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Original Article

Prediction of Post-Embolization Recurrence of Anterior Communicating Aneurysms with A1 Segment Asymmetry by Fluid Dynamic Analysis

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Objective: The increased surface pressure of the coil mass calculated by computational fluid dynamics (CFD) analysis has been reported to be associated with the recurrence of internal carotid aneurysms after coil embolization. In this study, we investigated the relationship between the pressure on the coil surface and the recurrence of anterior communicating aneurysms.

Methods: Among patients with anterior communicating aneurysms who underwent coil embolization at a volume embolization rate of 20% or more without using a stent, only one proximal anterior communicating artery (A1) was visualized by magnetic resonance angiography (MRA). A virtual post-coiling model was created by eliminating the aneurysm at the neck position from the blood vessel model based on three-dimensional rotational angiography (3D-RA) data before treatment, and the neck plane was defined as the virtual coil plane. Using CFD analysis, the pressure difference (PD) was calculated by subtracting the average pressure of A1 from the maximum pressure on the virtual coil surface and dividing by the dynamic pressure of A1 for normalization. PD was statistically compared between the recurrent group and the non-recurrent group.

Results: Four of 10 patients with anterior communicating aneurysms exhibited recurrence. The PD was 2.54 ± 0.24 and 2.12 ± 0.26 in the recurrent and non-recurrent groups, respectively, and was significantly higher in the recurrent group ($p=0.038$). In the receiver operating characteristics (ROC) analysis, the area under the curve (AUC) was 0.917, and with a cutoff value of 2.31, the sensitivity was 1.000 and the specificity was 0.833.

Conclusion: PD was considered a predictor of recurrence after coil embolization in anterior communicating aneurysms with asymmetrical A1. Preoperative prediction of recurrence after cerebral aneurysm embolization may be possible using CFD analysis.

Keywords▶ cerebral aneurysm, coil embolization, computational fluid dynamics, pressure difference, recurrence after coil embolization

Introduction

Coil embolization for intracranial aneurysms is less invasive than clipping surgery but is more often associated with recanalization (recurrence) after treatment.[1] The dome, neck, large dome/neck ratio, low volume embolization rate, and rupture have been reported as risk factors for recurrence of intracranial aneurysms after coil embolization.[2–7] We applied computational fluid dynamics (CFD) to intracranial aneurysms, and reported an increase in the pressure difference (PD) on the surface of the coil mass using the feeding artery as the baseline to be a factor for recurrence of internal carotid aneurysms after coil embolization.[8] This factor is of clinical use because recurrence is predicted by simulating the pressure exerted on the coil mass using preoperative vascular information, but whether PD is related to the recurrence of aneurysms in other intracranial vessels is unclear. In this study, we evaluated whether PD is associated with the recurrence of anterior communicating aneurysms after coil embolization.

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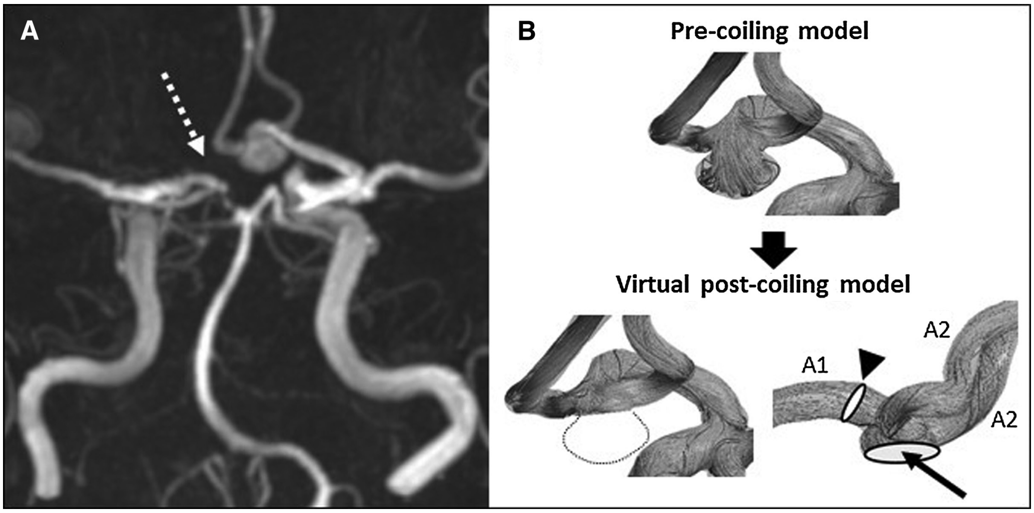

