Article published online: 2022-09-27

EDITOR'S CHOICE

The study of flow diversion effects on aneurysm using multiple enterprise stents and two flow diverters

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ABSTRACT

Background: Computer-based simulation is necessary to clarify the hemodynamics in brain aneurysm. Specifically for endovascular treatments, the effects of indwelling intravascular devices on blood stream need to be considered. The most recent technology used for cerebral aneurysm treatment is related to the use of flow diverters to reduce the amount of flow entering the aneurysm. To verify the differences of flow reduction, we analyzed multiple Enterprise stents and two kinds of flow diverters.

Materials and Methods: In this research, we virtually modeled three kinds of commercial intracranial stents (Enterprise, Silk, and Pipeline) and mounted to fit into the vessel wall, and deployed across the neck of an IC-ophthalmic artery aneurysm. Also, we compared the differences among multiple Enterprise stents and two flow diverters in a standalone mode.

Results: From the numerical results, the values of wall shear stress and pressure are reduced in proportion to the size of mesh, especially in the inflow area. However, the reduced velocity within the aneurysm sac by the multiple stents is not as significant as the flow diverters.

Conclusions: This is the first study analyzing the flow alterations among multiple Enterprise stents and flow diverters. The placement of small meshed stents dramatically reduced the aneurysmal fluid movement. However, compared to the flow diverters, we did not observe the reduction of flow velocity within the aneurysm by the multiple stents.

Key words: Aneurysm, computational fluid dynamics, flow diverter, multiple stents

Introduction

Intracranial aneurysm shown in Figure 1 is one of the cerebral vascular diseases characterized by weakening and bulging of a portion of an artery. There are two effective approaches to treat the detected aneurysm.[1] One approach is via clipping the neck of cerebral aneurysm while the other is via undergoing intravascular surgery. The advantage of this surgery is the fact that there is no need to open the skull to expose the surface of the brain vessel. Medical coils are delivered inside the aneurysm to allow the filling of the cavity, and ultimately, stabilize the disease. However, coiling technique is difficult in the wide-necked aneurysm because of the risk of the coil dropping from aneurysm to parent artery. To solve this problem, an Enterprise stent as an intracranial stent, has been developed to support coils packed in the aneurysmal cavity. Several reports showed that the placement of multiple stents across the aneurysm neck improves the efficiency of flow diversion by reducing aneurysmal inflow.[2,3] By using multiple stents and overlapping them at the neck of aneurysm, the effect of thrombosis was completed in a short time. By focusing on the flow diverting effects, new devices for endovascular treatments of aneurysms called flow diverters have been developed.[4-6] Flow diverter stents block the inlet flow into the aneurysm to induce thrombosis and make a new path of blood flow in a stand-alone mode. Since the flow diverters consist of the small cell design, their placement and position in regard with the neck of the aneurysm is no longer an issue. To quantitatively evaluate the effects of flow diversion, computational fluid dynamics (CFD) has been a key technology. In the previous research, computational fluid dynamics studies were carried out focusing on the flow diverting effects by comparing different mesh pattern.[7-9] However, these studies use conventional stents to evaluate their flow diverting effects,

Access this article online	
Quick Response Code:	Website: www.asianjns.org
	DOI: 10.4103/1793-5482.106643

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and there is no study that compares the flow diversion effects among multiple stents and flow diverters. To overcome these limitations of computational fluid dynamics, in this paper, we present quantitative data by comparing three kinds of commercially available stents (Enterprise, Silk, and Pipeline) in a patient-specific model. Moreover, we verify the differences of flow reduction effects among multiple stents and flow diverters. This is the first study analyzing the flow alterations among multiple Enterprise stents and flow diverters.

