### **SUPPLEMENTARY DATA**

### **Geometry generation methods**

Three-dimensional images of the patients’ artery and embolization coil were generated as digital imaging and communication in medicine (DICOM) data from 3D-DSA data. The geometry data were converted to stereolithography (STL) data using 3D visualization software, Amira 5.6 (FEI Company, Hillsboro, OR, USA). The lumen of the embolization coil was filled manually to assume complete embolization.

### **Mesh generation methods**

Computational unconstructed volume grids were generated using ANSYS ICEM CFD 15.0 (ANSYS, Inc., Canonsburg, PA, USA) based on the STL geometry data of the artery and coils. Tetrahedral grids were arranged in the lumen of the vessel with an average size of 0.2 mm. In the vicinity of the vessel wall, seven-layer prism grids were fitted with a height of 0.3 mm. The grids of the coil were also generated using the same methods. Extended tubes 75 mm long were connected to all inlets and outlets.

### **Computational conditions**

Blood flow was analyzed using ANSYS CFX 15.0 (ANSYS, Inc.). We considered the blood as a Newtonian fluid with a density and viscosity of 1,100 kg/m3 and 0.0036 Pa･s, respectively. The flow field was assumed to be incompressible, laminar flow since the Reynolds number based on the diameter of the vessel and flow speed at the ICA was approximately 600. The vascular wall and surface of the coil were defined as rigid, non-slip boundaries. Unsteady flow analysis was performed over two heartbeats (1.8 s) with a 5 × 10–4 s time step.

## **Hemodynamic parameters**

A pressure difference (*PD*) was developed to determine the presence of thin-walled regions in unruptured aneurysms.[1] In this study, *PD* is formulated as:



where ** is the density of blood, *P* is arbitrary pressure, *Pavg* is the average pressure on the parent artery, and *vin* is the average velocity at the aneurysmal inlet.

The values for all the CFD parameters were sampled from the second systole in the analyzed pulsation.

## **Statistical methods**

Continuous variables were analyzed using the Kolmogorov–Smirnov test to determine whether the re-treatment and non-retreatment groups exhibited normal distribution. Fisher’s exact test was used to analyze the nominal scales. A *P* value less than 0.05 was considered statistically significant. We examined significant differences for each hemodynamic, morphological, and clinical parameter between the re-treatment and non-retreatment groups. Univariate logistic analysis was also performed for each parameter. If the sample size for the parameters are less than ten, Firth’s bias-adjusted estimates were applied. We confirmed multicollinearity for the variables with a *P* value of less than 0.1 and performed multivariable logistic analysis using the variables with a variance inflation factor (VIF) less than 10. Step-wise selection using the *P* value was performed; the variables were selected until the *P* value was less than 0.05 by iteration of the multivariable logistic analysis. Two-way interaction terms were considered after the variables were selected. In addition, the Hosmer-Lemeshow goodness-of-fit test was performed for the final logistic regression models. To estimate how accurately the final model will perform in practice, leave-one-out (100-fold) cross-validation was performed. Receiver operating characteristic (ROC) analysis was performed for the combined parameter to obtain a cutoff value. The cutoff value was defined using Youden’s index. [2, 3]

## **Supplementary Table 1, 2, and 3**

Supplementary table 1　Fisher's exact test for clinical parameters

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Total (n=100) | Non-retreatment (n=74) | Re-treatment (n=26) | *P* value |
| n | % | n | % | n | % |
| Location | (ICA) | 59 | 59.0% | 46 | 62.2% | 13 | 50.0% | 0.382 |
| (MCA) | 12 | 12.0% | 7 | 9.5% | 5 | 19.2% |
| (ACA) | 15 | 15.0% | 12 | 16.2% | 3 | 11.5% |
| (VABA) | 14 | 14.0% | 9 | 12.2% | 5 | 19.2% |
| Sex (Male) | 28 | 28.0% | 17 | 23.0% | 11 | 42.3% | 0.077  |
| History of alcohol consumption | 8 | 8.0% | 4 | 5.4% | 4 | 15.4% | 0.200  |
| Bleb | 18 | 18.0% | 12 | 16.2% | 6 | 23.1% | 0.553  |
| DM | 4 | 4.0% | 3 | 4.1% | 1 | 3.8% | 1.000  |
| HT | 44 | 44.0% | 28 | 37.8% | 16 | 61.5% | 0.042\* |
| Hyperlipidemia | 21 | 21.0% | 13 | 17.6% | 8 | 30.8% | 0.170  |
| Family history of SAH | 14 | 14.0% | 9 | 12.2% | 5 | 19.2% | 0.511  |

