol/L	23.7 ± 2.7	22.9 ± 2.2	.19
Base excess, mmol/L	−0.6 ± 2.5	−1.5 ± 2.2	.09
Lactate, mg/dL	27.0 ± 16.4	28.5 ± 15.2	.41

[a]DCI, delayed cerebral ischemia; Hb, hemoglobin; Ht, hematocrit; WBC, white blood cell.

RESULTS

A total of 1262 TCD examinations performed up to SAH day 14 were analyzed (a mean of 8.9 per patient). DCI occurred in 28 of the 142 patients (19.7%), and the clinical characteristics of the groups with or without DCI are compared in Tables 1 and 2. The mean age of the patients with DCI was 57.0 ± 10.0 years, which was significantly younger than the mean age of the patients without DCI (63.4 ± 12.4 y, $P = .012$). Meanwhile, BFVs on TCD were significantly higher in patients who developed DCI vs those without DCI, except on day 1 and day 3. The mBFV of patients with DCI increased progressively between SAH days 3 and 5 before subsequently showing a decrease, and the condition did not happen in patients without DCI (Figure 1). The mean mBFV between SAH days 1 and 14 of patients with DCI was 103.7 ± 22.4 cm/s, which was significantly higher than the mean mBFV of patients without DCI (77.9 ± 25.7 cm/s, $P < .001$).

Three other clinical variables were also significantly associated with DCI, including high diastolic blood pressure on admission ($P < .01$), a large amount of blood in the suprasellar cisterns (Table 3, $P < .05$), and performance of decompressive craniectomy ($P < .01$). The SAH sum score and IVH sum score were not significantly different between patients with and without DCI (Tables 3 and 4). Although the associations were not specifically significant, the presence of intracerebral hematoma ($P = .054$) was highly associated with an increased risk of DCI.

The I/C mBFV of 121 patients was available. According to ROC analysis, the I/C mBFV had a higher detection rate for patients with DCI compared with the conventional absolute mBFV (Figure 2). When ROC curves displaying the overall

TABLE 2. Radiological Characteristics, Treatment, and Transcranial Doppler Findings of Patients With or Without Delayed Cerebral Ischemia[a]

Characteristic	No DCI	DCI	*P* Value
Radiological findings			
Modified Fisher grade			.61
1	21 (18.4)	3 (10.7)	
2	38 (33.3)	9 (32.2)	
3	15 (13.2)	6 (21.4)	
4	40 (35.1)	10 (35.7)	
ICH, %	28 (24.6)	12 (42.9)	.054
Hydrocephalus, %	38 (33.3)	9 (32.1)	.90
Location of ruptured aneurysm, %			.75
ACA	40 (35.1)	11 (39.3)	
ICA	29 (25.4)	9 (32.2)	
MCA	34 (29.8)	6 (21.4)	
Posterior circulation	11 (9.7)	2 (7.1)	
Aneurysm size, mm			.08
≤12	94 (82.5)	25 (89.3)	
13–24	18 (15.8)	1 (3.6)	
≥25	2 (1.7)	2 (7.1)	
Treatment			
Operation			.58
Microsurgical clipping, %	109 (95.6)	28 (100.0)	
Endovascular coiling, %	5 (4.4)	0 (0.0)	
Decompressive craniectomy, %	42 (35.6)	18 (64.3)	.008
Statin, %	23 (20.2)	7 (25.0)	.58
TCD findings			
mBFV, cm/s	77.9 ± 25.7	103.7 ± 22.4	<.001

[a]ACA, anterior cerebral artery; DCI, delayed cerebral ischemia; ICA, internal carotid artery; ICH, intracerebral hematoma; mBFV, mean blood flow velocity; MCA, middle cerebral artery; TCD, transcranial Doppler.

diagnostic utility for DCI were drawn, the area under the curve was 0.86 (95% confidence interval: 0.76-0.96) using the I/C mBFV and 0.80 (0.71-0.88) by the conventional method. The mBFV threshold value that best discriminated between patients with and without DCI was 1.5 for the I/C mBFV and 125 cm/s for the absolute velocity. With the use of these threshold values, the sensitivity, specificity, and positive predictive of the I/C mBFV and absolute velocity for predicting DCI was 77.0%, 80.0%, and 51.3% vs 67.9%, 71.9%, and 37.3%, respectively.

Angiography data of 26 patients with DCI in whom the I/C mBFV could be calculated were available (Table 5). In our analysis, the angiographic vasospasm in patients with the I/C mBFV ≥1.5 found no significant difference between anatomical locations. However, most angiographic vasospasm in patients with the I/C mBFV <1.5 occurred on the anterior cerebral artery and the artery of the posterior circulation ($P = .008$).

