Hemodynamic Characteristics at the Rupture Site of Cerebral Aneurysms: A Case Study

BACKGROUND AND IMPORTANCE: Hemodynamics play an important role in the mechanisms of aneurysm formation, growth, and rupture. However, little is known about the hemodynamics of rupture sites.

CLINICAL PRESENTATION: We incidentally acquired 3-dimensional images before and at the moment of rebleeding of a cerebral aneurysm in a patient. Comparison of these 2 images enabled precise identification of the rupture site. On the basis of computational fluid dynamics simulation, we propose that there are characteristic hemodynamic parameters of the rupture site in cerebral aneurysms. We evaluated flow velocity, wall shear stress (WSS), pressure, and the oscillatory shear index to determine characteristic parameters at the rupture site. Among the hemodynamic parameters in the cardiac cycle, the rupture site was most markedly distinguished by a combination of low WSS at end diastole and high pressure at peak systole. The flow patterns around the rupture site uniquely changed in the cardiac cycle. The rupture site was an impingement zone at peak systole. Flow separation at the rupture site was observed at end diastole.

CONCLUSION: In this case, a region with low WSS at end diastole and high pressure at peak systole was at the rupture site. A possible mechanism of rupture in this particular aneurysm is that low WSS at end diastole caused degeneration and thinning of the aneurysm wall and that high pressure at peak systole (impingement zone) resulted in rupture of the thinning wall.

KEY WORDS: Bleb, Cardiac cycle, Cerebral aneurysm, Computational fluid dynamics, Pressure, Rupture site, Wall shear stress

Hemodynamic factors play an important role in the rupture of cerebral aneurysms. Several studies have suggested that wall shear stress (WSS) might be an important hemodynamic parameter for the initiation, growth, and rupture of aneurysms. Although there are a few hemodynamic studies on blebs or their formation, characteristic hemodynamic patterns at the rupture site remain unclear. One of the reasons is that it is difficult to precisely determine the rupture site without bias.

We experienced a rare case concerning real-time imaging of aneurysmal rebleeding. In this case, we incidentally acquired 3-dimensional (3-D) images before and at the moment of rebleeding. Comparison of these 2 images enabled us to exactly identify the rupture site. Computational fluid dynamics (CFD) simulation of the aneurysm was performed to determine characteristic patterns of hemodynamic parameters related to the rupture site.

CLINICAL PRESENTATION

Patient

A 62-year-old woman was admitted to our hospital because of subarachnoid hemorrhage. The World Federation of Neurosurgical Societies grade was IV. Three-dimensional computed tomographic angiography (CTA) showed a ruptured...
aneurysm in the left distal anterior cerebral artery (ACA; Figure 1A). The maximum size of the aneurysm was 5.8 mm. We planned to perform coil embolization for the aneurysm. After the induction of general anesthesia, a 7F guiding catheter was positioned at the left internal carotid artery (ICA). No intravenous injection of heparin was given. For the first angiogram, 3-D rotational angiography (RA) was performed with an injected volume of 21.5 mL at flow rates of 3.2 mL/s. The 3-D RA showed rebleeding of the aneurysm (Figure 1B and Video 1, Supplemental Digital Content 1, http://links.lww.com/NEU/A488 which shows the rotational angiographic run of the left internal carotid artery showing rebleeding from the aneurysm). The vital signs of the patient were stable during the procedure. Blood pressure was maintained at approximately 90/60 to 110/80 mm Hg. Her heart
rate was approximately 60 to 70 bpm. It was unclear when rebleeding occurred. No obvious change in the shape or size of the aneurysm was observed during the angiographic run of 3-D RA. We performed coil embolization as quickly as possible. We first inserted a Trufill DCS Orbit coil (Cordis Neurovascular, Miami Lakes, Florida). A total of 10 coils were inserted with a packing density of 26.9%, and the extravasation was stopped (Figure 1D). Because of massive subarachnoid hemorrhage, the patient died 5 days after the intervention.

