Article published online: 2023-12-15

Predicting Morphological Changes to Vessel Walls Adjacent to Unruptured Cerebral Aneurysms Using Computational Fluid Dynamics

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Asian J Neurosurg 2023;18:764–768.

Abstract

Objective This study compared intraoperative findings with preoperative computed tomography angiography (CTA) and computational fluid dynamics (CFD) analysis of perianeurysmal findings for the indication of possible vessel wall thinning.

Materials and Methods Participants comprised 38 patients with unruptured middle cerebral artery aneurysms treated by surgical clipping at our hospital between May 2020 and April 2021. We defined parent artery radiation sign (PARS) as the presence of each of the following three findings in CFD analysis based on preoperative CTA: (1) impingement of the stream line on the outer parent vessel wall of the aneurysm; (2) radiation of wall shear stress vectors outwards from the same site; and (3) increased wall pressure compared with the surrounding area. CFD analysis showing PARS was compared with intraoperative findings.

Results In all nine cases with PARS, no morphological abnormalities were found in the same area on CTA. However, intraoperative findings showed thinning of the parent artery wall in one of the nine cases and formation of a very small mass in three cases, differing from CTA findings. All nine patients underwent additional clipping and/or wrapping and coating at the site of PARS.

Conclusion Detecting thinning of the vessel wall or the presence of a microaneurysm may be difficult in endovascular therapy, which is based on the visualization of the vessel lumen. CFD analysis suggests the necessity of confirming findings for the vessel wall around an aneurysm by direct manipulation, as the presence of PARS may indicate partial thinning of the vessel wall or formation of a microaneurysm.

Keywords
- computational fluid dynamics
- middle cerebral artery
- morphological change
- unruptured intracranial aneurysm

article published online
December 15, 2023

DOI https://doi.org/10.1055/s-0043-1771367.
ISSN 2248-9614.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

In the treatment of unruptured cerebral aneurysms, catheterization (such as with the use of coil embolization and flow diverters) has recently been gaining popularity over conventional surgical clipping.[1,2] In addition, computational fluid dynamics (CFD) analysis can evaluate the outer wall of a vessel both morphologically and hydrodynamically, allowing visualization of where pressure can be expected to increase on vessel and aneurysm walls, and how wall shear stress will be applied.[3,4]

Several studies have reported that CFD analysis of the outer walls of vessels around unruptured cerebral aneurysms enables preoperative blood flow evaluation and is useful for determining treatment strategies.[4]

When unruptured cerebral aneurysms are treated by surgical clipping at our hospital, some cases are encountered in which, counter to predictions made based on preoperative imaging, minimal aneurysm formation and wall thinning are observed in the parent artery outside the aneurysm.

The presence of a bleb is said to increase the risk of rupture in unruptured cerebral aneurysms.[5] Treatment of the area is therefore considered more important when a brevis is present. If a small morphological change, such as a microaneurysm, is identifiable in the parent artery adjacent to the cerebral aneurysm, the need for treatment of that part of the aneurysm is likewise elevated. This study was conducted to investigate whether CFD analysis can be used to predict micromorphological changes in the parent artery adjacent to an unruptured cerebral aneurysm.

We compared intraoperative findings with results of CFD analysis using preoperative computed tomography angiography (CTA) to investigate potential predictors of morphological changes in vessels outside the aneurysm.

Materials and Methods

Participants in this study comprised of 38 patients with unruptured middle cerebral artery (MCA) aneurysms treated by craniotomy between May 2020 and April 2021. In the CFD analysis based on preoperative CTA, parent artery radiation sign (PARS) was defined as the presence of each of the following three findings: (1) collision of the stream line with the outer parent vessel wall of the aneurysm; (2) radiation outwards from the wall of shear stress vectors from the same site; and (3) increased wall pressure compared with the surrounding region. CTA images were taken using a 320-row camera (Aquilion ONE; Canon, Tokyo, Japan). CTA images were processed using a Ziostation2 image-processing workstation (Ziosoft, Tokyo, Japan) to extract blood vessels around the mass, and CFD images were created with hemoscope Project Manager 2015 (EBM/AMIN, Tokyo, Japan). Magnetic resonance imaging (MRI) could also be used to assess vascular structures, but as CTA was performed preoperatively in all patients at our institution and MRI was performed only in some cases, CTA images were used for analysis in this study. The range of wall pressures was adjusted to within the range of 0.17 to 0.60 mm Hg so that the pressure change would be around the aneurysms. Stream lines were delineated using the cross-sections of blood vessels proximal to the aneurysms. The consent of patients for presentation of their case details was obtained and the study was approved by the hospital ethics committee.