The prognosis is significantly worse in patients with the I/C mBFV ≥1.5 compared with those <1.5 (Table 6, $P = .031$). In patients with the I/C mBFV ≥1.5, the rate of good outcome or moderate disability was low, but the mortality rate was extremely high, because 6 of the 39 (15.4%) patients died. In DCI patients, there was no significant difference in Glasgow Outcome Scale score between those treated with intra-arterial fasudil hydrochloride hydrate and with angioplasty (Table 7, $P = .88$).

DISCUSSION

The present study showed that: (1) DCI occurred in 28 of 142 patients with SAH (19.7%); (2) predictors of DCI were younger age, high diastolic blood pressure on admission, large amount of blood in the suprasellar cisterns, and decompressive craniectomy; and (3) the I/C mBFV was more predictable than the conventional absolute mBFV for identification of vasospasm according to ROC analysis, and the cutoff value for predicting DCI was an I/C mBFV of 1.5. The prognosis is significantly worse in patients with I/C mBFV ≥1.5 compared with those <1.5.

The most accurate and reliable method of detecting vasospasm is conventional angiography.[8-11] A meta-analysis was recently elucidated in 26 trials comparing TCD with cerebral angiography in patients with SAH and concluded that TCD of the MCA has a high specificity (99%) and a high positive predictive value (97%), but a low sensitivity (67%). This meta-analysis also found

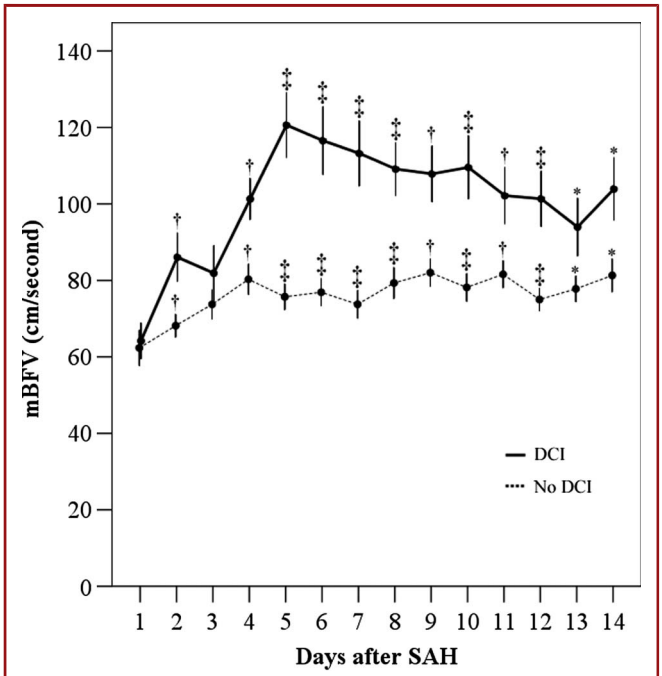

FIGURE 1. *Maximal mean blood flow velocity after SAH in patients with or without DCI. Velocities were significantly higher in patients who developed DCI, except on days 1 and 3. The mBFV of patients with DCI increased progressively between days 3 and 5. Values are the mean ± SE. *P < .05, †P < .01, ‡P < .001. mBFV, mean blood flow velocity; DCI, delayed cerebral ischemia; SAH, subarachnoid hemorrhage.*

TABLE 3. Subarachnoid Hemorrhage Score of 10 Cisterns and Subarachnoid Hemorrhage Sum Score[a]

	No DCI	DCI	*P* Value
Interhemispheric fissure	1.32 ± 0.74	1.46 ± 0.84	.38
Quadrigeminal cistern	1.36 ± 0.83	1.36 ± 0.49	.97
Rt. suprasellar cistern	1.67 ± 0.72	2.00 ± 0.47	.024
Lt. suprasellar cistern	1.68 ± 0.73	2.04 ± 0.51	.016
Rt. ambient cistern	1.40 ± 0.76	1.43 ± 0.50	.96
Lt. ambient cistern	1.40 ± 0.77	1.46 ± 0.51	.78
Rt. basal sylvian fissure	1.55 ± 0.71	1.71 ± 0.85	.37
Lt. basal sylvian fissure	1.68 ± 0.80	1.64 ± 0.83	.84
Rt. lateral sylvian fissure	1.54 ± 0.79	1.75 ± 0.89	.18
Lt. lateral sylvian fissure	1.69 ± 0.80	1.61 ± 0.92	.78
SAH sum score	15.28 ± 5.28	16.46 ± 3.56	.40

[a]DCI, delayed cerebral ischemia; lt., left; rt., right; SAH, subarachnoid hemorrhage.