Materials and Methods

Stent design

Figure 2 shows the procedure for creating virtual 3D geometry of the flow diverters from two helices. We constructed the stents from oppositely oriented helix. Blue line in Figure 2 shows clockwise helix whereas red line is counterclockwise helix. By placing these two types of spirals, we virtually reconstructed two kinds of commercial flow diverters, Silk and Pipeline. Figure 3 shows the geometry of mesh of each flow diverter, and Table 1 shows the parameters that determined the shape. α and β are the angles of two wires of mesh. L is the length of each side, and R is the diameter of wire. Mesh area of Silk and Pipeline are 0.07 mm^2 and 0.12 mm^2, respectively. Coverage rate is a ratio between area of wire and area of cylinder surface. Figure 4 shows the 3D models of Enterprise, Silk, and Pipeline stents. Diameter of the Silk and the Pipeline is 4 mm, and the length is 20 mm. We obtained the geometry of the Enterprise stent by using micro-CT scan. The resolution of micro-CT images was 20-μm and a 5-cm maximum field view. Diameter of Enterprise stent is 4 mm, and the length is 40 mm.

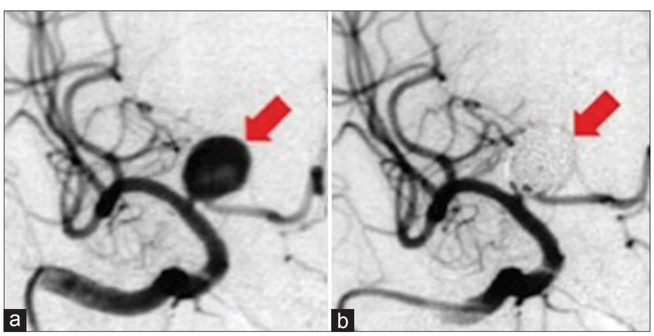

Figure 1: Fluoroscopic image of cerebral aneurysm (a) before surgery (b) after treatment with Enterprise stent and coils. Contrast media circulating in the blood stream do not enter to the aneurysm after the coil embolization. Red arrows point at the aneurysm

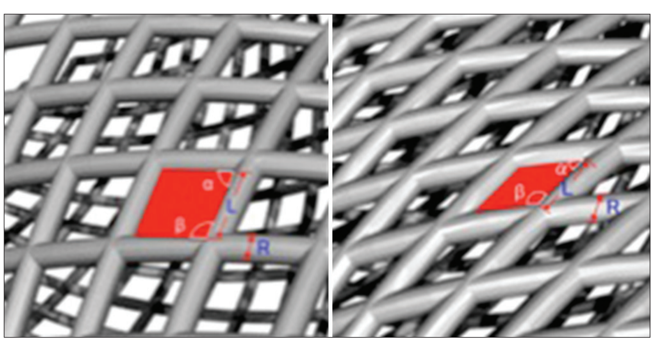

Figure 3: Mesh geometry of stent; left: Silk, right: Pipeline

Anatomical model for computational fluid dynamics

Figure 5 shows a patient-specific aneurysm model served as control and all cases studied with stents for computational fluid dynamics analysis. The object is a part of IC-ophthalmic artery, and this is a major artery of the head and the neck that supplies blood to the brain in the human anatomy. A sphere-shaped object in this artery pointed by black arrow in Figure 5 is an aneurysm. We reconstructed this model

Table 1: Parameter of mesh

	Silk	Pipeline
Angle: α	90°	44°
Angle: β	90°	136°
Length	0.346 mm	0.317 mm
R	42 μm	45 μm
Mesh area	0.12 mm^2	0.07 mm^2
Coverage rate	20.60%	31.06%