\**P*<0.05

ICA, Internal carotid artery; MCA, Middle cerebral artery; ACA, Anterior communicating artery; VABA, Vertebral artery and basilar artery; DM, Diabetes mellitus; HT, Hypertension; SAH, Subarachnoid hemorrhage

Supplementary table 2　Parametric or nonparametric test for hemodynamic and morphologic data

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | Total (n=100) | Non-retreatment (n=74) | Re-treatment (n=26) | *P* value | Statistical method |
| Mean | SD | Mean | SD | Mean | SD |
| *Ane.V\** | pre-Embo. | 0.522  | 0.193  | 0.522  | 0.192  | 0.522  | 0.198  | 0.891  | Mann–Whitney U-test |
| post-Embo. | 0.011  | 0.017  | 0.008  | 0.013  | 0.017  | 0.023  | 0.036\* | Mann–Whitney U-test |
| Reduc. Rate | 0.977  | 0.036  | 0.982  | 0.029  | 0.962  | 0.049  | 0.034\* | Mann–Whitney U-test |
| *Ane.VMax\** | pre-Embo. | 1.662  | 0.288  | 1.663  | 0.291  | 1.659  | 0.287  | 0.991  | Mann–Whitney U-test |
| post-Embo. | 0.886  | 0.521  | 0.867  | 0.521  | 0.940  | 0.530  | 0.538  | Student's t-test |
| Reduc. Rate | 0.477  | 0.287  | 0.489  | 0.286  | 0.441  | 0.291  | 0.372  | Mann–Whitney U-test |
| *NeckVIn\** | pre-Embo. | 0.904  | 0.221  | 0.920  | 0.206  | 0.857  | 0.259  | 0.213  | Student's t-test |
| post-Embo. | 0.259  | 0.300  | 0.236  | 0.262  | 0.326  | 0.389  | 0.732  | Mann–Whitney U-test |
| Reduc. Rate | 0.724  | 0.310  | 0.754  | 0.270  | 0.641  | 0.396  | 0.492  | Mann–Whitney U-test |
| *NeckVInMax\** | pre-Embo. | 1.598  | 0.257  | 1.603  | 0.260  | 1.584  | 0.252  | 0.884  | Mann–Whitney U-test |
| post-Embo. | 0.826  | 0.495  | 0.809  | 0.478  | 0.875  | 0.547  | 0.574  | Mann–Whitney U-test |
| Reduc. Rate | 0.488  | 0.297  | 0.501  | 0.285  | 0.450  | 0.331  | 0.425  | Mann–Whitney U-test |
| *NeckMF* | pre-Embo. | 0.628  | 0.331  | 0.606  | 0.317  | 0.693  | 0.367  | 0.270  | Mann–Whitney U-test |
| post-Embo. | 0.103  | 0.167  | 0.086  | 0.135  | 0.152  | 0.234  | 0.219  | Mann–Whitney U-test |
| Reduc. Rate | 0.824  | 0.240  | 0.854  | 0.186  | 0.737  | 0.341  | 0.259  | Mann–Whitney U-test |
| *NeckPD* | pre-Embo. | 0.193  | 0.393  | 0.174  | 0.399  | 0.244  | 0.381  | 0.444  | Mann–Whitney U-test |
| post-Embo. | 0.333  | 0.453  | 0.357  | 0.393  | 0.265  | 0.596  | 0.959  | Mann–Whitney U-test |
| Incre. Rate | 0.262  | 4.541  | 0.093  | 4.752  | 0.742  | 3.924  | 0.147  | Mann–Whitney U-test |
| *NeckPDMax* | pre-Embo. | 1.197  | 0.749  | 1.121  | 0.703  | 1.411  | 0.844  | 0.161  | Mann–Whitney U-test |
| post-Embo. | 2.030  | 1.162  | 1.996  | 1.169  | 2.126  | 1.160  | 0.663  | Mann–Whitney U-test |
| Incre. Rate | 1.378  | 3.145  | 1.750  | 3.207  | 0.320  | 2.749  | 0.079  | Mann–Whitney U-test |
| *CoilPD* | 0.427  | 0.547  | 0.445  | 0.462  | 0.376  | 0.747  | 0.972  | Mann–Whitney U-test |
| *CoilPDMax* | 2.790  | 2.125  | 2.555  | 1.281  | 3.461  | 3.530  | 0.207  | Mann–Whitney U-test |
| *VER* | 0.232  | 0.050  | 0.238  | 0.051  | 0.215  | 0.047  | 0.049\* | Mann–Whitney U-test |
| AneurysmVolume (mm3) | 299.097  | 381.186  | 278.720  | 287.864  | 357.091  | 573.328  | 0.543  | Mann–Whitney U-test |
| NeckArea (mm2) | 23.141  | 13.559  | 21.523  | 12.441  | 27.745  | 15.694  | 0.093  | Mann–Whitney U-test |
| Age (years) | 60.000  | 12.538  | 59.500  | 13.144  | 61.423  | 10.730  | 0.715  | Mann–Whitney U-test |

