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Hemodynamic Features of Unruptured Cerebral Aneurysms before Rupture: A CFD Study

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Abstract

Objective: This study was designed to identify hemodynamic features of aneurysms prior to rupture in comparison with unruptured aneurysms. Materials and Methods: A retrospective data of four large unruptured aneurysms (pre-ruptured group) with sufficient films just pre-rupture was used. Matched with the same location and similar sizes, another four unruptured aneurysms (unruptured group) were in accordance with controls during the same time period and flow simulations were performed for hemodynamic analysis. Results: Compared with the unruptured group, the pre-ruptured group had significantly more irregular aneurysm shape, higher aspect ratio and lower aneurysm-averaged wall shear stress (p = 0.031, p = 0.039 and p = 0.042, respectively). Although pre-ruptured aneurysms had lower low wall shear stress (WSS) area and higher oscillatory shear index value, there was no significant difference between groups. Conclusions: Irregular shape, higher aspect ratio and low wall shear stress were relative with unruptured ICA aneurysms in predicting rupture. Those patients with these risk factors should be more prone to treatment even if with an unruptured aneurysm.

Keywords

Aneurysm, Hemodynamic, Morphological, Computational Fluid Dynamics

1. Introduction

Although unruptured cerebral aneurysms carry a relatively low risk of rupture, preventive interventions are

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commonly considered because of the poor prognosis of intracranial hemorrhage. Current treatments of cerebral aneurysms carry a small but significant risk that can exceed the natural risk of aneurysm rupture, making the development of methods to better define the rupture risk of cerebral aneurysms very valuable for clinicians [1] [2]. Computational fluid dynamics (CFD) have been widely used in pursuing hemodynamic parameters that can stratify rupture status of cerebral aneurysms [3]-[5]. However, the published reports controversial for both high and low WSS show to be relative with aneurysm rupture risk. To reveal the relationship between rupture risk and hemodynamic factors, it is important to demonstrate the hemodynamic features of cerebral aneurysms just before their rupture. These studies have been limited to a small number of aneurysms, which has prevented the establishment of statistical associations between hemodynamic characteristics and aneurysm rupture [6] [7]. So far, the purpose of this study was to statistically confirm previous trends relating qualitative hemodynamic characteristics and aneurysm rupture by using image-based CFD analysis.

2. Methods

2.1. Patient Selection

This study was performed after an approval of the Ethics Committee of the Affiliated Hospital of Luzhou Medical College. A retrospective data from January 2013 to December 2014 were reviewed in all the clinical records and image films of our hospital. Four patients had sufficient 3D digital subtraction angiography (3D-DSA) just several days before rupture. Followed by, all of the four patients who undertook subarachnoid hemorrhage several days after DSA (Table 1), were cohorted into the pre-ruptured group. In this study, aneurysm size was categorized based on the International Study of Unruptured Intracranial Aneurysms (ISUIA) criteria (small, <10 mm; large, 10 - 25 mm; giant, >25 mm). Controls, which presented without SAH history, were selected as the unruptured group during the same time period. The included criteria of unruptured group were: 1) Cerebral aneurysms were in the same location and with the similar size (10 mm - 25 mm); 2) The DSA films of the cerebral aneurysm were sufficient for CFD; 3) The cerebral aneurysms diagnosed as dissecting aneurysms were excluded. During that period, a total of 386 patients with 439 aneurysms were admitted. Of them, four patients showed large ICA aneurysms (ophthalmic and communicating segments). According to the criteria above, four large unruptured ICA aneurysms were finally included as the unruptured group.

All the clinical records and aneurysm morphological features were included as follows (Table 1): Age, sex, hypertension, aneurysm size, aneurysm shape, size ratio (SR) and aspect ratio (AR) were collected [8] [9]. In this study, the aneurysm shape was divided into regular and irregular. Aneurysm shape was classified either as regular or irregular. Irregular aneurysms were defined as aneurysms with multiple irregularities due to bleb formations. The classification of internal carotid artery (ICA) segments was according to Bouthillier classification, that is, C6, ophthalmic; C7, communicating [10].

2.2. Image Reconstruction and CFD Modeling

The 3D images were firstly segmented the using standard proprietary software and saved the segmented surface

Table 1. Baseline characteristics of 8 patients between groups.