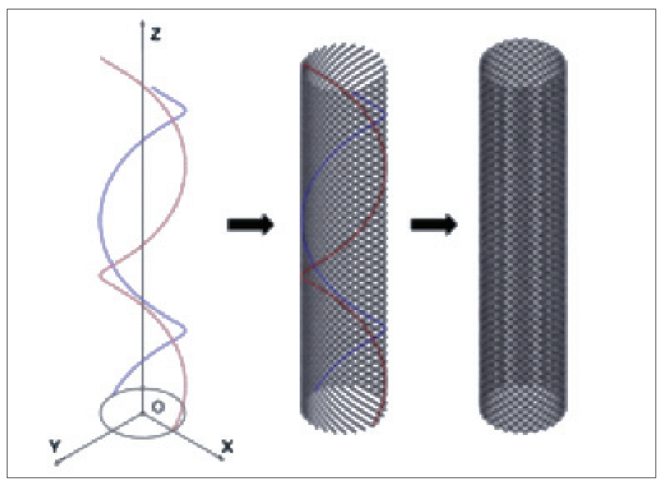

Figure 2: Procedure for creating 3D shape of flow diverter stent: Silk

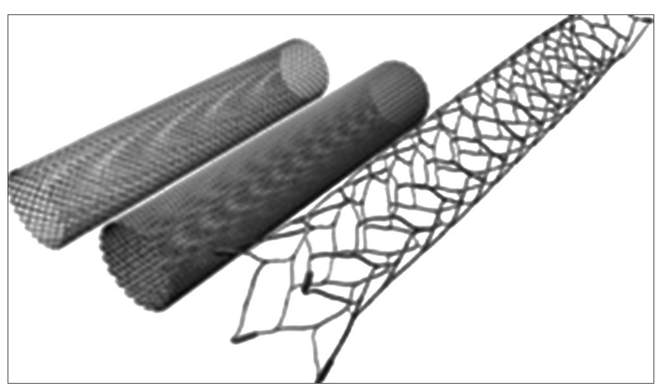

Figure 4: 3D data on stents, left: Silk, center: Pipeline, right: Enterprise

based on the clinical image data from 3D digital subtraction angiography (Philips Health Care, Best, The Netherlands). The diameter of the inlet is 5.88 mm, and the diameter of each outlet is 1.02 mm, 2.83 mm and 3.55 mm. Neck length of aneurysm is 4.75 mm and longitudinal diameter is 7.84 mm.

Fitting stents to vessel wall

In this study, we virtually mounted the stents to fit into the vessel wall and deployed across the aneurysm neck. We prepared five cases for CFD analysis as shown in Figure 5. They are: No stent case (Control), one Enterprise stent case (Enterprise), two overlapped multiple Enterprise stent cases (Multiple Enterprise), one flow diverter case (Silk), and one flow diverter case (Pipeline).

Property of working fluid

Although the blood is well-known to be non-Newtonian in general, we treated it as Newtonian in this study because apparent viscosity becomes nearly constant in an artery with relatively large diameter (1.0 mm) due to high velocity and shear rate.[10] The density and viscosity of blood were 1050 kg/m^3 and 3.5×10^{-3} Pas.

Numerical scheme and boundary condition

The governing equations include the Navier-Stokes equation of incompressible flows and the equation of continuity, where ρ is the density and u is the velocity.

$$\nabla \cdot u = 0 \quad (1)$$

$$\frac{\partial u}{\partial t} + (u \cdot \nabla) u = -\frac{1}{\rho} \nabla p + \nu \nabla^2 u \quad (2)$$

In this calculation, we considered the flow in the cerebral aneurysm as incompressible, laminar, and steady-state. Also, we set Reynolds number as 600 to confirm dynamic similarity. The value of Reynolds number; i.e., 600, signifies the systolic phase wherein the flow volume is the maximum between pulsatile cycles. The definition of Reynolds number is as follows, where V is the mean velocity, D is the diameter of vessel inlet, and $\nu = \mu/\rho$ is the kinematic viscosity.

$$Re = VD/\nu \quad (3)$$

Based on this equation and parameter of inlet diameter of artery model (5.88 mm), inlet velocity is 0.34 m/s. This calculation employs the finite-volume method, appropriate for complex geometry of vessels. All fluid regions are discretized with computational grids consisting of approximately 10-15 million tetrahedral elements. We created these elements by STAR-CCM, and the maximum element size is 0.03 mm. Regarding the calculation scheme, we selected the three-dimensional segregated solver and second-order implicit formulation in time. Pressure-Velocity coupling method is SIMPLE, and pressure term is PRESTO method. Momentum term of the Navier-Stokes equation is discretized with second-order upwind difference scheme and solved by algebraic multigrid (AMG).