Fig. 1 Patients in whom one proximal anterior cerebral artery (A1) was not delineated by preoperative MRA were selected as the subjects (**A**, dotted arrow). A virtual post-coiling model was prepared by deleting the aneurysm from the pre-coiling model prepared from 3D-RA data (**B**). The plane of the aneurysmal neck was defined as the coil surface in the virtual post-coiling model (arrow) and the cross-section of A1 at a point 1 mm proximal to the aneurysm was the inlet plane (arrowhead). 3D-RA: three-dimensional rotational angiography; MRA: magnetic resonance angiography

Materials and Methods

Subjects

Consecutive patients who underwent endovascular treatment for anterior communicating aneurysms during the period from January 2013 to December 2016 were evaluated. The subjects of this study were selected using the following criteria: (1) Saccular aneurysm of the anterior communicating artery with one proximal anterior cerebral artery (A1) not visualized by MRA (**Fig. 1A**), (2) coil embolization was performed without stenting, (3) a volume embolization rate, which is the volume ratio between the aneurysm and the coil, of ≥20% was achieved, (4) a follow-up period of at least 1 year after endovascular treatment, and (5) preoperative three-dimensional rotational angiographic (3D-RA) images were obtained and available for computational modeling. The patients were regularly followed up every 6 months by MRA, underwent angiography when recanalization was suspected, and if necessary, received additional endovascular treatment. The recurrence of aneurysms was defined as exacerbation of the Raymond–Roy classification or necessity of re-treatment, and the patients were classified into recurrent and non-recurrent groups.[9] The volume embolization rate was calculated by dividing the coil volume by the aneurysm volume. The aneurysm volume was calculated from the data of rotational angiography using a 3D workstation (Allura 3D-RA workstation, Philips Medical Systems, Best, the Netherlands).[2]

CFD simulation

DICOM data of 3D-RA (Philips Healthcare, Best, the Netherlands) were used for analysis. For vascular extraction, data were converted to standard triangulated language data using Amira (version 5.6, Maxnet Co., Ltd., Tokyo, Japan). These 3D images were imported to ANSYS ICEM CFD software (version 16.2, ANSYS Inc., Canonsburg, PA, USA) and used as a pre-coiling model. A virtual post-coiling model was created by deleting the dome of the aneurysm at the neck, and the plane at the neck of the aneurysm was defined as the coil surface. The inlet plane was defined as the cross-section of A1 at the point 1 mm proximal to the aneurysm (**Fig. 1B**).

Next, the vascular model was meshed using ANSYS ICEM CFD software. A path 75 mm long was added on the proximal side of the internal carotid artery, and the infusion port was sufficiently elongated. Blood was modeled as a Newtonian fluid with a density of 1100 kg/m^3 and a viscosity of 0.0036 Pa·s. The vascular wall and coil surface were defined as rigid walls in the no-slip boundary condition. Using ANSYS CFX (version 16.2, ANSYS Inc.), simulation was implemented by setting the mean flow rate at 0.254 L/min and assuming two pulses, each with a duration of 0.9 sec (1.8 sec), as inflow conditions of the internal carotid artery, and the pressure at the exit plane was set at 0 Pa.[10] The time step of simulation calculation was 0.005 sec. Calculation was performed for 2 pulses, and the results in systole of the second pulse were used for analysis.[11]

Table 1 Clinical characteristics and hemodynamic data for all included patients

Factors	Recurrence (n = 4)	Stable (n = 6)	P value
Age (year)	55.1 ± 8.7	69.8 ± 6.0	0.082
Female sex	2 (50)	2 (33)	1.000
Ruptured aneurysm	3 (75)	2 (33)	0.524
Dome size (mm)	8.21 ± 4.93	7.58 ± 2.10	1.000
Neck size (mm)	2.81 ± 1.49	3.49 ± 0.98	0.352
Initial result			0.933
Class 1 (Complete)	1 (25)	2 (33)	
Class 2 (Residual neck)	2 (50)	3 (50)	
Class 3 (Residual aneurysm)	1 (25)	1 (17)	
ASPECT ratio	1.96 ± 0.20	2.36 ± 1.36	0.762
Volume embolization ratio	24.8 ± 4.94	23.6 ± 2.33	0.762
Maximum wall shear stress (Pa)	50.3 ± 26.5	36.5 ± 14.7	0.476
Average wall shear stress (Pa)	27.3 ± 26.8	11.6 ± 4.9	0.476
Maximum pressure at coil plane (Pa)	4572 ± 5198	3633 ± 3634	0.914
Average pressure at inlet plane (Pa)	3893 ± 4452	3011 ± 3239	0.762
Average velocity at inlet plane (cm/s)	63.5 ± 37.5	69.4 ± 23.0	0.476
Pressure difference	2.54 ± 0.24	2.12 ± 0.26	0.038

Values are No. (%) or mean ± standard deviation.