No.	Ag	Presenting symptoms	HTN	MD	Location	SR	AR	Shape	TI
Pre-ruptured case 1	64	Severe headache	No	13.8	Lt C7	2.65	1.50	Irregular	5 days
Pre-ruptured case 2	57	Headache	No	15.9	Lt C6	4.17	2.69	Irregular	2 days
Pre-ruptured case 3	62	Severe dizziness	No	19.3	Lt C7	4.46	1.89	Irregular	3 days
Pre-ruptured case 4	58	Health examination	Yes	13.6	Lt C6	3.61	1.39	Irregular	2 days
Unruptured case 1	68	Trauma	No	15.8	Lt C6	2.17	1.76	Regular	4 months
Unruptured case 2	63	Health examination	Yes	13.7	Lt C7	3.64	1.42	Regular	4 months
Unruptured case 3	54	Health examination	No	12.6	Rt C6	3.52	1.79	Regular	6 months
Unruptured case 4	57	Mild dizziness	No	11.3	Lt C7	3.23	1.31	Regular	5 months

HTN = hypertension, Lt = left, Rt = right, SR = size ratio, AR = aspect ratio, MD = maximum diameter (mm), TI = time interval.

geometry into a standard tessellation language (STL) format. Prior to meshing, the aneurysm model was subdivided into the aneurysm sac and the parent artery regions. Each model was imported into the ICEM CFD (ANSYS Inc., Canonsburg, Pa., USA) to create around 1 million finite volume tetrahedral element grids with 4 layers of prism elements for accurate calculation of WSS [1] [11] [12].

ANSYS CFX 14.0 (ANSYS Inc., Canonsburg, Pa., USA) was then used to solve the flow governing Navier-Strokes equations, incompressible and Newtonian blood flow. The density and dynamic viscosity of blood were specified as 1060 kg/m^3 and 0.004 N s/m^2, respectively. The blood vessel wall was assumed to be rigid with no-slip boundary conditions. A pulsatile velocity profile is obtained by Transcranial. A traction-free boundary condition was applied to the outlets. The initial pressure and velocity were set to zero. 800 time steps (0.001 s/step) were set for each cardiac cycle. Two cardiac cycles were simulated for numerical stability. Results from the second cardiac cycle were collected as output for hemodynamics post-processing.

2.3. Hemodynamics Analysis

Hemodynamic parameters, including time-averaged WSS (TAWSS), oscillatory shear index (OSI) and low WSS area (LSA), were calculated based on the simulated pulsatile flow simulations. In this study, TAWSS distributions were normalized by the parent artery averaged TAWSS in the same patient to allow comparison among different cases. LSA was defined as the area of the aneurysm wall exposed to a TAWSS below the threshold that was 10% of parent artery TAWSS and then normalized by the aneurysm sac area. For quantitative comparison, TAWSS and OSI were further averaged over the aneurysm sac.

2.4. Statistical Analysis

SPSS 17.0 software was used for statistical analysis (SPSS, Chicago, Illinois). For continuous parameters, the Mann-Whitney test was performed. Fisher's exact test was used appropriately for categorical parameters. α = 0.05 was set as test level.

3. Results

3.1. Clinical Records and Aneurysm Features

The average age of this study was 60.3 years. Of which, female was occupied 5 persons, and the remained 3 persons were males. The symptoms at admission included headache, dizziness, trauma, and health examination. The specific clinical records and aneurysm features were summarized in **Table 1**. After the statistical analysis, there were no significant differences in all clinical records, size and size ratio between groups (**Table 2**). However, the aspect ratio and shape were significant between groups (**Table 2**). The difference of AR and shape were statistically significant between groups (p = 0.039 and p = 0.000). All of the pre-ruptured Cerebral aneurysms (100%) were irregular with daughter blebs. On the contrary, all the aneurysms in unruptured group were regular interestingly.

Table 2. Patient demographics and aneurysms morphology in pre-ruptured and unruptured aneurysms.

	Pre-ruptured group (n = 4)	Unruptured group (n = 4)	p value*
Mean age ±SD, y	60.2 ±5.4	60.5 ±6.4	0.982
Male sex, n (%)	1/4	2/4	0.873
Hypertension, n (%)	3/4	2/4	0.658
Maximum size ±SD, mm	15.7 ±4.3	13.4 ±3.1	0.334
Size ratio (SR)	3.7 ±1.2	3.2 ±0.9	0.417
Aspect ratio (AR)	1.8 ±0.7	1.5 ±0.3	0.039
Irregular shape, n (%)	4/4	0/4	0.000

*Mann-Whitney test or Fisher's exact test as appropriate.

3.2. Hemodynamic Characteristics

TAWSS distributions were showed in **Figure 1**. In pre-ruptured group, TAWSS was lower within the aneurysm sac compared with that in the parent arteries. However, the TAWSS was comparable between groups. In addition, a lower WSS magnitudes was found in the pre-ruptured group.