TABLE 5. Locations of Angiographic Vasospasm in Delayed Cerebral Ischemia Patients[a]

	I/C mBFV ≥1.5	I/C mBFV <1.5	*P* Value
Locations of vasospasm			.008
ICA	2 (10.0)	0 (0)	
ACA	1 (5.0)	3 (50.0)	
MCA	4 (20.0)	0 (0)	
ICA + MCA	2 (10.0)	0 (0)	
ACA + MCA	6 (30.0)	0 (0)	
CA + ACA + MCA	4 (20.0)	0 (0)	
Bilateral ACA + MCA	1 (5.0)	1 (16.7)	
Posterior circulation	0 (0)	2 (33.3)	
Total	20	6	

[a]ACA, anterior cerebral artery; ICA, internal carotid artery; I/C mBFV, mean blood flow velocity rate of the ipsilateral to contralateral middle cerebral arteries; MCA, middle cerebral artery.

that TCD of other arteries showed no evidence of accuracy to detect vasospasm.[18] In addition, cerebral infarction may occur in some patients without apparent vasospasm on angiography. The sensitivity and predictive value of TCD are limited, and sophisticated methods for identifying patients with a high risk for cerebral vasospasm and DCI after SAH are further necessitated. In the present study, analysis with the I/C mBFV achieved a higher detection rate of patients who developed DCI after SAH than the absolute mBFV according to ROC analysis. Lee et al[33] reported that use of TCD to predict cerebral infarction after SAH had a sensitivity of 69.6% and a specificity of 77.1%, while Suarez et al[6] reported values of 70% and 73%, respectively. In the current study, TCD had a higher sensitivity (77.0%) and specificity (80.0%) when the I/C mBFV was used, and this rate was more closely related to clinically significant vasospasm in patients with aneurysmal SAH than absolute flow velocity indices. That is, to say, we can improve the low sensitivity of TCD for DCI.

To examine a further correlation between TCD and angiogram data, we analyzed correlation between the I/C mBFV and the location of angiographic vasospasm (Table 5). Our findings highly implicated that, for the MCA and the internal carotid artery, the I/C mBFV tended to show 1.5 and more when angiography shows cerebral vasospasm. For the other arteries such as the anterior cerebral artery and the artery of the posterior circulation, there seemed to be no indication to use the I/C mBFV to detect vasospasm.

TABLE 4. Intraventricular Hemorrhage Score of 4 Ventricles and Intraventricular Hemorrhage Sum Score[a]

	No DCI	DCI	*P* Value
Rt. lateral ventricle	0.86 ± 0.86	0.93 ± 0.98	.84
Lt. lateral ventricle	0.84 ± 0.86	0.93 ± 0.81	.51
Third ventricle	0.75 ± 1.04	0.79 ± 1.07	.86
Fourth ventricle	0.79 ± 1.17	0.75 ± 1.08	.92
IVH sum score	3.25 ± 3.37	3.39 ± 3.38	.84

[a]DCI, delayed cerebral ischemia; IVH, intraventricular hemorrhage; lt., left; rt., right.

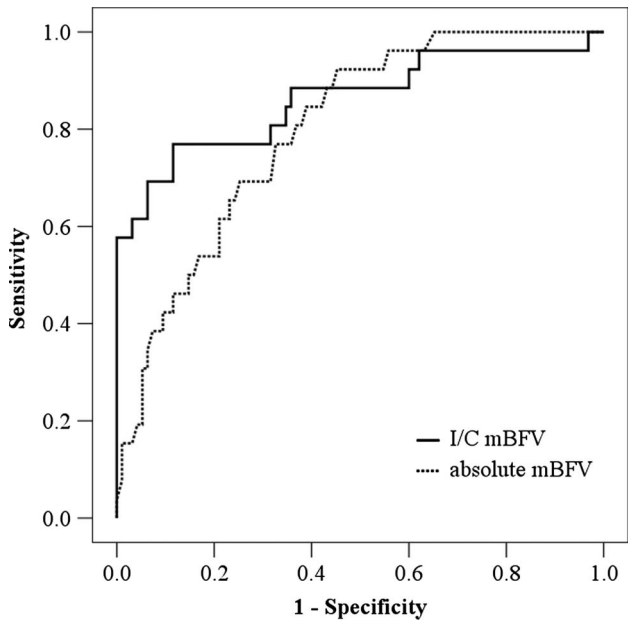

FIGURE 2. *Receiver operating characteristic curves comparing the absolute mean mBFV and the I/C mBFV for prediction of DCI. The area under the ROC curve for the I/C mBFV was 0.86 (95% confidence interval: 0.76-0.96), while that for the absolute mBFV was 0.80 (0.71-0.88). mBFV, mean blood flow velocity; I/C mBFV, mBFV of the ipsilateral to contralateral middle cerebral artery; ROC, receiver operating characteristic; DCI, delayed cerebral ischemia.*