The PD was calculated as a CFD parameter using the following equation:

$$\text{Pressure difference} = \frac{P_{max} - P_{ave}}{\frac{1}{2}\rho V_{in}^{2}}$$

P_{max} is the maximum pressure on the coil surface, P_{ave} is the average pressure at the inlet plane (A1), ρ is 1100 kg/m^3, and V_{in} is the average flow rate at the inlet plane (A1). PD was calculated by subtracting P_{ave} from P_{max} as the degree of increase in the pressure from the inlet plane to the neck plane, and the value was divided by the arterial pressure at the inlet plane for non-dimensionalization.[8] As other factors, the maximum and mean of the wall shear stress applied to the coil surface were calculated.

Statistical analysis

Group-wise comparisons were made using the Mann–Whitney U test or Fisher's exact test. The predictive power of the parameter was evaluated by creating a receiver-operating characteristic (ROC) curve and calculating the area under the curve (AUC) with a 95% confidence interval (CI). The optimal cutoff value of the continuous variable of the present data set was defined using ROC curve analysis. The level of significance was defined as $p < 0.05$. All analyses were carried out using SPSS (IBM SPSS Statistics 23, Chicago, IL, USA).

Results

Of the 44 patients who underwent coil embolization for anterior communicating aneurysms between 2013 and 2016, 25 remained after excluding 2 in whom stenting was used concomitantly, 5 who were retreatments after coiling, 9 in whom the volume embolization rate of <20%, and 4 who were not followed up (including those who died) because of severe subarachnoid hemorrhage. Of these patients, 10 in whom one A1 was not delineated by MRA were analyzed. Four of them had recurrence. The characteristics of the aneurysms and results of fluid dynamic analysis in the two groups are shown in **Table 1**. No significant difference was observed between the two groups in age, percentage of females, percentage of ruptured aneurysms, aneurysm or neck size, aspect ratio, or volume embolization rate. Among the fluid dynamic parameters, no significant difference was observed in the maximum pressure on the coil surface, mean pressure or mean blood flow velocity at the inlet plane (A1), or wall shear stress. However, the PD was 2.54 ± 0.24 and 2.12 ± 0.26 in the recurrent and non-recurrent groups, respectively, and was significantly higher in the recurrent group ($p=0.038$). The AUC of the ROC curve was 0.917, and the sensitivity and specificity were 1.000 and 0.833, respectively, with a cutoff value of 2.31 (**Fig. 2**).

Representative cases

Recurrent case

A 56-year-old man was transported due to headache and vomiting, and was diagnosed with subarachnoid hemorrhage. For the ruptured anterior communicating artery, intra-aneurysmal coil embolization was performed,

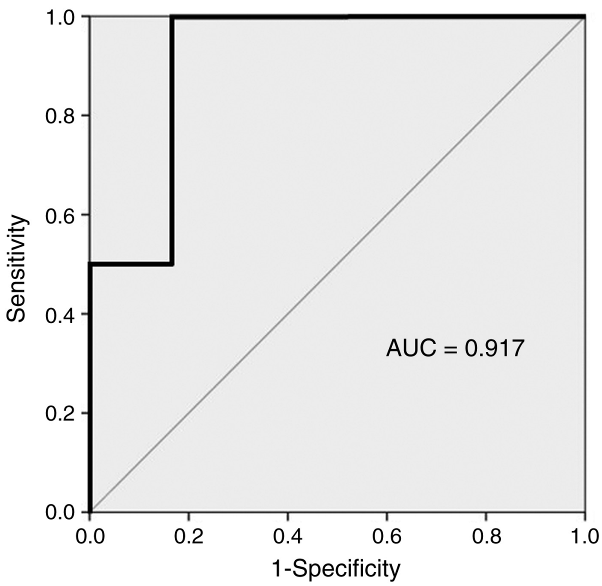

Fig. 2 In the ROC curve analysis for the prediction of aneurysm recurrence after coil embolization, the AUC was 0.917. With a cutoff value of 2.31, the sensitivity was 1.000 and the specificity was 0.833. AUC: area under the curve; ROC: receiver operating characteristic