Hemodynamic parameters between groups were shown in **Table 3**. Aneurysm-averaged TAWSS in the pre-ruptured group was significantly lower than that in the unruptured group using the Mann-Whitney test (p = 0.048). However, the value of LSA in the pre-ruptured group was larger than that in the unruptured group with no significance (p = 0.085). Similarly, aneurysm-averaged OSI in pre-ruptured group was higher than that in unruptured group with no significance (p = 1.000).
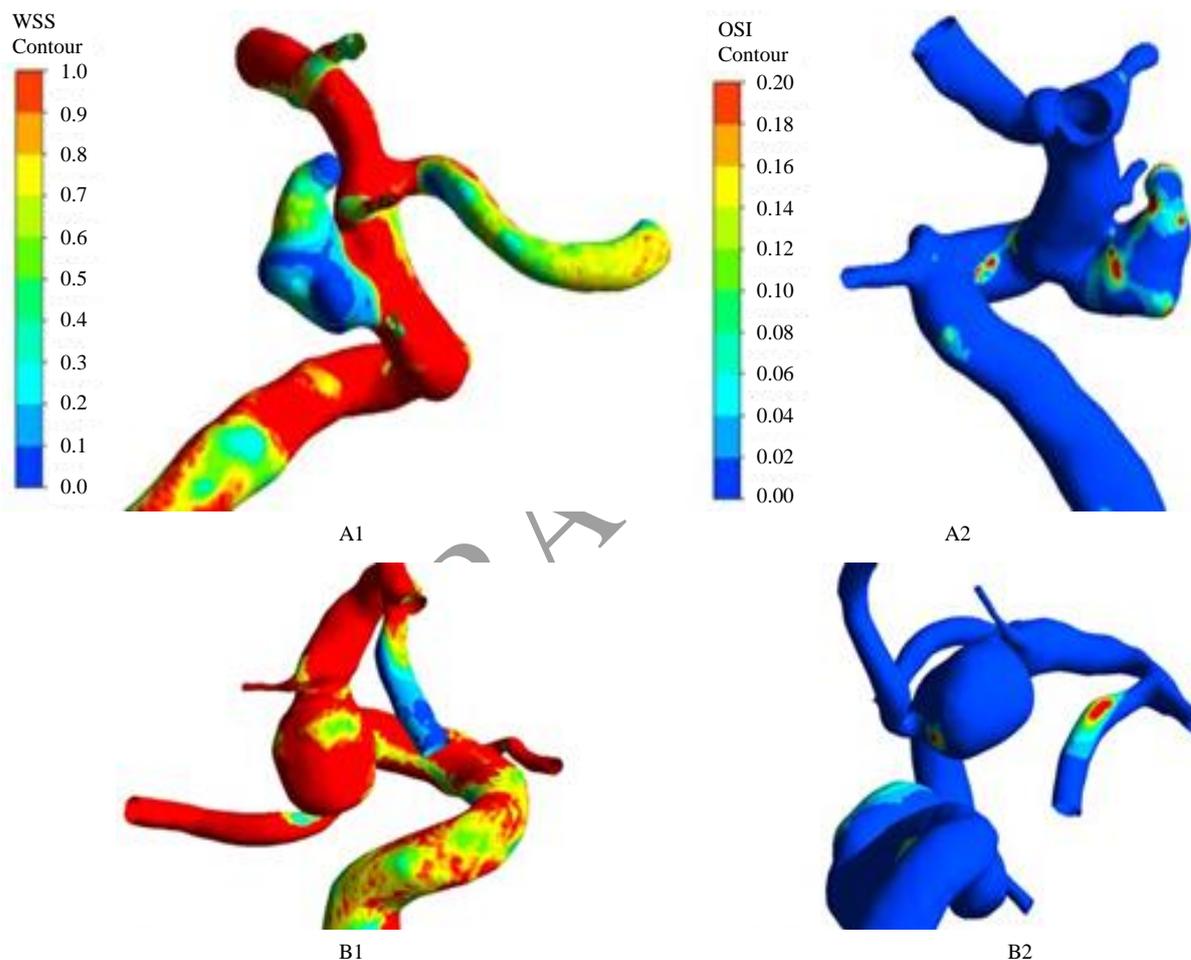
Figure 1. Hemodynamic characteristics of 2 representative PCoA aneurysms. (A1) (A2) Ruptured aneurysms; (B1) (B2) Unruptured aneurysms. (1) WSS; (2) OSI; The figure legends showed that ruptured aneurysms have irregular shape, lower WSS, higher OSI.

Table 3. Univariate analysis of hemodynamic parameters between groups.

