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Hemodynamic Alterations after Stent Implantation in 15 Cases of Intracranial Aneurysms

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Abstract

Background—Stent-assisted coiling technology has been widely used in the treatment of intracranial aneurysms. In current study, we investigated the intra-aneurysmal hemodynamic alterations after stent implantation and its association with aneurysm location.

Methods—We first retrospectively studied 15 aneurysm cases (8 internal carotid artery-ophthalmic artery (ICA-OphA) aneurysms and 7 posterior communicating artery (PcoA) aneurysms) treated with Enterprise stents and coils. Then based on patient-specific geometries before and after stenting, we built virtual stenting computational fluid dynamics (CFD) simulation models.

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Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Results—Before and after stent deployment, the average Wall Shear Stress (WSS) on the aneurysmal sac at systolic peak changed from 7.04 Pa (4.14 Pa, 15.77 Pa) to 6.04 Pa (3.86 Pa, 11.13 Pa), $P = 0.001$; and the spatially averaged value of flow velocity in the perpendicular plane of aneurysm dropped from 0.5 m/s (0.28 m/s, 0.7 m/s) to 0.33 m/s (0.25 m/s, 0.49 m/s), $P = 0.001$, respectively. Post-stent implantation, WSS in ICA-OphA aneurysms and PcoA aneurysms decreased by 14.4% ($P = 0.012$) and 16.6% ($P = 0.018$) respectively, and flow velocity also reduced by 10.3% ($P = 0.029$) and 10.5% ($P = 0.013$), respectively. Changes in WSS, flow velocity, and pressure were not significantly different between ICA-OphA aneurysms and PcoA aneurysms ($P > 0.05$). Stent implantation did not significantly change the peak systolic pressure in both aneurysm types.

Conclusion—After stent implantation, intra-aneurysmal flow velocity and WSS decreased independent of aneurysm type (ICA-OphA and PcoA). Little change was observed on peak systolic pressure.

Keywords

intracranial aneurysm; stent; hemodynamics; velocity; wall shear stress; pressure

Introduction

In the endovascular treatment of intracranial wide-necked aneurysm, stent (such as Enterprise, Neuroform, etc.) assisted coiling technology has been widely used. The main function of the stent is to avoid coil herniation [4, 17, 23]. However, many studies suggest that stent may have an impact on patients' intra-aneurysmal hemodynamics [2, 9, 11, 12, 25]. Decreased flow velocity indicative of stagnant blood flow, may promote the process of thrombosis. Wall Shear Stress (WSS) is the friction force between flowing blood and vessel endothelial surface and has been found to play an important role in the recurrence of aneurysm. Areas with low velocity and WSS are subject to increased risk of thrombus [2, 21]. Therefore, in addition to preventing coil herniation, whether and how much the stent also affects the hemodynamics of intracranial aneurysm, remain important questions to be answered.

Previous studies showed that hemodynamic alterations might be associated with the location, size and shape of the aneurysm. However, these studies are limited to animal model, in-vitro silicone-based model, computational aneurysm model based on virtual stent deployment, or only single case treated clinically, thus the results may not reflect the real changes in human body during the clinical treatment [13, 25]. Recently Kono[14] studied 16 real cases of vertebral artery aneurysm treated with Enterprise stent, and investigated the impact of vessel straightening on flow velocity during and after stent implantation. However, they did not investigate the changes in WSS and pressure, and failed to include ophthalmic artery aneurysm and Posterior communicating artery aneurysm, which are more common than vertebral artery aneurysm.

In addition, there are also issues related to the method of stent deployment. Augsburger and Kono only developed model that covered the orifice of aneurysm, thus the length is quite different from the real stent[1, 14]. "Direct placement method" directly bends uniform stent

tubes to fit the inside of parent vessel, but could not represent real stenting situation and stent adherence is also limited [9-12]. "Finite Element Method" simulates the real stent deployment procedure, considering the material properties and the constraint conditions. Although it improves the accuracy of stent placement, it is time-consuming and not suitable for a large cohort study [2-3]. "Fast Virtual Stenting (FVS)" uses only deformable meshes, simple geometrical constraints, and neglects material properties. It greatly reduces the time of stent deployment, but with poor accuracy, especially for complex tortuous blood vessels [16-26].

Therefore, to address the limitations of these aforementioned studies, we retrospectively studied 15 real aneurysm cases (including ICA-OphA and PcoA aneurysms) treated with Enterprise stents and coils, and reconstructed aneurysm model from Digital Subtraction Angiography (DSA). We also applied an improved FVS technique to study the hemodynamic changes before and after stent implantation, and better understand the significance of stenting in the treatment of aneurysm.

