

## Short Communication

# Computational Fluid Dynamics for Predicting Delayed Cerebral Ischemia after Subarachnoid Hemorrhage

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- Computational fluid dynamics
- CT angiography

**Abstract**

**Background and purpose:** Delayed cerebral ischemia (DCI) is a significant cause of morbidity and mortality after aneurysmal subarachnoid hemorrhage (SAH). Recently, we reported the various hemodynamic characteristics of ruptured aneurysm with computational fluid dynamics (CFD). The aim of this study was to assess whether CFD was useful to predict the development of DCI after SAH.

**Materials and methods:** This was a single-center, retrospective, observational study. We investigated 53 consecutive patients with SAH. CFD was analyzed by subtraction 3-dimensional computed tomography angiography performed within 72 hours after onset.

**Results:** Six of 53 patients (11.3%) had DCI. There were no significant differences in age, SAH grades at admission, amount of subarachnoid or intraventricular blood, aneurysm location and treatment modalities (clipping or coiling) between patients with and without DCI. Concerning the CFD analysis, the areas of extracranial ICA and distal parent artery were tended to be smaller (14.1 mm<sup>3</sup> vs 18.0 mm<sup>3</sup>, 3.58 mm<sup>3</sup> vs 4.67 mm<sup>3</sup>, respectively), and the flow velocity in distal parent artery also tended to be higher (0.640 m/s vs 0.469 m/s) in patients with DCI than without DCI, but there were no significant differences.

**Conclusions:** This study first describes the possibility of CFD analysis to predict the subsequent development of DCI after SAH. CFD analysis may be useful to predict the DCI in SAH patients, because it is possible to detect the slight differences described above on CT angiography data obtained at admission.

**ABBREVIATIONS**

SAH: Subarachnoid Hemorrhage; DCI: Delayed Cerebral Ischemia; CFD: Computational Fluid Dynamics; ICA: Internal Carotid Artery; WFNS: The World Federation of Neurosurgical Societies; FV: Flow Velocity

**INTRODUCTION**

Delayed cerebral ischemia (DCI) still remains a major cause of morbidity and mortality after aneurysmal subarachnoid hemorrhage (SAH) [1]. It has been reported that many factors such as early brain injury, cerebral vasospasm, arteriolar constriction, thrombosis and dysfunction in microcirculation or veins, and cortical spreading ischemia may be involved in the development of DCI [2]. Early vasospasm on admission was also

reported to be associated with neurological worsening and poor outcome [3]. In addition, it has been reported that cerebral blood flow reduction in first 3 days after SAH on computed tomography (CT) perfusion was a predictor for the development of DCI [4].

Computational fluid dynamics (CFD) uses patient-specific geometry models to characterize the pathophysiological mechanisms of aneurysm initiation, growth and rupture [5]. Recently, we reported the various hemodynamic characteristics of ruptured aneurysm with CFD [6-8]. However, the relationships between hemodynamics with CFD and development of DCI after SAH have not been investigated. Thus, the aim of this study was to determine whether CFD was useful to predict the development of DCI after SAH.

## MATERIALS AND METHODS

CFD analysis is performed as previously described [8], and briefly as follows. The patient-specific geometries are generated as stereo lithography (STL) (Mimics 16.0; Matelialis Japan, Yokohama, Japan) from preoperative 3-dimensional (3D) CT angiography using Aquilion One (Toshiba Medical System, Otawara, Japan). Vessels with diameters under 1 mm are excluded from analysis (Magics 17.0; Matelialis Japan, Yokohama, Japan), because it is judged that blood vessels with high Reynolds numbers have turbulent or transition flow and are unsuitable for analysis of laminar flow. The STL is remeshed to improve the quality of the surface triangles (3-matic 6.0; Matelialis Japan, Yokohama, Japan). The computational hybrid meshes are generated with tetrahedral and prism elements (ANSYS ICEM CFD16.1; ANSYS, Inc., Canonsburg, PA, USA). Tetrahedral element sizes range from 0.1 to 0.6 mm for the fluid domain. Six prismatic boundary layers with a total thickness of 0.15 mm cover the surface to ensure an accurate definition of the velocity gradient. A straight inlet extension is added to the cervical (C5) segment of the internal carotid artery (ICA) or intradural (V4) segment of vertebral artery to obtain fully developed laminar flow.