Determination of the Rupture Site

The 3-D images of the aneurysm before and at the moment of rebleeding were obtained by 3-D CTA (Figure 1A) and 3-D RA (Figure 1B), respectively. Vessels and aneurysms were segmented by adjusting the threshold curve of the volume-rendered image on the workstation, resulting in the output of 3-D surfaces. Thresholds were adjusted to maintain the same reference diameter (ie, the diameter of the left callosomarginal artery) when comparing the 2 images. With the use of engineering design software, 3-matic (Materialise NV, Leuven, Belgium), these 2 images were fused semiautomatically based on the geometry of the left ACA (Figure 1C). We used a 3-point registration algorithm by choosing 3 points located at similar regions on both 3-D images. We then performed a global registration algorithm by selecting the same surface regions of both images. The fused image showed some dissociation of the 2 images because the 3-D CTA image included the bilateral ACAs whereas the 3-D RA image contained only the left ACA owing to the aplastic anterior communicating artery. In addition, the quality of the 3-D CTA was insufficient to reconstruct a 3-D image of the left pericallosal artery. However, fusion of the images was feasible by use of the 3-D images of the proximal portion of the left ACA and the left callosomarginal artery. The rupture site was exactly identified with the fused image (Figure 1C). The edge of the rupture site was defined as the intersection of the isosurface representations of the 3-D RA and 3-D CTA images. The size of the rupture site was 1.5 × 1.6 mm.

CFD Simulation

For the CFD simulation, we used the 3-D RA image, which had higher resolution than the 3-D CTA image, except for at the rupture site. The surface geometry of 3-D CTA encircled by the edge of the rupture site was used to complement the 3-D RA image. The image for the simulation included the petrous portion of the ICA, the middle cerebral artery (M1), and the left ACA. The image did not contain the anterior communicating artery because it was aplastic. Other small vessels such as the ophthalmic artery, posterior communicating artery, and anterior choroidal artery were removed.

The fluid domain was meshed by the use of ANSYS ICEM CFD software (version 13.0; ANSYS Inc, Canonsburg, Pennsylvania) to create finite-volume tetrahedral elements and wall prism elements. The number of elements was approximately 500 000. Blood was modeled as a newtonian fluid with a density of 1056 kg/m³ and a viscosity of 0.0035 kg/m·s. A rigid-wall no-slip boundary condition was implemented at the vessel walls. We performed a pulsatile-flow simulation with ANSYS CFX (version 13.0; ANSYS Inc). A blood velocity waveform of the left ICA of this patient was obtained by carotid ultrasonography under general anesthesia after the intervention. In an ultrasound examination, the blood pressure was 105/78 mm Hg and heart rate was 65 bpm. Blood pressure and heart rate values were similar to those at rerupture. The waveform of the flow velocity was translated into the volumetric waveform by use of the area of a cross section of the ICA (0.14 cm²). The volumetric waveform was used to create the inlet boundary condition (Figure 2).
pressure was imposed at the outlets. The width of the time step for calculation was set at 0.005 second. Calculations were performed for 3 cardiac cycles, and the result of the last cycle was used for analysis. We examined 4 hemodynamic parameters: velocity, static pressure, WSS, and the oscillatory shear index (OSI), as defined by Ku et al.9 To perform the simulation, we used a laptop computer (DELL Precision 4500; Dell Computer Corp, Austin, Texas). For a validation study of the CFD simulations, we created 2 types of finer-volume mesh to show grid independence. The numbers of elements were approximately 1 000 000 and 1 500 000, respectively. The profiles of flow velocity on a cut plane in the ICA were obtained and compared among the models with the different grid densities.

To determine hemodynamic characteristics at the rupture site, we defined 4 parts of the aneurysm wall as regions of interest: the rupture site, 2 unruptured blebs (defined as unruptured bleb-1 and unruptured bleb-2), and the whole dome of the aneurysm (Figure 3A and 3D). In each area, peak systolic, end-diastolic, and time-averaged WSS and static pressures were measured. The OSI was also examined. The mean and standard deviation of each hemodynamic parameter in each area were calculated from the spatial distributions. To clarify characteristic hemodynamic parameters at the rupture site, we calculated Z scores of the rupture site and the 2 unruptured blebs on the basis of the mean and standard deviation of the spatial distributions of each variable on the whole dome. For example, the Z score of WSS at peak systole on the rupture site was calculated as the mean of WSS at peak systole on the rupture site minus the mean of WSS at peak systole on the whole dome divided by the standard deviation of WSS at peak systole on the whole dome. Using this method, we standardized the hemodynamic variables of each region of interest on the dome.