Results

Figure 6 shows the results of numerical simulation. From the left side, it shows the results of vessel model without stent (*N*-1, *N*-2, *N*-3, and *N*-4), Enterprise stent (E-1, E-2, E-3, and E-4), multiple Enterprise stents (ME-1, ME-2, ME-3, and ME-4), Silk (S-1, S-2, S-3, and S-4), and pipeline (*P*-1, *P*-2, *P*-3, and *P*-4). Each model contains visualized data on streamline, velocity of cross section around the neck of aneurysm, blood pressure, and wall shear stress. Based on these results, the flow into the aneurysm is affected by mesh pore size and pore density.

Streamline

From the streamline plotted to visualize aneurysm flow patterns, vortex flow occurred in the case of control [Figure 5, N-1].

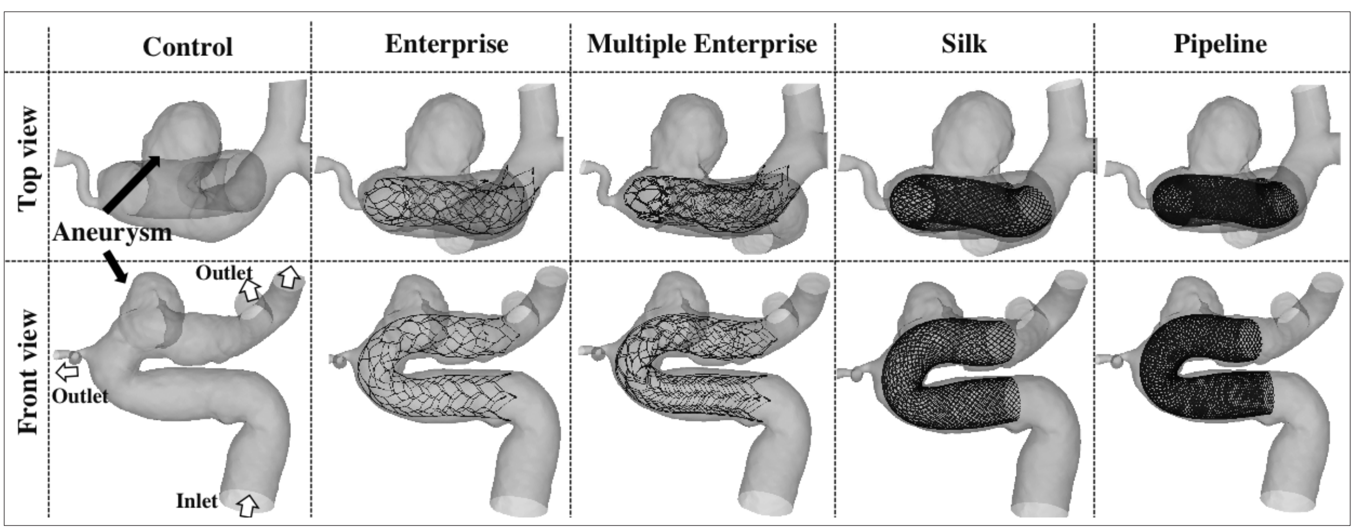

Figure 5: Analyzed five cases by computational fluid dynamics in this study. No stent case: Control, one enterprise stent case: Enterprise, two overlapped multiple Enterprise stent case: Multiple Enterprise, one flow diverter case: Silk, and one flow diverter case: Pipeline