TABLE 6. Glasgow Outcome Scale Scores of the Patients Who Had the I/C mBFV Not Less Than or Less Than 1.5[a]

	I/C mBFV ≥1.5	I/C mBFV <1.5	*P* Value
GOS scores			.031
4–5	8 (20.5)	35 (42.7)	
2–3	25 (64.1)	42 (51.2)	
1	6 (15.4)	5 (6.1)	
Total	39	82	

[a]GOS, Glasgow Outcome Scale; GOS score of 1 indicates death; 2, persistent vegetative state; 3, severe disability; 4, moderate disability; and 5, good recovery; I/C mBFV, mean blood flow velocity rate of the ipsilateral to contralateral middle cerebral arteries.

The crucial risk factors to predict DCI after SAH were the presence of thick clots in the basal cisterns or blood in the ventricular system.[34] Other possible risk factors for DCI involved younger age,[35] female sex,[19] cigarette smoking,[36,37] poor clinical grade,[19,38] high systolic blood pressure,[19] fever,[38] high glucose level,[19] poor modified Fisher scale score,[19] large amount of subarachnoid blood,[37] intracerebral hematoma,[19] and intravascular volume depletion.[39] In the present study, we identified 4 predictors of DCI: young age, high diastolic blood pressure on admission, large amount of subarachnoid blood at suprasellar cisterns, and decompressive craniectomy.

A younger age was associated with a significantly higher incidence of DCI (P = .012). Magge et al[35] investigated that increasing stiffness of the cerebral vasculature associated with advancing age may explain the lower incidence of angiographic vasospasm in the elderly, and they suggested that older patients may require less aggressive prophylactic treatment for vasospasm.

A relationship between vasospasm and the modified Fisher grade, SAH sum score, or IVH sum score has been reported.[29,30] Our study showed that the volume of SAH or IVH was not a significant predictor of vasospasm; meanwhile, a large amount of subarachnoid blood in the suprasellar cisterns was significantly related to DCI ($P < .05$). Moreover, we found that the diastolic blood pressure on admission was significantly higher in patients who developed DCI than in those who did not ($P < .01$). Rosen et al[40] also reported that the admission diastolic blood pressure is one of the risk factors for a large SAH volume. Our findings were consistent with this report (Figure 3). Furthermore, we found that hematoma in the suprasellar cisterns is most closely related to vasospasm.

Decompressive craniectomy has been shown to improve outcomes in patients experiencing massive ischemic infarction and severe head trauma; however, the role of craniectomy in aneurysmal SAH is less well defined.[41] We performed decompressive craniectomy in SAH patients who had large intracerebral hematomas and/or Sylvian fissure hematomas to reduce the intracranial pressure or to elevate the perfusion pressure. In our series, 18 (64.3%) of 28 patients with DCI underwent decompressive craniectomy, and this percentage was significantly higher than for patients without DCI ($P < .01$). In addition, although the correlation was not significant, an increase of DCI tended to be along with intracerebral hematoma (P = .054). We speculate that elevated intracranial pressure may also be a risk factor of DCI.

We did not find any correlation between the neurological status (Hunt and Hess grade or Glasgow Coma Scale) and the development of DCI, contrary to a previous report. Among the 142 patients who met all of the inclusion criteria, 29 patients (20.4%) were in Hunt and Hess grade 1 or 2 and 113 patients (79.6%) were in grades 3-5 (Table 1). We consider that this finding may depend on the higher proportion of poor grade patients than in previous reports.[19,38] This difference presumably can arise simply because our Department of Emergency and Critical Care Medicine particularly handles severe cases.