RESULTS

With regard to the fusion image of the aneurysm (Figure 1C), the 2 images of 3-D CTA and 3-D RA showed a small gap on the aneurysm dome. There was an approximately 0.4-mm maximum gap between the surface of the 3-D CTA image and that of the
3-D RA image. In some parts of the image, the surface of the 3-D CTA image was outside that of the 3-D RA image (Figure 1C), whereas in other parts, the relationship was the opposite (data not shown). We do not consider that the size or shape of the aneurysm was changed after rebleeding because it was previously demonstrated that the mean error distance of 3-D CTA and 3-D RA is approximately 0.40 mm.

With regard to the validation study, we obtained almost identical profiles of the area-averaged flow velocity on the cut plane among the 3 models with different grid densities. (See the supplemental Figure A-B, http://links.lww.com/NEU/A489). Figure 1 shows a cut plane in the internal carotid artery and a line on the cut plane [black line], as well as the contour of velocity at end diastole on the cut plane. The vectors of flow on the cut plane are also shown with lengths that denote the velocity. Figure 2 shows the flow velocity during the cardiac cycle on the cut plane among 3 different grid densities. Mesh-1 corresponds to the initial mesh conditions. The number of elements is approximately 500 000. Mesh-2 and mesh-3 correspond to the finner mesh conditions. The numbers of elements are approximately 1 000 000 [mesh-2] and 1 500 000 [mesh-3]. The 3 curves are almost identical. The maximum difference among these 3 models during the cardiac cycle is 1.5%. The maximum difference of the velocity among the models was 1.5% during the cardiac cycle. The profiles of the velocity on the line on the cut plane at end diastole or peak systole among the 3 models were also almost identical. (See Figures 3 and 4, Supplemental Digital Contents 2 [C-D], http://links.lww.com/NEU/A489). The profiles of flow velocity on the line at end-diastole [Figure 3] and at peak systole [Figure 4] among 3 different grid densities are shown. The 3 profiles are almost identical. The maximum difference among these 3 models on the line is 2.0%. These results indicate that the initial mesh conditions are valid for the computational fluid dynamic simulation. The maximum difference of the velocity among the models was 2.0%. Therefore, we concluded that the initial mesh conditions were valid for the CFD simulation. The cycle-averaged velocity and WSS at the ICA were 0.45 m/s and 2.9 Pa, respectively, which were within expected physiological levels.

We analyzed the overall results of the CFD simulation and found a trend for the rupture site to have low WSS and high pressure on the dome surface at any time in the cardiac cycle. In addition, the rupture site was the impingement zone at peak systole (Figure 3). There were 3 blebs including the rupture site. All 3 blebs had low WSS. The 2 unruptured blebs had lower pressure than the rupture site (Figure 3). The OSI showed no distinctive trend at the rupture site (data not shown).

The hemodynamic parameters at the regions of interest are summarized in the Table. According to the Z scores, WSS at end diastole and pressure at peak systole showed the most distinctive deviation at the rupture site. The OSI did not show as much deviation as the other 2 parameters. These results indicated that the rupture site was most markedly distinguished by the combination of low WSS at end diastole and high pressure at peak systole. The unruptured blebs-1 and blebs-2 also had low WSS. However, these 2 blebs had comparatively low pressure.

Therefore, the rupture site was discriminated by high pressure at peak systole among the 3 blebs. The flow patterns around the site of rupture were uniquely changed. The flow at peak systole directly impinged on the rupture site (Figure 4A), which led to high pressure at peak systole. The flow at end diastole turned away at the proximal part of the rupture point (Figure 4B), and flow separation, which caused low WSS in this area, was observed. These changes in flow patterns in the cardiac cycle were unique to the rupture site and could explain characteristic patterns of the hemodynamic parameters at the rupture site.

DISCUSSION

We performed a CFD simulation for a rare case in which the rupture site was precisely identified. This site was characterized by the combination of low WSS at end diastole and high pressure at peak systole. This site was also an impingement zone. Flow patterns at the rupture site were uniquely changed in the cardiac cycle.