Results

The participants (11 men, 27 women) had a mean age of 67.1 years (range, 44–83 years), and mean size of the mass was 5.6 mm (range, 3–10 mm). None of the patients had fibromuscular dysplasia, Ehlers-Danlos syndrome, polycystic kidney, or other predisposing factors. Nine patients showed PARS, and CTA did not show any morphological abnormalities in the same areas. However, intraoperative findings showed thinning of the parent artery wall in one of the nine cases and formation of a very small mass in three cases, differing from the CTA findings. Additional treatments such as clipping or encapsulation were required in these cases. In the remaining five cases, intraoperative findings suggested that the area considered as parent vessel wall on preoperative CTA was actually part of the aneurysmal wall. Case details are summarized in ►**Table 1**. Some representative cases are described below.

Table 1 Nine cases showing parent artery radiation sign

Case	Age (y)	Sex	Aneurysm size (mm)	Morphological change	Additional treatments
1	43	Male	9	Microaneurysm	Clipping + coating
2	77	Female	4	Microaneurysm	Clipping + coating
3	70	Female	7	Microaneurysm	Clipping + coating
4	71	Female	4	Wall thinning	Clipping + coating
5	74	Male	6	Including aneurysm	Clipping + coating
6	74	Female	3	Including aneurysm	Clipping + coating
7	72	Female	5	Including aneurysm	Coating
8	63	Female	5	Including aneurysm	Clipping + coating
9	68	Female	4	Including aneurysm	Clipping + coating

Case 1: A 44-Year-Old Man with Right MCA

Preoperative CTA showed a saccular aneurysm at the bifurcation of the MCA, but CFD showed PARS adjacent to the aneurysm (►**Fig. 1A–C**). Intraoperative imaging revealed formation of a very small aneurysm in the area between the aneurysm and bifurcating vessel consistent with PARS (►**Fig. 1D**), and additional clipping was performed.

Case 4: A 71-Year-Old Woman with Left MCA

Preoperative CTA images showed a saccular aneurysm at the bifurcation of the MCA, but CFD showed PARS adjacent to the aneurysm (►**Fig. 2A–C**). Intraoperative imaging revealed a red area suggestive of vessel wall thinning in a portion of the parent artery coincident with the PARS (►**Fig. 2D**). Additional clipping and coating were performed.

Case 5: A 74-Year-Old Man with Left MCA

Preoperative imaging showed a wide-necked saccular aneurysm at the bifurcation of the MCA, but CFD showed PARS at the M2 bifurcation (►**Fig. 3A–C**). On intraoperative imaging, the area coinciding with the PARS was actually part of the aneurysm wall (►**Fig. 3D**).

The aneurysm was red, suggestive of thinning, and required multiple clipping and coating procedures.

Discussion

CFD analysis extracts the vascular surface structure from CTA and digital subtraction angiography (DSA) images, constructs a three-dimensional structure, and analyzes how mechanical loads are applied to the three-dimensional structure using virtual fluid.[4]

Accurate depiction of the vascular surface structure is important and in the case of aneurysms that occur at the bifurcation of small arteries, these small arteries are poorly depicted during analysis, making correct analysis difficult.[4,6] In addition, observation of aneurysms from all directions is difficult for aneurysms located deep in the skull.[7] As a result, this study limited analysis to unruptured aneurysms of the MCA. The large number of female patients is roughly in line with the male-to-female ratio of cerebral aneurysms, which is approximately 1:2.[8]

We limited our analysis in this investigation to unruptured aneurysms of the MCA, and defined PARS as the presence of all three of the following findings: 1) impingement of stream lines on the wall of the outer parent vessel wall of the aneurysm; 2) radiation of wall shear stress vectors outward from the same region; and 3) increased wall pressure compared with the surrounding region. Although several reports have described findings predictive of wall irregularity in aneurysms, this is the first study to focus on vessels outside the aneurysm.[4]

In addition, morphological changes in the parent artery can be predicted by CFD analysis in the presence of PARS, but could not be predicted using preoperative CTA alone. This finding may be very useful in formulating treatment strategies for unruptured cerebral aneurysms in the future. In general, bloodstreams collide at vascular bifurcations. The occurrence of cerebral aneurysm is considered to be one of the subsequent changes. In this study, morphological changes were thought to