Materials and methods

Study Population

We selected consecutive cases of intracranial aneurysm treated with Enterprise stent-assisted coil embolization in our institution from October 2013 to December 2013. The inclusion criteria were: 1) patients with aneurysms that were treated with an Enterprise stent-assisted coil embolization; 2) aneurysms located at ICA-OphA or PcoA; 3) adequate resolution of the instantaneous 3D-DSA images post-treatment for CFD analysis. Exclusion criteria were: 1) patients treated with other type of stents; 2) insufficient 3D-DSA imaging quality for CFD analysis. The indication of stent-assisted coiling in this study is aneurysm with neck width >4 mm or a dome-to-neck ratio $<2:1$ [5]. All medical data were gathered for diagnostic purpose, and the study was approved by Ethics Committee of our institution.

Aneurysm and stent deployment modeling

All 3D aneurysm geometries were obtained from DSA images. We first segmented and smoothed the images using Geomagic Studio (version 12.0 Geomagic, Research Triangle Park, NC) and saved the surface geometries as Wall Shear Stress (STL) format file. We then used the improved Fast virtual stenting (FVS) technique[22] to simulate the process of Enterprise stent implantation (Cordis Neurovascular, Miami, FL) that generally includes 3 steps: (1) pre-processing, in which parent vessel is isolated and simplex mesh is created to best fit the vessel along its centerline using vessel-specific initialization; (2) expansion of simplex mesh to makes the deployed simplex mesh a good apposition to the wall of parent vessel; (3) post-processing, in which we map the stent on the deployed simplex mesh and sweep the wires into 3D structure. The deployed stent was incorporated into the aneurysm geometry with ICEM CFD version 14.0 (ANSYS Inc., Canonsburg, PA). We improved FVS in both vessel-specific rapid initialization and adaptive expansion force, which can lead to better efficiency and accuracy of stent implantation, comparing with existing FVS algorithm.

CFD modeling

Computational fluid dynamic modeling was performed by numerically solving the continuity and Navier–Stokes momentum equations for an unsteady blood flow using the commercial software ANSYS CFX 14.0 (ANSYS Inc., Canonsburg, Pa., USA), based on the finite volume method. Volumetric mesh was created and defined by ANSYS ICEM (ANSYS Inc., Canonsburg, Pa., USA). Mesh dependency tests were also performed to ensure the stability of the simulations. The final grids contained approximately 1 million and 5 million tetrahedral elements for the untreated and Enterprise-treated models respectively. Blood was assumed to be an incompressible Newtonian fluid with a density of 1.06 g/cm³ and viscosity of 0.04 g/cm per second. Because patient-specific information was not available, pulsatile flow boundary conditions were set based on the superposition of blood flow waveforms of the common internal carotid artery from Doppler ultrasonography of normal human subjects in the transient analysis. Vessel walls were assumed to be rigid, and non-slip boundary conditions were applied. The pressure distribution along the parent artery and in the aneurysm was then computed using the drop in pressure calculated during the CFD simulations with respect to $p=10000\text{Pa}$ prescribed at the outlet [12]. The flow waveforms were scaled to achieve a mean inlet WSS of 15 dyne/cm under pulsatile conditions. The unsteady flow solutions were advanced in time using 1000 time steps per cycle for 2 cycles with a fully implicit scheme and efficient solution algorithm[21]. Results of the second cycle were used for characterizing hemodynamics of aneurysm. WSS, pressure of aneurysm and velocity in the perpendicular plane of aneurysm corresponding to pre- and post-implantation of aneurysm models were calculated and compared at the systolic peak.

Statistical Analysis

All data (before and after stent implantation), if normally distributed, were summarized as mean $\pm$ SD and analyzed with paired-samples or independent-samples t-test; or summarized as median (interquartile range), if not normally distributed, and analyzed with paired Wilcoxon test. $P<0.05$ was regarded as statistically significant. Statistical analysis was performed with SPSS 17.0.

Results

1. Patients Characteristics and stenting

The mean age of enrolled patients was 53.2 ± 7.6 years. The average age for men ($n=8$) was 52.0 ± 9.6 years and for women ($n=7$) was 54.6 ± 5.1 years. Their information was summarized in Table 1. Each patient only received one Enterprise stent (Fig. 1A and Fig. 2A).