Several reports have compared hemodynamic parameters between unruptured and ruptured aneurysms. Shojima et al and Cebral et al described the hemodynamic characteristics of...
bleb formation. However, to the best of our knowledge, no reports have evaluated hemodynamic patterns of the rupture site, probably because it is difficult to precisely determine the point of rupture. A rupture site can possibly be identified by surgeons directing attention to ruptured aneurysms in open surgery. However, this is not precise because of surrounding hematomas, a limited operative view under the microscope, and deformation of the aneurysm by manipulations. Even if the site of rupture can be observed, determining this site on a 3-D reconstructed image without any bias is impossible. Although blebs are likely to be rupture sites, such geometric analysis cannot provide evidence of rupture sites. We incidentally encountered rebleeding while performing 3-D RA. This 3-D image enabled us to overcome this difficulty in exactly identifying the point of rupture. Although there are a few reports regarding 3-D images during rebleeding, this is the first report to investigate hemodynamic characteristics at the rupture site.

In our study, the rupture site was characterized by the combination of low WSS at end diastole and high pressure at peak systole. Most of the previous CFD studies on cerebral aneurysms used time-averaged WSS.1-3 Our study results suggest that it may be necessary to investigate each hemodynamic parameter, taking into account the dimension of time in the cardiac cycle. For example, in our case, the rupture site was the impingement zone at peak systole but not at end diastole, and flow separation was not observed at peak systole but was observed at end diastole. A number of studies have proposed that concentrated inflow jets and complex flow patterns such as flow separation are correlated with aneurysm rupture.2,14-17 Our results are consistent with these previous studies if we take the cardiac phase into consideration. Therefore, we propose that it may be necessary to evaluate hemodynamic characteristics while considering changes in these parameters during the cardiac cycle.

A number of reports have described that WSS may have an important role in aneurysm rupture. Some studies have shown that low WSS or an area of low WSS is associated with aneurysm rupture,4,5,16 and others have demonstrated that high WSS is associated with aneurysm rupture.2 In these previous studies,1-3,18 area-averaged WSS on the whole dome was measured. In our study, we focused on WSS on the rupture site. Shojima et al8 described that bleb formation is associated with a high WSS gradient in a large region of low WSS. Cebal et al1 demonstrated that blebs form at or adjacent to regions of high WSS. Although both of these studies focused on blebs, they examined hemodynamics using geometry of aneurysms before bleb formation; therefore, our results are not comparable to their results. Cebal et al also described that formation of blebs results in a lower WSS state with formation of a countercurrent vortex, which is consistent with our results.

WSS is converted to biological signals on endothelial cells, and it modulates gene expression and cellular function in vessel walls.5,19 It is considered that a WSS of approximately 2.0 Pa is suitable for maintaining the structure of arteries and that a WSS < 1.5 Pa will cause degeneration of the vessel wall.5 In our case, cycle-averaged WSS on the dome or the rupture site was 2.6 or 1.4 Pa, respectively (Table). WSS at end diastole was 0.15 Pa, which is much lower than 1.5 Pa; therefore, this appears to be too low to maintain normal cellular function in endothelial cells. The possible mechanism of rupture of the cerebral aneurysm in our case is that low WSS at end diastole caused degeneration and thinning of the aneurysm wall and that high pressure at peak systole resulted in rupture of the thinning wall. Low cycle-averaged WSS (1.4 Pa) may be sufficient to cause degeneration of the aneurysm wall. However, it is also possible that extremely low WSS at end diastole (0.15 Pa) may be necessary for thinning of the aneurysm wall. Further studies are needed to investigate the importance of hemodynamic variables while taking the cardiac phase into consideration.

With regard to the interpretation of high pressure at the rupture site, Shojima et al20 stated that local pressure elevation at the aneurysm is small and that it may have less effect on the rupture of aneurysms than expected. In our case, at peak systole, the pressure at the rupture site was 1.57 mm Hg (1936 Pa – 1757 Pa = 209 Pa) above the mean pressure. This local pressure elevation, 1.57 mm Hg, was 1.4% to 1.7% of the peak pressure in our patient (90-110 mm Hg), and it was 12.8% of the intraaneurysmal pulse pressure of 12.29 mm Hg (1757 Pa – 119 Pa = 1638 Pa). This small pressure elevation may not adversely affect endothelial cells. We consider local pressure elevation to be an indicator of the impingement zone, which may be important.
for rupture of aneurysms, as previously demonstrated. In addition, the combination of a low WSS area and an impingement zone may be necessary for rupture. Namely, impingement flow on a thinning wall caused by low WSS may lead to rupture of aneurysms. Because we studied only a single case, this assumption may be unique to this case and cannot be generalized.