resulting in a volume embolization rate of 32.0% (**Fig. 3A**). However, as recanalization was observed after 7 months, coil embolization was performed again (**Fig. 3B**). According to CFD analysis using the virtual post-coiling model of this patient, the maximum pressure on the coil surface and mean pressure on the inlet plane were 2060 Pa (**Fig. 3C**) and 1755 Pa, respectively, and as the mean flow rate of the feeding artery was 0.44 m/s, the PD was calculated to be 2.87, which was higher than the cutoff value.

Non-recurrent case

A 69-year-old man was transported with disturbance of consciousness due to subarachnoid hemorrhage. Multiple cerebral aneurysms were noted, and because the largest anterior communicating aneurysm was considered to have been ruptured, coil embolization was performed for this lesion, resulting in a volume embolization of 22.7% (**Fig. 3D**). No recurrence was noted by follow-up angiography performed after 1 year (**Fig. 3E**). According to CFD analysis, the pressures on the coil surface and inlet plane were 1715 Pa (**Fig. 3F**) and 1443 Pa, respectively, and the PD calculated by assuming the mean flow velocity of the feeding artery as 0.52 m/s was 1.73, which was lower than the cutoff value.

Discussion

This is the first report suggesting that the correlation between the recurrence of cerebral aneurysms after coil embolization and PD observed in internal carotid aneurysms also applies to anterior communicating aneurysms with asymmetry of A1.[8] The PD estimated by simulation of the pressure on the virtual coil surface from preoperative vascular information is useful for preoperative outcome prediction. In this study, recurrence was observed in four (80%) of the five patients in whom the PD was above the cutoff value, which was 2.31, and in none of the five patients in whom it was below the cutoff value. According to the report by Nambu et al. on internal carotid aneurysms, as recurrence was observed in 7 (64%) of the 11 patients in whom the PD was 2.83 or above but in none of the 39 patients in whom it was below 2.83, the PD is considered to be a useful predictor for internal carotid aneurysms.[8] The cutoff value was 2.83 in internal carotid aneurysms but was lower at 2.31 in anterior communicating aneurysms. As the pressure is lower in more distal blood vessels, the PD is also considered to be smaller, but it must also be evaluated in aneurysms of other distal vessels such as the middle cerebral artery.

In CFD analysis of anterior communicating aneurysms, the absolute blood flows of the bilateral A1s and the difference between the left and right A1s should be made closer to those in the actual *in vivo* environment.[12] To reduce these errors, the subjects were restricted to those in whom one A1 was not delineated by MRA to perform analysis by limiting the feeding artery to one A1. The high frequency of recurrence (in 4 of the 10 patients) observed in this study in patients with asymmetrical A1 was consistent with the previous report that recurrence was significantly more frequent in patients with asymmetrical A1 than in those with symmetrical A1.[7]

In previous reports on recurrence of aneurysms, the aneurysm or neck size was a risk factor, but in this study, it did not differ significantly between the recurrent and non-recurrent groups. The percentage of ruptured aneurysms was 75% (3/4) in the recurrent group and 33% (2/6) in the non-recurrent group, but the difference was not significant. The absence of significance was due to the small number of patients, and it is necessary to accumulate more cases and evaluate the relationship of these factors with PD.

If the PD is high before surgery for a cerebral aneurysm, suggesting that the risk of recurrence after coil embolization is high, the following two measures may be taken: One is clipping surgery, after which recurrence is reported to be