2. Hemodynamic changes

2.1 Spatially averaged changes in peak systolic velocity and shear stress—

Intra-aneurysmal hemodynamics before and after stenting in the 15 cases were summarized in Table 2. Both flow velocity and WSS decreased after stent implantation, from 0.5m/s (0.28, 0.7) to 0.33 m/s (0.25 m/s, 0.49 m/s), and from 7.04 Pa (4.14 Pa, 15.77 Pa) to 6.04 Pa (3.86 Pa, 11.13 Pa), respectively, and the changes were statistically significant ($P=0.001$). As

shown in Figures 1 (D, E) and 2 (D, E), flow velocity was significantly reduced after stent implantation.

2.2 Compare aneurysms by location—In the ICA-OphA aneurysm, there were complex flow streamlines and the formation of a vortex before stenting (Fig. 1B, D), and reduced number of flow streamlines but no change of vortex after stenting (Fig. 1C, E). In the PcoA aneurysm, there were also complex flow streamlines prior to stenting (Fig. 2B, D), and weaker streamlines as well as disappearance of the vortex after stenting (Fig. 2C, E), indicating reduced blood flow velocity within the aneurysm. Within ICA-OphA aneurysms, before and after stent implantation, WSS and flow velocity changed from 6.03 Pa (2.49 Pa, 14.38 Pa) to 5.16 Pa (2.29 Pa, 9.7 Pa), a 14.4% reduction, $P = 0.012$; and from $0.29 \text{ m/s} \pm 0.13 \text{ m/s}$ to $0.26 \text{ m/s} \pm 0.15 \text{ m/s}$, a 10.3% reduction, $P = 0.029$, respectively. Within PcoA aneurysms, WSS changed from 7.24 Pa (4.81 Pa, 25.1 Pa) to 6.04 Pa (3.86 Pa, 24.31 Pa) after stent implantation, a 16.6% reduction, $P = 0.018$; and flow velocity decreased from $0.38 \text{ m/s} \pm 0.22 \text{ m/s}$ to $0.34 \text{ m/s} \pm 0.21 \text{ m/s}$, a 10.5% reduction, $P = 0.013$ (Table 3–4). The changes in WSS and flow velocity were similar between ICA-OphA and PcoA aneurysms, $P > 0.05$ (Table 5). In summary, both flow velocity and WSS decreased in ICA-OphA and PcoA aneurysms after stenting, the extent to which did not differ by the location of the aneurysms.

2.3 Spatially averaged change in peak systolic pressure—Intra-aneurysmal pressure did not change significantly after stent implantation in 15 cases (Table 2). Subgroup analysis by the ICA-OphA and PcoA aneurysms also did not change the conclusion (Table 3–4).

Discussion

Our study on hemodynamic changes among 15 aneurysm cases before and after stent implantation showed: 1) post-stenting, both intra-aneurysmal flow velocity and WSS decreased and the reductions were similar between ICA-OphA and PcoA aneurysms. Considering the extent of reduction in flow velocity inside the aneurysmal sacs, the blocking effect of Enterprise stent was limited compared with flow diverter [13, 25]. Meanwhile, WSS on the aneurysm wall was reduced because WSS is associated with the gradient of the velocity. WSS is a critical hemodynamic factor during the initiation, growth and rupture of intracranial aneurysms and the change of WSS after stenting may affect the remodeling of the aneurysms. The initiation, growth and rupture of aneurysm involves a really complex process. Hemodynamic factor was only one of the risk factors, other factors such as hypertension, alcohol consumption, genetic and molecular parameters should also be considered. Francis [6] and Metaxa [20] reported that high WSS and an increase in the WSS gradient were observed in the formation of aneurysm and represented “dangerous” hemodynamics likely to induce aneurysm remodeling. Meanwhile, Meng [19] demonstrated that a combination of low WSS and high oscillatory shear index were associated with the growth and rupture of large atherosclerotic aneurysm phenotypes, while high WSS combined with a positive WSS gradient were associated with the growth and rupture of small or secondary bleb aneurysm phenotypes. In addition to the hemodynamic factors, other risk factors including genetic, molecular and pathological factors had also been shown