Most CFD studies use typical flow rate waveforms, probably because computer scientists or engineers usually perform CFD simulations. However, in the present case, we obtained the patient-specific waveform by ultrasonography and used it as the inlet boundary condition of the simulation. In our institution, as clinical neurosurgeons, we perform CFD simulations ourselves. This situation enables us to obtain necessary data immediately when we encounter this type of case in which the hemodynamics appear to be interesting. Because Karmonik et al demonstrated that patient-specific waveforms may be necessary for accurate calculation of WSS, our study may be more reliable than studies using typical flow waveforms.

In our CFD study, we simplified several properties such as the viscoelasticity of the vessel wall and the nonNewtonian property of the blood for technical reasons. Although the main hemodynamic features are supposed to be preserved, these simplifications may cause differences between the results of CFD simulation and the in vivo state. As stated in the Results section, we consider that the shape or size of the aneurysm was not changed after rebleeding, although there was a slight gap in the fused image. If the shape or size is changed, the CFD results may differ. In addition, our results may be unique to this particular aneurysm. Further studies need to investigate whether presumed rupture sites based on geometry or direct surgery will have the same hemodynamic characteristics.

CONCLUSION

We present a rare case in which the rupture site of an aneurysm was precisely identified in a 3-D image. When performing CFD simulation of the aneurysm, we demonstrated that the rupture site had low WSS at end diastole and high pressure at peak systole and was an impingement zone. Because this is a single case, these findings may be unique to this particular aneurysm and cannot be generalized. In addition, the rupture observed was due to rebleeding, not to rupture of an unruptured aneurysm. However, our findings provide insight into the hemodynamics of rupture sites.

Disclosures

Dr. Kono received financial support from the Japan Labour Health and Welfare Organization as research funds to promote hospital functions. The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES


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COMMENTS

Computational fluid dynamics is attracting increased attention for describing hemodynamics in cerebral aneurysms. A well-conducted patient study, as described in this work, is important to demonstrate its capabilities and limitations. Identifying hemodynamic parameters related to the rupture site is instructive; however, it should be kept in mind that in addition to mechanical parameters, biological parameters not accessible to the simulations described here may be of importance.

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This is an interesting case report of an aneurysm that ruptured during image acquisition. The rare image allowed the authors to determine the rupture site and to characterize the hemodynamics at that location using computational fluid dynamics techniques. Different from the common approach of comparing the hemodynamic stress on the whole aneurysm wall between ruptured and unruptured cases, this study is the first to narrow down the region of interest to the rupture site. Improved interpretation of the findings of this work likely requires patient-specific knowledge of the mechanical properties of the aneurysm wall and a better understanding of the role that hemodynamics play in the mechanobiology of the aneurysm wall.

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The authors provide us with a report of a unique case that combines the opportunity of acquiring a 3-dimensional imaging data set of the intraprocedural rerupture of a ruptured distal anterior cerebral artery aneurysm during treatment with coil embolization. The authors combine this with the application of computational fluid dynamics methods and demonstrate that the predicted hemodynamic forces indeed support that the aneurysm should rupture in the location of the dome that actually ruptured. Only a handful of studies provide imaging of the rupture of an aneurysm (eg, the work by Van Rooij et al1), and again only a very small number of studies have attempted to evaluate the fluid dynamics environment in an aneurysm known to rupture (eg, those by Sforza et al2 and Cebral et al3). The present study adds to this because it allowed the authors to estimate the size of the rupture opening in the aneurysm dome, to pinpoint its exact location, and to predict the hemodynamic forces acting on this part of the dome. The results of this study are not necessarily generalizable and unfortunately do not necessarily help us to decide if and when a given aneurysm will rupture, but they underline that the routine application of computational fluid dynamics studies may add a dimension to the evaluation of aneurysms beyond anatomic and statistical consideration and may add to the immeasurable clinical judgment calls with which neurosurgeons are faced.

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