Parameters	Pre-ruptured group (n = 4)	Unruptured group (n = 4)	p value[*]
TAWSS	0.30 ±0.06	0.48 ±0.13	0.048
LSA	12.39 ±4.63	6.28 ±5.16	0.085
OSI	0.05 ±0.04	0.04 ±0.03	1.000

[*]LSA, low wall shear stress area; OSI, oscillatory shear index; TAWSS, time-averaged wall shear stress.

4. Discussion

The pathophysiology of cerebral aneurysms is complex and poorly understood. Current theories implicate genetic factors, perianeurysmal environment, and vascular wall biology in combination with hemodynamics as the determinants of whether aneurysms will progress and ultimately rupture [13] [14]. Although hemodynamics is widely considered important in the process, there is no consensus on whether regions of low or high flow are the most critical in promoting the events responsible for rupture.

There are few studies reported the multiple pre-ruptured aneurysms in hemodynamics. Pereira *et al.* [5] performed a case-control study to evaluate the use of computed hemodynamics to detect which cerebral aneurysms were prone to rupture. According to their 4 small cerebral aneurysms, the WSS-derived parameters were lower than that in control cohorts. However, there was no significant difference between groups. Takao *et al.* [15] performed a similar research, and showed that significant difference was found between ruptured and unruptured with the minimum WSS However, all their cases were 5 - 10 mm in size, which prone to basis. Recently, Duan *et al.* [16] published their matched case-control study, which included six patients with posterior communicating artery aneurysms that eventually ruptured within 7 days. Compared with the controls, the lower WSS was significantly related with posterior communicating artery aneurysms rupture. The mean aneurysm size was small and it was not clear whether the cases were rebleeding or not. In our study, these four cases also had the short time interval between 3D angiography and rupture. After the CFD simulation, we found that the aneurysm-averaged TAWSS was significantly lower in these rare cases than that in the controls. Our results were consistent with those previous studies. After analyzing all large aneurysms from a single ICA location, we further supported that lower WSS was found to be associated with pre-ruptured aneurysms.

Currently WSS were controversial in predicting aneurysm rupture status. Meng *et al.* [4] proposed a new concept that both low and high WSS could drive cerebral aneurysms growth and rupture via different biologic mechanisms. In our unruptured group, the aneurysms showed relatively high WSS. Although the control cases had maintained stable over at least 3 months, the time intervals were still short. Leaving untreated, we are not sure whether these aneurysms will undergo growth or rupture in the future.

Morphological features of aneurysms were effective and reproducible to treatment decision [17]. Irregular shape or blebs were strongly suggested to treatment, even for those unruptured aneurysms. Some previous reports and our results were also in favor of that. Irregular shape was showed more prone to rupture, in addition, more complex flow pattern and larger low WSS areas could be found commonly in aneurysms with irregular shape. Aneurysm size remained conflicting with rupture risk. Cebral *et al.* [18] reported a series of 62 aneurysms in which CFD analysis was performed on patient-specific models and CFD findings were correlated with a clinical history of prior rupture. They found that unruptured aneurysms more commonly had simple stable flow patterns, large impingement regions, and large jet sizes, while ruptured aneurysms had disturbed flow patterns, small impingement regions, and narrow jets. Of these characteristics, only impingement size reached statistical significance, possibly due to the small sample size. However, impingement size did not reach statistical significance in our study, may be due to lagerer sample size in our cases. According to the ISUIA of rupture risk in aneurysm size, the rupture risk was 0.05%/y in aneurysms <10 mm in diameter and 1%/y for those with aneurysms ≥10 mm in diameter [10].

The demographic factors, such as age, sex, and hypertension, should be also taken into consideration before treatment decision. Peng *et al.* [19] reported a series of 664 cases of rupture aneurysm, showed that demographic factors, such as age, gender, and hypertension were all with no significant difference in predicting aneurysm rupture. However, A meta-analysis showed these factors had a significant association with an rupture risk of aneurysm, *i.e.*, patients older than 60, female, and Japanese or Finnish descent were prone to aneurysm rupture [10] [12].

There are several limitations to the present study, including the retrospective nature, the sample of patients, and the limited follow up duration, and the lack of logistic analysis of factors. Nevertheless, due to the fact that this study was designed to identify hemodynamic features of aneurysms prior to rupture in comparison with unruptured aneurysms, the results of this study may serve as a reference for such aneurysms and provide the basis for future studies.

5. Conclusion

Irregular shape, higher aspect ratio and low wall shear stress were relative with unruptured ICA aneurysms in

predicting rupture. Those patients with these risk factors should be more prone to treatment even if with an unruptured aneurysm.

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