to be involved in this process. Francis[6] identified that genetic risk factors such as SerpinA3 and CDKN2BAS, and molecular risk factors such as nitric oxide synthase and IL-1 β were all associated with the progression of cerebral aneurysm. Frosen[7, 8] and Krings[15] also suggested that the pathological factors such as the loss of mural cells and mural smooth muscle cells could eventually lead to the aneurysm rupture. Some researchers have indicated that the stenting also plays a potentially biological role in accelerating intimal covering and subsequent occlusion of partially-occluded aneurysms[18, 29]. Therefore, we believe that stent placement not only prevents coil herniation, but also reduces the growth and recanalization of the embolized aneurysms. 2) The pressure change after stent implantation was not statistically significant. It is difficult for clinicians to monitor patient's intra-aneurysmal pressure change before and after stenting, so the change of pressure was rarely discussed in the previous studies. Shobayasi[26] studied the impact of virtual Neuroform stent implantation in a case of a large ICA-OphA aneurysm and found that the flow velocity within the aneurysm was reduced by 14%, but the pressure was only reduced by 4mmHg, which was much larger than our result. Makoto[13] virtually implanted an Enterprise stent into an ICA-OphA aneurysm, and reported that mean pressure at the inflow zone of aneurysm dropped from 43.56Pa to 28.23Pa and mean pressure at the dome of aneurysm dropped from 8.06Pa to 1.7Pa, similar to our findings. Our results also showed that there was no significant difference in peak systolic pressure before and after stenting, which may be due to the following reasons: When the stent is implanted, the flow resistance increases. Because the outlet pressure in our computational models was set to be a constant 10000 Pa, the pressures at the inlet and inside the aneurysm were increased in order to keep the flow rate steady. On the other hand, enterprise stent has large interval porosity and very limited effect on resisting blood flow, thus the increment of pressure inside the aneurysm was small compared to the baseline of 10000Pa and the statistical analysis showed no significant change for the systolic pressure in the aneurysms.

Currently there is a lot of research interest on hemodynamic changes associated with stenting, but there is no firm conclusion yet. Tanemura[27] investigated the effect of virtual Enterprise stent implantation in one saccular aneurysm model and one blister-like aneurysm model, and reported the decrease in WSS and flow velocity within the aneurysm. Nevertheless, the number of cases in these researches was very small and may not represent the real changes from the clinical treatment. Kono[14] studied 16 cases of sidewall cerebral aneurysm treated with the Enterprise stent (actual stenting), found that stenting had two times effects on reduction in flow velocity than straightening of vessels. These results agreed on the effect of stenting on reducing flow velocity within the aneurysm. However, our study also showed unremarkable change of intra-aneurysmal pressure after the stenting. The main finding of this study confirmed the effect of stenting on the reductions of WSS and flow velocity in intracranial aneurysms and showed similar changes for both ICA-OphA and PcoA aneurysms. Furthermore, as Hong[10] and Rayz[24] reported, stent-assisted coiling showed a lower recurrence rate than conventional coiling in treatment of intracranial aneurysms, and areas with low flow velocity and WSS are subject to higher chance of thrombus. Therefore, besides holding the coils in the aneurysmal cavity, the stent might also play an important role in lowering recurrence rate by decreasing the flow velocity and WSS in the aneurysmal sac.

This study has several limitations. First, it did not study the hemodynamic changes in aneurysm models with various shape, size, and location. Second, hemodynamic parameters were set uniformly, blood vessels were assumed to have rigid wall, which may not reflect the physiology of human body and individual variations. Third, we only investigated the role of hemodynamic effects of intracranial stents without coiling, which was also a crucial factor in the process of treatment.

Conclusion

In conclusion, this study confirmed the effect of stenting on the reductions of WSS and flow velocity in intracranial aneurysms and showed similar changes for both ICA-OphA and PcoA aneurysms. Future study is necessary to understand the effect of stent-assisted coiling for the treatment of intracranial aneurysms.

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Fig 1.

(A) Case 3, a representative case of ICA-OphA aneurysm with Enterprise stent. Hemodynamics (streamline, velocity, WSS and pressure) at the systolic peak before and after stenting. (B) Streamlines before stenting showed blood entering at the distal neck of the aneurysm (black arrow). (C) After stenting, the streamlines inside the aneurysm became weaker (black arrow). (D) The impact of stenting on the distribution of flow velocity (intra-aneurysmal flow velocity in the perpendicular plane to the axis of the parent artery) occurred mainly near the center. (E) After stenting implantation, velocity close to the center changed

significantly. (F)/ (G) After stent implantation, WSS of aneurysm was markedly reduced, especially at the top of the aneurysm (red arrow). There was little change on aneurysm wall pressure before and after stent implantation. Note: ICA-OphA: internal carotid artery-ophthalmic artery; PcoA: posterior communicating artery

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Fig 2.

(A) Case 9, a representative case of PcoA aneurysm with an Enterprise stent.