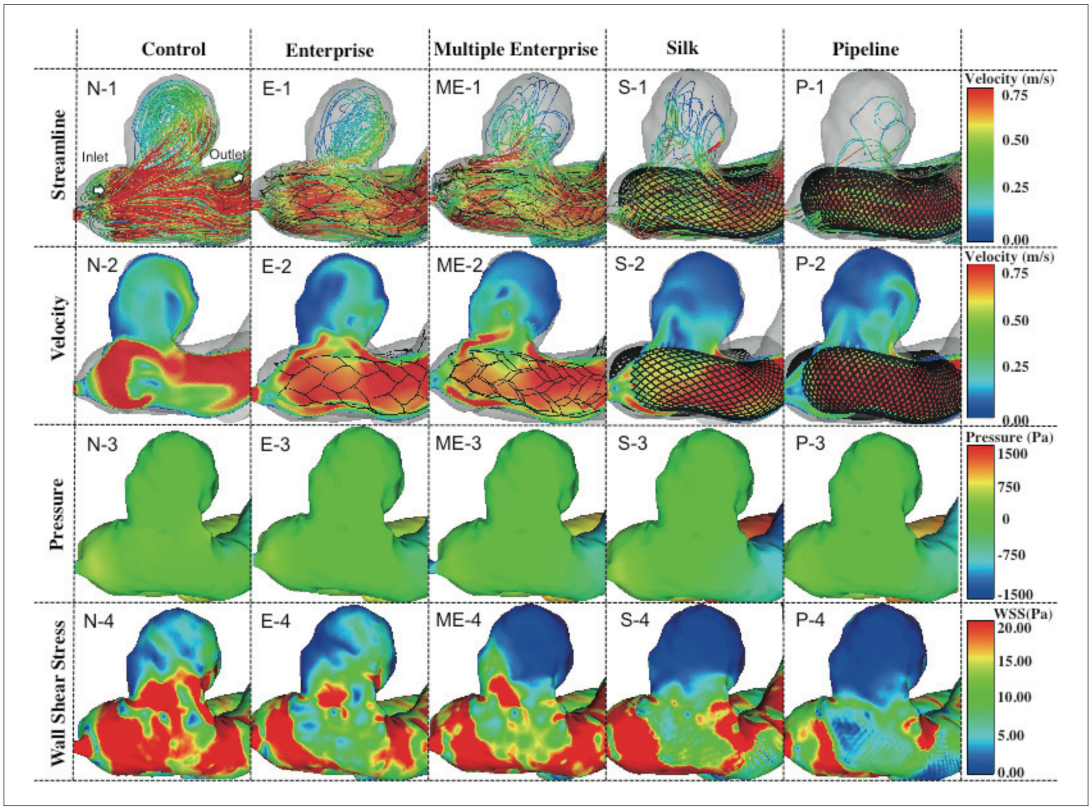

Figure 6: Visualized results of numerical simulation of four models. N: Control model, E: Enterprise stent model, ME: Multiple Enterprise stent model S: Silk model, P: Pipeline model

Vortex in aneurysm becomes small in the following order: Enterprise stent, multiple Enterprise stents, Silk, and Pipeline. Moreover, mesh structure of the stents blocked the blood flow and decreased its velocity. Number of streamline was reduced relative to the increment of pore density. Especially in the case of S-1 (Silk) and *P*-1 (Pipeline), flow diverting effects reduced the volume of blood flow from the main artery into the aneurysm.

Velocity

The results of the velocity distribution of cross section around the neck of aneurysm are shown in Figure 5 (N-2, E-2, ME-2, S-2, and *P*-2). Velocity of blood flow rapidly declined based on the stent structure. The most distinguishing feature is the case of Pipeline whereby the velocity of inner aneurysm was drastically reduced while the velocity of the main artery inside of the stent increased. Also, around the metallic-wire, there were low velocity areas that may lead to aggregation of platelets and thrombus of vessel. Figure 7 represents the quantitative data on root mean square (RMS) velocity magnitude within the aneurysm. In each case, the velocity magnitude is averaged in the area of the aneurysm, and the red part in Figure 7 is region of interest (ROI). The graph shows the reduction percentage of RMS velocity magnitude compared to the control.