For the fluid domain, 3D incompressible laminar flow fields are obtained by solving the continuity and Navier-Stokes equations. Numerical modeling is performed using a commercially available CFD package (ANSYS CFX 16.1; ANSYS, Inc., Canonsburg, PA, USA). Blood is assumed to be an incompressible Newtonian fluid with a blood density of 1056 kg/m<sup>3</sup> and a blood dynamics viscosity of 0.0035 Pas. Because patient-specific flow information was not available, pulsatile boundary conditions are based on the superposition blood-flow waveforms of the common carotid artery as characterized by Doppler ultrasound in normal human subjects for transient analysis. Traction-free boundary conditions are applied at outlets.

Flow in the control CFD is a model with Navier-Stokes equations and the equation of continuity, given by

$$\nabla \cdot \mathbf{v} = \text{div} \cdot \mathbf{v} = 0$$

$$\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} = -\frac{1}{\rho} \nabla p + \frac{\mu}{\rho} \nabla^2 \mathbf{v} + \mathbf{F}$$

Where  $\mathbf{v}$  is the velocity of the flow,  $p$  the pressure,  $\rho$  the density,  $\mu$  the viscosity of the fluid, and  $\mathbf{F}$  is the force.

C1-3 segment, M1 segment, A1 segment, and basilar artery were defined as the parent arteries of aneurysms at the ICA, middle cerebral artery, anterior communicating artery (Figure 1A-C), and basilar artery, respectively [7].

This was a single-center, retrospective, observational study. The subjects of this study were 53 consecutive patients (13 males and 40 females), 26 to 90 years of age (mean 60.0 years) who met the following inclusion criteria: >20 years of age at onset, subtraction 3D CT angiography performed within 72 hours after onset, saccular aneurysm as the cause of SAH confirmed on 3D CT angiography, aneurysmal obliteration by clipping or coiling within 48 hours after admission. Excluded from the study were patients who died within 14 days after onset. The World Federation of Neurosurgical Societies (WFNS) SAH grading scale

at admission included 38 patients of grade I-III and 15 patients (28.3%) of grade IV-V. The ruptured aneurysm location was anterior communicating artery in 11 patients, internal carotid artery in 21, middle cerebral artery in 18, basilar arteries in one, and distal anterior cerebral artery in two.

All patients received intravenous fasudil chloride from one day post-surgery to Day 14 post-hemorrhage. Additional treatment was administered to maintain normovolemia, prevent meningitis, pneumonia and hypoxia, and correct anemia and hypoproteinemia. All patients with DCI were treated with hypertensive hypervolemic therapy. DCI was defined as otherwise unexplained clinical deterioration (i.e., a new focal deficit, decrease in the level of consciousness, or both) or a new infarct on CT that was not visible on admission or immediate postoperative scans, or both. Other potential causes of clinical deterioration, such as hydrocephalus, rebleeding, or seizures, were rigorously excluded [2].