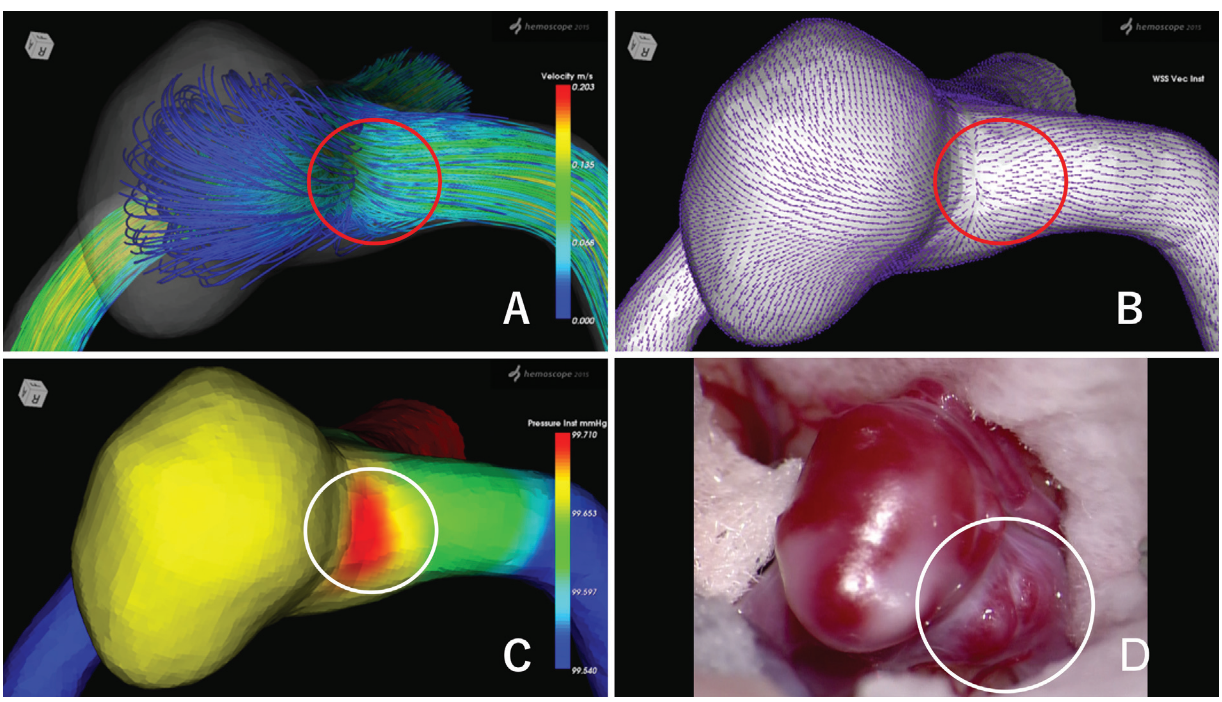

Fig. 1 Computational fluid dynamic images and intraoperative view in Case 1, showing collision of the stream line (**A**) with the extra-aneurysmal parental vessel wall, radial spread of wall shear stress vectors (**B**), and (**C**) partial increase in wall pressure adjacent to the aneurysm within the encircled area. The intraoperative view (**D**) shows a microaneurysm (*circle*) adjacent to the aneurysm.