Pressure

The pressure for each model is summarized in the third line of Figure 6. From these images, it is difficult to see clear differences among these cases. Therefore, we quantified pressure on three regions of the aneurysm. Inflow covers an area of neck of aneurysm near the inlet. Dome covers the tip of the aneurysm, and outflow covers the neck area on the side of the outlet. We obtained and averaged the data from 10 points in the rectangle area (0.1×0.1 mm). Figure 8 demonstrates the quantitative data on pressure over three regions of the aneurysm. There

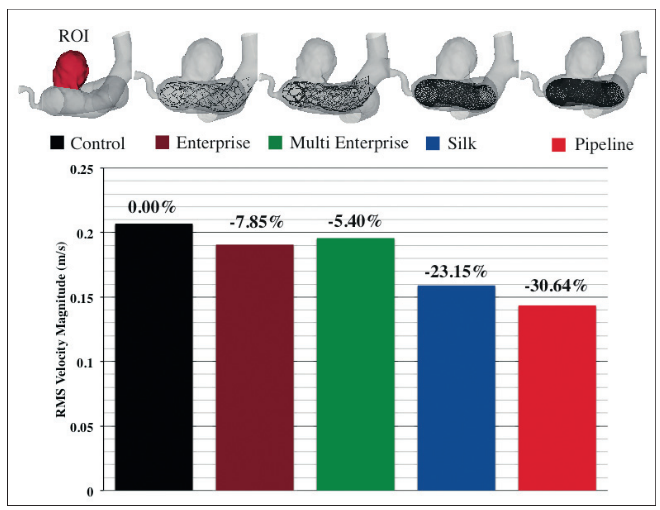

Figure 7: Averaged root mean square (RMS) velocity magnitude within the aneurysm. Red part shows the ROI. Percentage values represent velocity reduction of each case compared to the control

was a strong tendency indicating that pressure decreased from the inlet to the outlet. The reduction of blood pressure is recognized after the placement of intravascular devices. Mean pressure value at the inflow zone of each case is as follows: Control 43.56 Pa, Enterprise stent 28.23 Pa, Multiple Enterprise stents 12.44 Pa, Silk −4.97 Pa, and Pipeline −2.37 Pa. Around the distal area of aneurysm, pressure was reduced by the placement of stents. Mean pressure value at the dome of aneurysm in each case is as follows: Control 8.06 Pa, Enterprise stent 1.70 Pa, Multiple Enterprise stents 1.00 Pa, Silk −0.11 Pa, and Pipeline 1.44 Pa. The pressure around the outflow region is as follows: Control −16.63 Pa, Enterprise stent −10.46 Pa, Multiple Enterprise stents -28.84 Pa, Silk −6.14 Pa, and Pipeline −0.69 Pa.

Considering the device effects of treatment, we focused on the inflow area. Enterprise stent caused the reduction of blood pressure, and its effect became clear with multiple Enterprise stents. On the other hand, in the case of flow diverters, such as Silk and Pipeline, blood pressure became negative pressure due to the effect of flow diversion. This is because the blood flow within the aneurysm is sucked into the main artery. Moreover, the region where we estimated as the inflow zone and the outflow zone in the Control case do not coincide with the same region of the flow diverters because vortex flow within the aneurysm cannot be seen in the case of Silk and Pipeline from the results of streamline in Figure 6. Thus, blood flow of the inflow zone became unstable and indicated the negative pressure. Blood pressure at the dome was lowered by the placement of Enterprise stent and flow diverters. However, the difference of value is small except for the control.

Wall shear stress

Figure 6 (*N*-4, E-4, ME-4, S-4, and *P*-4) shows the results of wall shear stress over the aneurysm. In *N*-4, local high shear stress was observed around the neck. Especially around the area of neck, wall shear stress was decreased by placing Enterprise stent, Silk, and Pipeline. Area of low wall shear stress spread according to the mesh density of stents. Figure 9 summarizes the quantitative data on wall shear stress over the aneurysm. In the area of inflow, the value of wall shear stress is reduced in proportion to the smallness of mesh.