## RESULTS

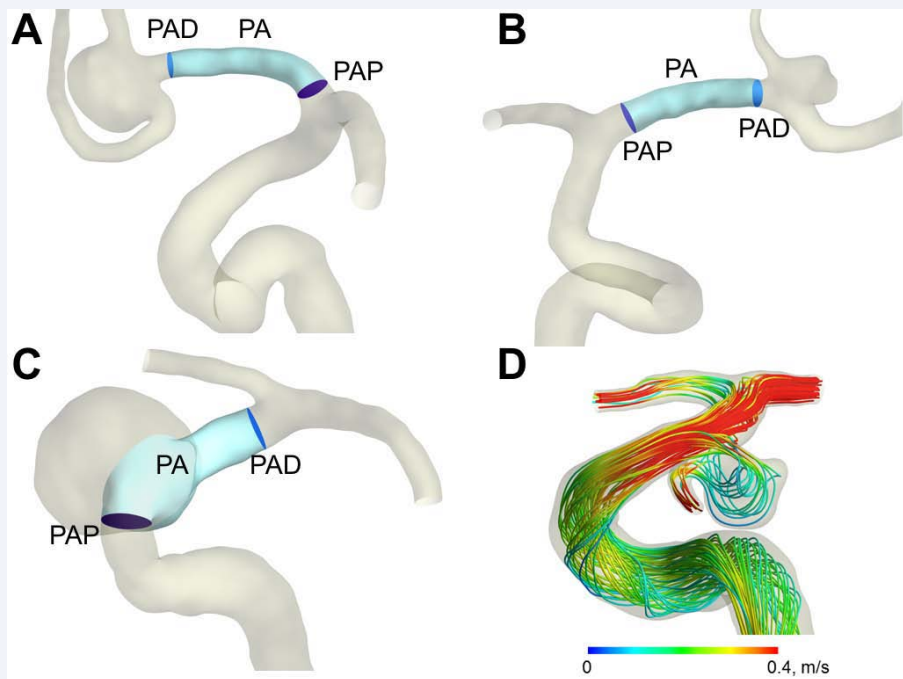
Six of 53 patients (11.3%) had DCI. There were no significant differences in age, WFNS grades at admission, amount of subarachnoid or intraventricular blood, aneurysm location and treatment modalities (clipping or coiling) between patients with and without DCI (Table 1). The areas of extracranial ICA and distal parent artery were tended to be smaller, and the time-averaged flow velocity (FV) in distal parent artery also tended to be higher in patients with DCI than without DCI, but there were no significant differences (Table 2).

## DISCUSSION

CFD holds a prominent position in the patient-specific evaluation of intracranial aneurysms and hemodynamic parameters have shown the correlation with aneurysm initiation, growth and rupture [5]. Recently, we reported hemodynamic characteristics of ruptured aneurysm with CFD: for example, rupture status [6], rupture point [7], and hemostatic patterns [8] were characterized by hemodynamic parameters on CFD analyses. However, to our knowledge, no study has shown the relationships between hemodynamic characteristics obtained with CFD and DCI after SAH.

Early vasospasm on admission and early reduction of cerebral blood flow on CT perfusion were reported to be associated with delayed neurological worsening and poor outcome [3,4]. Similarly, there was the trend that early narrowing of distal parent artery was associated with the subsequent development of DCI in this study. Detection of early vasospasm needs catheter angiography and standardized definition, but the definitions were different among previous trials [3]. Early autoregulatory failure, detected using near-infrared spectroscopy and transcranial Doppler, has also been reported to predict DCI [9]. Using transcranial Doppler is widely accepted in SAH management, but the target vessel is almost limited to MCA, and it is difficult to analyze the FV in ACA and ICA. On the other hand, CFD uses patient-specific geometry models, and thus it is possible to analyze all major cerebral arteries according to the parent artery of each aneurysm.