Hemodynamics (streamline, velocity, WSS and pressure) at the systolic peak before and after stenting. (B) Streamlines before stenting showed blood entering at the distal neck of the aneurysm, forming two complex vortexes. (C) After stenting, the vortex in the upper left corner of the aneurysm disappeared. (D)/(E) The impact of stenting on the distribution of flow velocity (intra-aneurysmal flow velocity in the perpendicular plane to the axis of the parent artery) occurred mainly in surrounding area, velocity also changed notably. (F)/(G)

After stent implantation, WSS was significantly reduced, especially at the neck of the aneurysm. There was no significant change on aneurysm wall pressure after stent implantation. Note: ICA-OphA: internal carotid artery-ophthalmic artery; PcoA: posterior communicating artery

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Table 1

Case No.	Sex, Age	Aneurysm Site	Neck Width (mm) [†]	Aneurysm Size (mm) [‡]	Stent Diameter (mm)	Stent Length (mm)	Dome-to-neck ratio
1	F, 52	rt ICA-ophA	4.82	3.54	4.5	22	0.73
2	M, 48	lt ICA-ophA	5.12	5.62	4.5	22	1.09
3	M, 65	rt ICA-ophA	3.38	2.79	4.5	28	0.83
4	F, 58	lt ICA-ophA	3.07	1.72	4.5	22	0.56
5	M, 45	lt ICA-ophA	5.16	7.97	4.5	22	1.54
6	M, 42	lt ICA-ophA	7.95	5.12	4.5	28	0.64
7	F, 55	rt ICA-ophA	1.45	1.31	4.5	28	0.90
8	M, 61	rt ICA-ophA	8.15	9.47	4.5	22	1.16
9	M, 46	lt PcoA	4.51	5.82	4.5	22	1.29
10	F, 62	rt PcoA	5.32	3.53	4.5	22	0.66
11	F, 53	rt PcoA	4.55	2.34	4.5	22	0.51
12	M, 45	lt PcoA	4.88	4.45	4.5	28	0.91
13	F, 46	rt PcoA	6.75	8.09	4.5	28	1.19
14	M, 64	lt PcoA	3.88	2.58	4.5	22	0.66
15	F, 56	rt PcoA	4.65	3.51	4.5	28	0.75

[†] Measurement parameter definitions: Neck Width represented the largest axial diameter at the orifice of the aneurysm. Aneurysm Size was defined as the length from the neck center to the dome of the aneurysm. Stent Diameter and Stent Length were defined as the diameter and length of the Enterprise stent. Dome-to-neck ratios were calculated as aneurysm size to the neck width. All the size measurements were calculated on the Siemens Medical workstation using 3D.

Table 2

Hemodynamic changes Before and After stenting

Variables	Aneurysm		p value (2-tailed)
	Without stent	With stent	
WSS(Pa)	7.04(4.14,15.77)	6.04(3.86,11.13)	0.001
Velocity(m/s)	0.5(0.28,0.7)	0.33(0.25,0.49)	0.001
Pressure(Pa)	10556.6(10337.5,10619.2)	10564.5(10347.8,10628.6)	0.268

WSS: wall shear stress: Data are presented as mean±SD or median (IQR)

Table 3

Hemodynamic Changes in ICA-OphA aneurysms Before and After stenting

Variables	Aneurysm		p value (2-tailed)
	Without stent	With stent	
WSS(Pa)	6.03(2.49,14.38)	5.16(2.29,9.7)	0.012
Velocity(m/sec)	0.29±0.13	0.26±0.15	0.029
Pressure(Pa)	10530.1(10377,10618.9)	10573.3(10399.9,10622)	0.123

WSS: wall shear stress: Data are presented as mean±SD or median (IRQ)

Table 4

Hemodynamic changes in PcoA aneurysms Before and After stenting

Variables	Aneurysm		p value (2-tailed)
	Without stent	With stent	
WSS(Pa)	7.24(4.81,25.1)	6.04(3.86,24.31)	0.018
Velocity(m/s)	0.38±0.22	0.34±0.21	0.013
Pressure(Pa)	10652.43±517.1	10663.03±532.14	0.928

WSS: wall shear stress: Data are presented as mean±SD or median (IQR)

Table 5

The Percentage of Hemodynamic changes between ICA-OphA and PcoA aneurysms After stenting

Variables	Aneurysm			
	ICA-OphA	p value(2-tailed)	PcoA	p value(2-tailed)
WSS(Pa)	14.4±11.2	0.62	16.6±10.5	0.6
Velocity(m/s)	10.3±8.7	0.8	10.5±9.1	0.79
Pressure(Pa)	0.41±0.11	0.27	0.36±0.14	0.24

WSS: wall shear stress;Data are presented as mean±SD.