We obtained the value of wall shear stress in the inflow area in the same manner as the pressure value: Control 7.24 Pa, Enterprise stent 4.74 Pa, Multiple Enterprise stents 0.92 Pa, Silk 0.38 Pa, and Pipeline 0.53 Pa. As for the dome area, the value of wall shear stress became nearly zero by placing flow diverter stents, such as Silk and Pipeline. The value is as follows: Control 2.25 Pa, Enterprise stent 1.43 Pa, Multiple Enterprise stents 0.64 Pa, Silk 0.29 Pa, and Pipeline 0.27 Pa. As for the outflow area, the value is as follows: Control 1.77 Pa, Enterprise stent 0.97 Pa, Multiple Enterprise stents 3.09 Pa, Silk 1.09 Pa, Pipeline 0.96 Pa. Aside from an exceptional case of multiple Enterprise stents around the outflow, wall shear stress within the aneurysm decreased as the pore size of stent was also lowered.

Discussion

The purpose of this article was to obtain quantitative data on flow diversion effects by comparing three kinds of commercially available stents in the patient-specific vessel model. Also, we verified the differences of flow reduction effects among multiple stents and flow diverters by computational fluid dynamics analysis. The study indicated that the mesh design such as size and density of pore affected the blood flow in the aneurysm. Flow diverters, Silk and

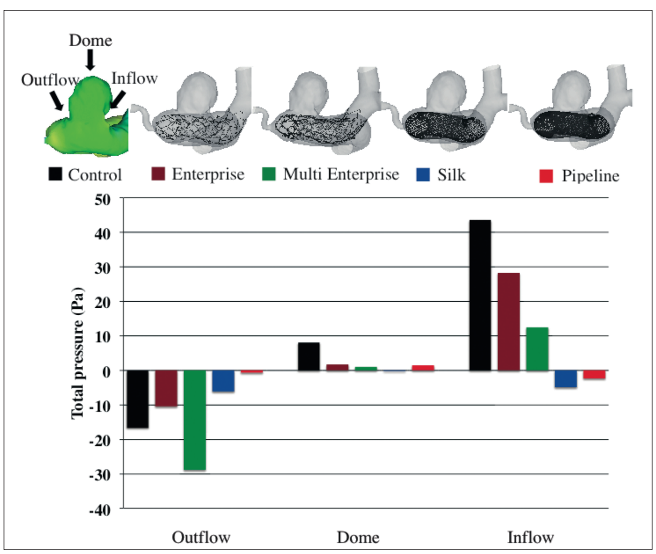

Figure 8: Quantitative data on pressure over three parts of the aneurysm. outflow: Neck part of aneurysm near the outlet, dome: The tip of aneurysm, inflow: Neck of aneurysm near the inlet

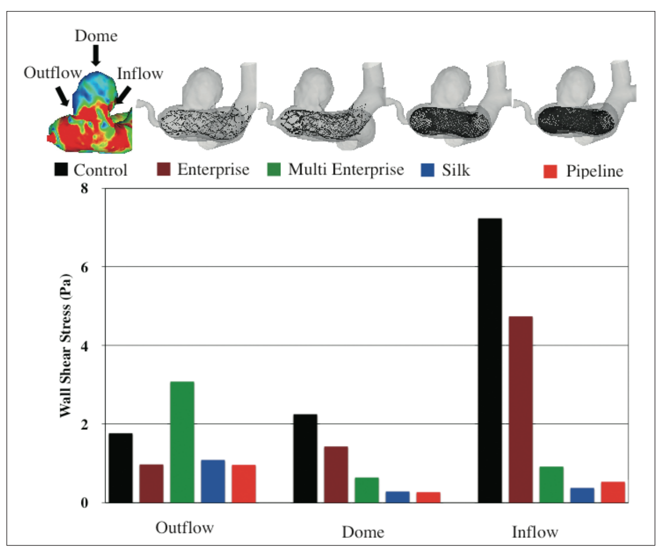

Figure 9: Quantitative data on wall shear stress over three parts on the aneurysm outflow: Neck of aneurysm near the outlet, dome: The tip of aneurysm, inflow: Neck of aneurysm near the outlet