In this study, the area of extracranial ICA and distal parent artery tended to be smaller and the FV in distal parent artery



**Figure 1** Schematic diagram of defining parent arteries of anterior communicating artery (A), middle cerebral artery (B), and internal carotid artery (C) aneurysms. Flow velocity (D) is visualized as the three-dimensional stream lines.  
Abbreviations: PA: Parent Artery; PAP: Proximal Parent Artery; PAD: Distal Parent Artery

**Table 1:** Baseline distribution of variables in the DCI and non-DCI groups.

	DCI (n=6)	Non-DCI (n=47)	Total
Mean age, years	59.7 ± 13.4	67.0 ± 15.5	66.2 ± 15.3
Sex			
Female, n	5 (83.3)	35 (74.5)	40 (75.5)
Fisher CT group			
1	0(0.0)	1(2.1)	1(1.9)
2	1(16.7)	18(38.3)	19(35.8)
3	4(66.7)	23(48.9)	27(50.9)
4	1(16.7)	5(10.6)	6(11.3)
World Federation of Neurosurgical Societies grade			
	2(33.3)	20(42.6)	22(41.5)
	3(50.0)	6(12.8)	9(17.0)
	0(0.0)	7(14.9)	7(13.2)
	1(16.7)	9(19.1)	10(18.9)
	0(0.0)	5(10.6)	5(9.4)
Aneurysm obliteration			
Clipping	4(66.7)	45(95.7)	49(92.5)
Coiling	2(33.3)	2(4.3)	4(7.5)
Aneurysm location			
ICA	3(50.0)	18 (38.3)	21(39.6)
Acom	0(0.0)	11 (23.4)	11(20.8)
Distal ACA	0(0.0)	2 (4.3)	2(3.8)
MCA	2(33.3)	16 (34.0)	18(34.0)
BA	1(16.7)	0 (0.0)	1(1.9)

**Abbreviations:** DCI: Delayed Cerebral Ischemia; ICA: Internal Carotid Artery; Acom: Anterior Communicating Artery; ACA: Anterior Cerebral Artery; MCA: Middle Cerebral Artery; BA: Basilar Artery  
Values in parentheses denote percentages; ± represents standard deviation.

**Table 2:** Morphological and hemodynamic parameters of parent artery in the DCI and non-DCI groups.

	DCI (n=6)	Non-DCI (n=47)	P value
Area@ICA (mm <sup>3</sup> )	14.1(9.32-16.4)	18.0 (14.1-21.1)	0.0852
Area@PAP (mm <sup>3</sup> )	5.05 (3.68-7.31)	5.75 (4.09-8.41)	0.535
Area@PAD (mm <sup>3</sup> )	3.58 (3.03-4.24)	4.67(2.87-7.02)	0.237
FV@ICA (m/s)	0.228 (0.184-0.245)	0.257 (0.227-0.284)	0.081
FV@PAP (m/s)	0.371 (0.368-0.50)	0.354 (0.230-0.531)	0.615
FV@FPA (m/s)	0.514 (0.446-0.514)	0.467 (0.265-0.593)	0.475
FV@PAD (m/s)	0.640 (0.511-0.888)	0.469 (0.308-0.672)	0.194

**Abbreviations:** DCI: Delayed Cerebral Ischemia; ICA: Extracranial Internal Carotid Artery; PAP: Proximal Parent Artery; PAD: Distal Parent Artery; FV: Flow Velocity; FPA: Fluid-Domain Parent Artery  
Data, median (interquartile range)  
P value, Mann-Whitney U tes

tended to be higher in patients with subsequent DCI, although extracranial ICA was thought to be hardly affected by SAH directly. The FV in the proximal part of the ICA may be diminished because of narrowing of the distal part of the ICA [10]. Similarly, narrowing of extracranial ICA may be due to the narrowing of distal parent artery. However, it is important to assess the effect of increased intracranial pressure by SAH in the future study. Furthermore, it will give useful information to detect DCI by clarifying hemodynamic characteristics of the other vessels, such as intra- and extracranial vertebral artery or posterior cerebral artery, with CFD analysis.

## CONCLUSION

This study first describes the possibility of CFD analysis to predict the subsequent development of DCI after SAH. CFD analysis may be useful to predict the DCI in SAH patients, because it is possible to detect the slight differences described above on CT angiography data obtained at admission. Lastly, larger studies are needed to confirm the usefulness of this new technique.

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