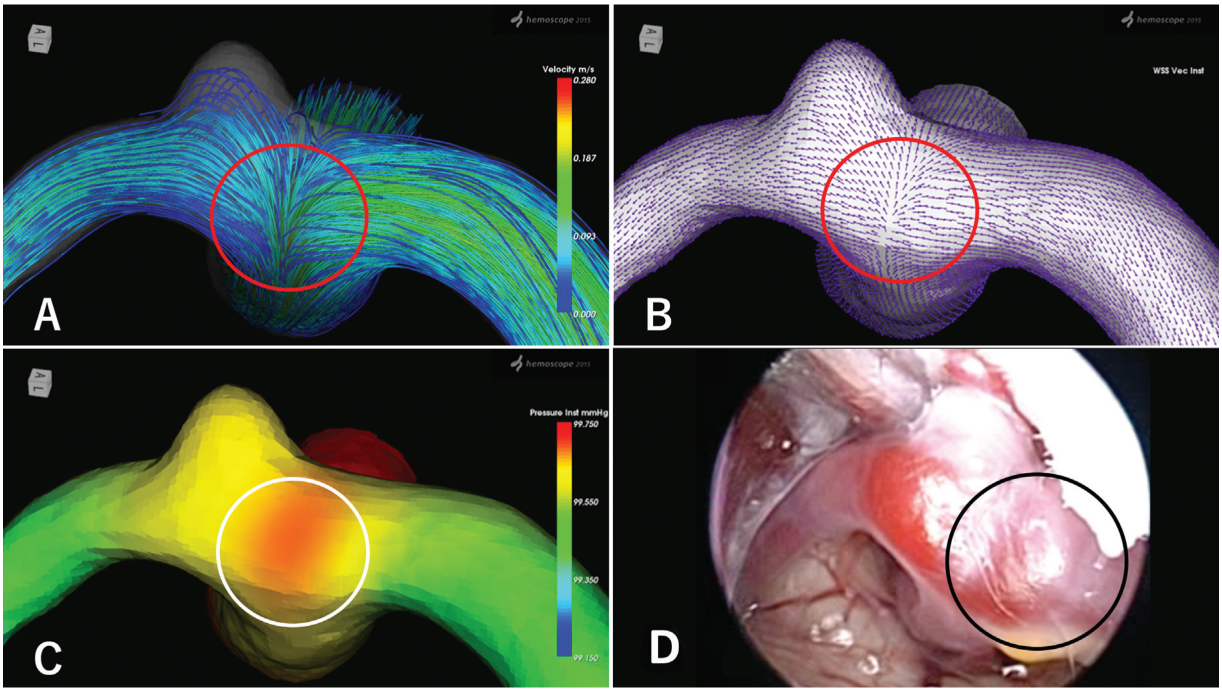

Fig. 2 Computational fluid dynamic images and intraoperative view in Case 4, showing the collision of the stream line (**A**) with the extra-aneurysmal parental vessel wall, radial spread of wall shear stress vectors (**B**), and (**C**) a partial increase in wall pressure adjacent to the aneurysm within the encircled area. Intraoperative view from the endoscope (**D**) shows thinning of the vessel wall (*circle*) adjacent to the aneurysm.