Pipeline, declined the velocity of blood flow into the aneurysm that resulted in the reduction of pressure and wall shear stress. Flow diverter was approved as a treatment of aneurysm in 2011. Also, it has been used at limited medical facilities in Europe and the United States. In the clinical study of 101 intracranial aneurysms treated by Pipeline, they estimated the safety and efficacy of the device.[11] They reported that complete cure of the target lesions in 52%, morphological improvement in 36%, and no improvement in 12%. They concluded that Pipeline is a technically straightforward and relatively safe modality for the treatment of aneurysm, which is often difficult to treat by the coil assist stent, such as Enterprise. This favorable clinical effect of flow diverter is consistent with our simulation. However, some studies on the numerical simulation of artificial vessel model with placement of flow diverter reported increased pressure on the aneurysmal wall.[12] Pressure effect on aneurysm after the placement of flow diverter is being discussed and remains as one of the key issues. However, their results are consistent with our results wherein reduction effect of velocity and wall shear stress is in proportion to high density and small size of pore. It is well-known that the wall shear stress on the vessel wall plays key roles on degradation and rupture of aneurysm.[13] There are two schools of theory; one is high WSS theory whereas the other is low WSS theory. However, an inflammatory and atherosclerotic process triggered by low WSS has been reported in the growth of aneurysm.[14-16] Low WSS within aneurysm sac over the long term will cause degradation of the aneurysm wall and lead to rupture.[17] In the present case study, the value of WSS and pressure around the inflow zone and the dome area dropped dramatically in each case. However, the decline of average RMS velocity magnitude is not significant in the case of multiple Enterprise stents compared to the case of Pipeline. From the results of Figure 7, the velocity reduction of multiple Enterprise stents and Pipeline are −5.40% and −30.64%, respectively. These results indicate that there is a possibility of increased risk of rupture in the case of multiple Enterprise stents, if the reduction effect of velocity within the aneurysm sac is not sufficient for clot formation. The current study has several limitations common to many computational fluid dynamics analyses that should be considered. These include: 1) assumption of vessel wall as a rigid body, 2) Newtonian blood properties and steady flow condition (rigid body and Newtonian blood properties may overestimate the pressure values), and 3) this study conducted numerical simulation in a single patient-specific vascular model at a location that may not be generalized. However, it is our hope that simulated results contribute to the understanding of hemodynamics in the aneurysm induced by various kind of stents.

The selection of the appropriate diameter and length of the device is a significant factor for efficiency of treatment. Implantation of an undersized device may result in poor fitness to the vessel wall with the risk of blood leakage. Placement of a device that exceeds the diameter of target artery may damage the tissue such as endothelial cells. Because of these clinical problems, proposed methods in this paper, "virtual stenting" demonstrate significant potentials to determine the flow alterations of different stents in an aneurysm model and extract the maximum outcome of treatment in advance of actual surgery. Consequently, this technology contributes to minimally invasive surgery. Moreover, our numerical simulation will contribute greatly toward designing optimized intravascular devices.

Conclusions

In this research, we present quantitative data on flow diversion effects by comparing three kinds of commercially available stents (Enterprise, Silk, and Pipeline) in the patient-specific vessel model. Also, we verify the differences of flow reduction effects for five cases (Control, one Enterprise, two overlapped Enterprise, one Silk, and one Pipeline). From the results, area of low wall shear stress and value of wall shear stress is reduced in proportion to the size of mesh, especially in the inflow area. Also, an Enterprise stent lowered blood pressure in the aneurysm, and its effect becomes clear with multiple Enterprise stents. Moreover, in the case of flow diverters, such as Silk and Pipeline, blood pressure becomes negative pressure due to the flow diversion effects. As for the change of velocity magnitude, the reduction percentage of multiple Enterprise stents and Pipeline are –5.40% and –30.64%, respectively. By using multiple stenting technique, we can expect the reduction effect of wall shear stress and pressure in the inflow and the dome areas. However, the reduction effect of velocity within the aneurysm sac by multiple stents is not as significant as flow diverters.

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How to cite this article: Kojima M, Irie K, Fukuda T, Arai F, Hirose Y, Negoro M. The study of flow diversion effects on aneurysm using multiple enterprise stents and two flow diverters. Asian J Neurosurg 2012;7:159-65.

Source of Support: Nil, **Conflict of Interest:** None declared.