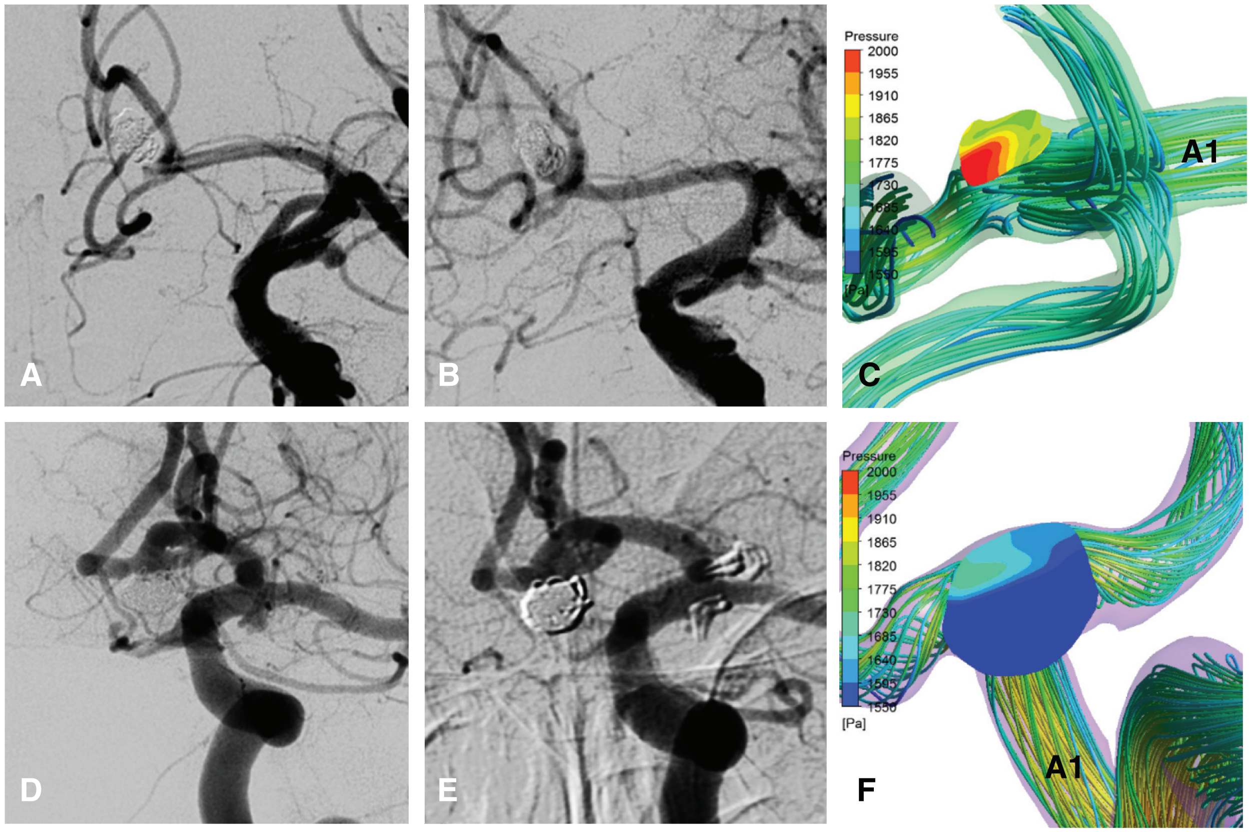

Fig. 3 In a recurrent case, the left anterior oblique view on left internal carotid artery angiography showed recanalization of the aneurysm after 7 months (**B**) compared with the image immediately after surgery (**A**). By analysis using a virtual post-coiling model, the maximum pressure on the coil surface was 2060 Pa (**C**). In a non-recurrent case, no intra-aneurysmal blood flow was noted after 1 year (**E**), similar immediately after surgery (**D**) by left internal carotid artery angiography. The maximum pressure on the coil surface was 1715 Pa (**F**).

significantly less frequent than after endovascular treatment.[1] The other is endovascular treatment using stents. One report stated that recurrence can be avoided by changing the shape of the parent artery due to the straightening effects of stenting.[13] As the PD is a factor dependent on the shape of the parent artery rather than the aneurysm, there are limitations that it cannot be used in the acute phase of rupture and that it may be changed by the straightening effects of the stent. Endovascular surgery is less invasive, and its indications are expected to be widened further if complications can be reduced by preoperative examination and more effective use of devices.[14,15] We began analysis of the PD using preoperative models because of the clinical usefulness of preoperative prediction of recurrence, but its validity must be evaluated using postoperative models.

Limitations

As this was a retrospective study of a small series of patients, prospective evaluation in a larger number of patients is necessary. Moreover, this study was conducted using patients with anterior communicating aneurysms with unilateral A1 hypoplasia; therefore, evaluation in patients with less A1 asymmetry is necessary. We evaluated the PD based on preoperative vascular information, but evaluation using actual postoperative vascular information is necessary.

Conclusion

In anterior communicating aneurysms with asymmetric A1, an increase in the PD was significantly correlated with recurrence after coil embolization. The PD may be useful for the prediction of recurrence of anterior communicating aneurysms and internal carotid aneurysms.

Disclosure Statement

The authors declare no conflicts of interest.

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