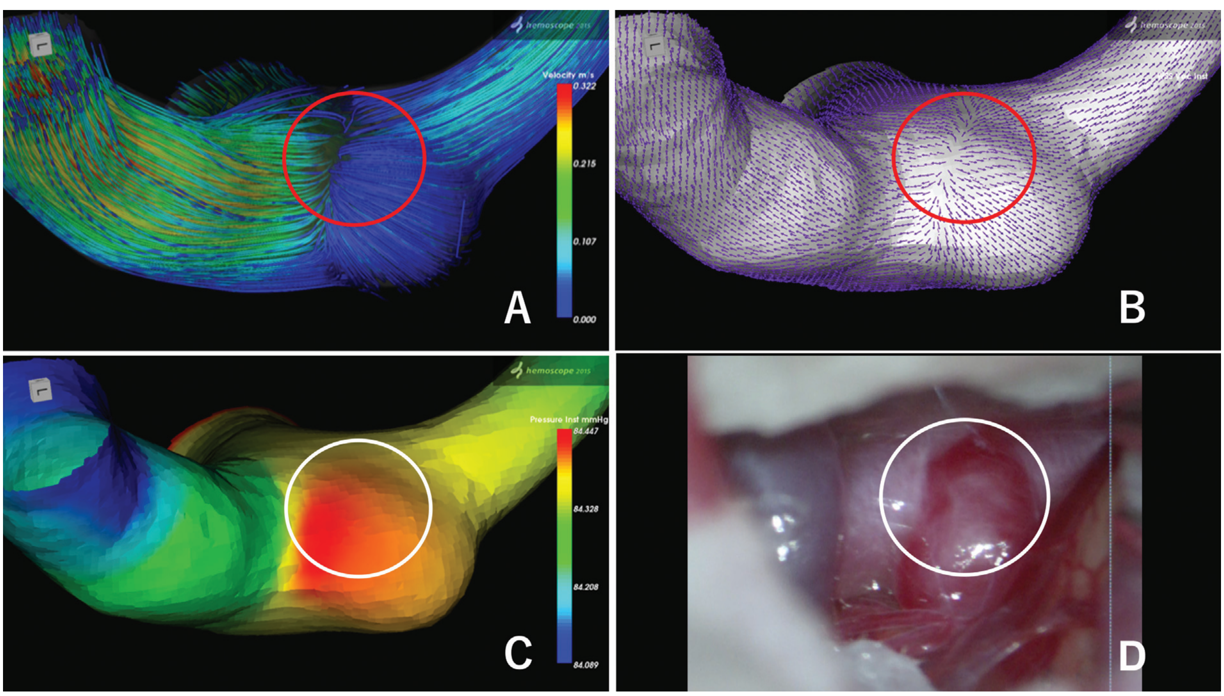

Fig. 3 Computational fluid dynamic images and intraoperative view in Case 5, showing collision of the stream line (**A**) with the extra-aneurysmal parental vessel wall, radial spread of wall shear stress vectors (**B**), and (**C**) a partial increase in wall pressure adjacent to the aneurysm within the encircled area. The intraoperative view (**D**) shows the region in which parent artery radiation sign (*circle*) is part of the aneurysm wall.

be caused by the impingement of fast-flowing blood on part of the parent artery, which was not within the aneurysm, and by the application of a large force to that part.

The fact that wall shear stress is applied in the direction of stretch for the vessel wall can be visualized by the presence or absence of vector dispersion, but in PARS, the only form of vector dispersion is radiating outward, distributed in all directions from a single point.

The lack of specific findings for wall shear stress pressure may be due to the fact that this parameter varies greatly with CTA absorption, and/or the range of window width and level values.

Recent studies have shown that fluctuating mechanical energy, that is, instability of blood flow, correlates positively with increases in the size of unruptured cerebral aneurysms by CFD analysis.[9]

In this investigation, the presence of PARS and morphological abnormalities outside the aneurysm may have been due to the fact that aneurysm formation caused changes in blood flow, and the area where pressure was concentrated in the parent artery outside the aneurysm, such as PARS, moved. Morphological changes again may have arisen in that PARS area, and the intraoperative findings were observed at that time. This may have been showing the process of aneurysm formation with multiple blebs or a giant aneurysm.

Another limitation of this study was that DSA was not performed before craniotomy for unruptured aneurysms at our institution, and we cannot rule out the possibility that DSA may have revealed micromorphological changes in the vessel wall. In any case, even external surface changes (including those of very small aneurysms) were slight, and endovascular treatment may not have detected wall thinning as an abnormal finding, making intervention difficult.

For aneurysms occurring in the anterior communicating artery or at the bifurcation of the internal carotid and posterior communicating arteries, which are known as sites prone to showing unruptured cerebral aneurysms and rupture, accurate depiction of vessels and evaluation of blood flow using CFD may be difficult. However, this situation may be improved by radiologists and evolving image-editing techniques.

For lesions in deep cranial regions where visibility is poor, confirming the same region with the naked eye may be difficult depending on the angle, even if PARS is observed on preoperative analysis. However, use of an endoscope may help obtain a deeper view.[7]

The findings of this study should be considered in light of some limitations. First, the number of PARS-positive cases was not large (9 cases), and morphological changes could not be ruled out among PARS-negative cases. However, morphological changes were observed in all nine PARS-positive cases. None of the negative cases showed the formation of any mass within the observable range. While the sensitivity is debatable, the specificity seems very high. Second, thinning was subjective and not quantitatively evaluated by the authors. Thinning is difficult to evaluate at our institution at this time because of the invasiveness and equipment required. This is an area for improvement in future studies. Third, the overall number of cases was not large, and insufficient for valid statistical evaluations. Fourth, this study used CFD analysis, which may have inductive and other biases because hemodynamics are assessed based on a simplified vascular structure. However, the utility of this method has been demonstrated in many papers, and we consider the influence of potential biases would have been minimal in this study. Another limitation of this study was that only Japanese subjects were included. These points need to be addressed with the accumulation of more cases, and additional studies in the future are desirable.

Conclusion

Detecting thinning of the vessel wall and the presence of very small aneurysms may be difficult in endovascular treatment, which is performed by visualizing the vessel lumen. Preoperative CFD analysis suggests that the presence of PARS may indicate partial thinning of the vessel wall outside the aneurysm or the formation of a microaneurysm, and that confirmation of findings for the vessel wall around the aneurysm by direct manipulation is necessary.

Authors' Contributions
K.S. helped in conceptualization, data curation, formal analysis, investigation, methodology, resources, validation, visualization, and writing—original draft. F.K. contributed to methodology, and writing—review and editing. K.M. helped in investigation. R.T. and Y.Y. were involved in methodology and investigation. Y.K. helped in resources and supervision. Y.H. helped in project administration.

Conflict of Interest
None declared.

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