TABLE 7. Glasgow Outcome Scale Scores of the Patients With Delayed Cerebral Ischemia Who Were Treated With Intra-arterial Fasudil Hydrochloride Hydrate or With Angioplasty[a]

	Intra-arterial Fasudil Hydrochloride Hydrate	Angioplasty	*P* Value
GOS scores			.88
4–5	5 (20.8)	1 (25.0)	
2–3	15 (62.5)	2 (50.0)	
1	4 (16.7)	1 (25.0)	
Total	24	4	

[a]GOS, Glasgow Outcome Scale; GOS score of 1 indicates death; 2, persistent vegetative state; 3, severe disability; 4, moderate disability; and 5, good recovery.

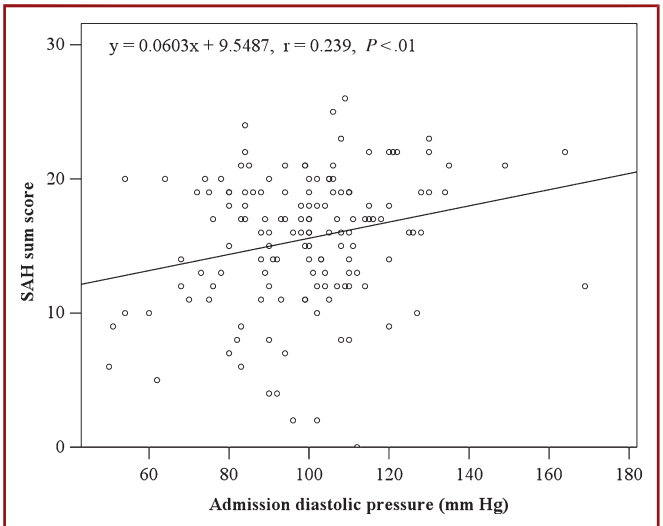

FIGURE 3. *Relation between the diastolic blood pressure on admission and the SAH sum score. SAH, subarachnoid hemorrhage.*

Limitations

There were 21 patients in whom TCD was only performed on one side, so that the I/C mBFV could not be evaluated. If craniotomy has been performed, TCD is easy to do through the burr hole. However, the contralateral side does not have a burr hole and TCD examination becomes difficult.

CONCLUSION

Our study demonstrated that the I/C mBFV can be a reliable predictor of clinically significant/symptomatic vasospasm in patients with aneurysmal SAH compared with the absolute flow velocity. Evaluation of the I/C mBFV and the combination of the I/C mBFV and the absolute flow velocity can improve the diagnostic accuracy of TCD to detect vasospasm, but further studies should be conducted to expand our findings.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENT

The authors present an analysis of the TCD data from patients admitted to their center between July 2003 and August 2009. Specifically, the authors analyzed mean blood flow velocities (mBFVs) in both middle cerebral arteries (MCAs). They calculated the ratio of ipsilateral MCA mBFV (ie, MCA with the highest mBFV) to contralateral MCA mBFV (I/C mBFV). They built ROC curves to compare reliability of the proposed index compared with standard absolute mBFV. They also studied delayed cerebral ischemia (DCI) defined as neurological deficits or CT evidence of cerebral infarction caused by vasospasm. The authors analyzed data from 142 patients and 1262 TCD studies. The study was retrospective. The authors report that the area under the ROC curve was 0.86 (95%CI 0.76-0.96) for I/C mBFV compared with 0.8 (95%CI 0.71-0.88) for absolute mBFV. The threshold that best discriminated was 1.5. The authors also report that the variables associated with DCI were younger age, high diastolic blood pressure recordings, large amount of blood in the suprasellar cisterns, and performance of decompressive craniectomy. The authors concluded that "in patients with aneurysmal SAH, the I/C mBFV shows a closer association with clinically significant vasospasm than the absolute mean flow velocity." This report is interesting. I agree with the authors that better methods or calculations to predict DCI are needed to hopefully improve patient outcome. However, the study has some shortcomings. First, the authors performed a comparison between the proposed I/C mBFV ratio and the absolute mBFV values but did not compared it with other ratios such as the Lindegaard ratio. The latter would be interesting. If their proposed ratio is better than what is being currently used then practitioners will be more inclined to use the proposed measurements. Second, the authors performed analyses of predictors of DCI. However, it is not clear as to whether all patients who met the criteria for DCI underwent cerebral angiography and complete studies to rule out other clinical conditions such as electrolyte imbalances, cardioembolic sources of emboli, and seizures. In addition, the authors report that their patients did not receive calcium-channel blockers but statins. Nimodipine has become the standard the care for patients with SAH. The authors did not explain the reasons for their patients not receiving nimodipine but some receiving statins. The latter has not been clearly demonstrated to be beneficial. Overall the article suggests that calculation of the I/C mBFV may be more useful than the absolute mBFV value.

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