\**P*<0.05

SD, Standard deviation; Ane., Aneurysm; V, Velocity; MF, Mass flow; PD, Pressure difference; Embo., Embolization; Reduc., Reduction; Incre., Increase.; VER, Volume embolization ratio

Supplementary table 3　Univariate logistic analysis for clinical data and hemodynamics

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | OR | 95% CI | *P* value | VIF |
| *Ane.V\** | pre-Embo. | 1.010  | 0.098  | 10.400  | 0.996  | 　 |
| post-Embo. | 5.51×1011 | 1.560  | 1.94×1023 | 0.046† | 7.441  |
| Reduc. Rate | 1.42×10-6 | 1.41×10-11 | 0.144  | 0.022† | 4.379  |
| *Ane.VMax\** | pre-Embo. | 0.952  | 0.200  | 4.540  | 0.951  | 　 |
| post-Embo. | 1.310  | 0.555  | 3.110  | 0.534  | 　 |
| Reduc. Rate | 0.548  | 0.112  | 2.680  | 0.458  | 　 |
| *NeckVIn\** | pre-Embo. | 0.266  | 0.033  | 2.130  | 0.213  | 　 |
| post-Embo. | 2.570  | 0.619  | 10.700  | 0.194  | 　 |
| Reduc. Rate | 0.326  | 0.082  | 1.300  | 0.113  | 　 |
| *NeckVInMax\** | pre-Embo. | 0.754  | 0.128  | 4.450  | 0.755  | 　 |
| post-Embo. | 1.310  | 0.528  | 3.260  | 0.558  | 　 |
| Reduc. Rate | 0.553  | 0.120  | 2.550  | 0.447  | 　 |
| *NeckMF* | pre-Embo. | 2.180  | 0.580  | 8.200  | 0.249  | 　 |
| post-Embo. | 8.090  | 0.648  | 101.0  | 0.105  | 　 |
| Reduc. Rate | 0.158  | 0.027  | 0.925  | 0.041† | 4.173  |
| *NeckPD* | pre-Embo. | 1.550  | 0.514  | 4.680  | 0.436  | 　 |
| post-Embo. | 0.643  | 0.240  | 1.720  | 0.380  | 　 |
| Incre. Rate | 1.040  | 0.927  | 1.160  | 0.531  | 　 |
| *NeckPDMax* | pre-Embo. | 1.650  | 0.918  | 2.950  | 0.094† | 1.396  |
| post-Embo. | 1.100  | 0.759  | 1.580  | 0.624  | 　 |
| Incre. Rate | 0.760  | 0.561  | 1.030  | 0.078† | 1.385  |
| *CoilPD* | 0.794  | 0.353  | 1.790  | 0.577  | 　 |
| *CoilPDMax* | 1.210  | 0.950  | 1.540  | 0.123  | 　 |
| *VER* | 2.83×10-5 | 7.58×10-10 | 1.060  | 0.051† | 1.112  |
| AneurysmVolume (mm3) | 1.000  | 0.999  | 1.000  | 0.380  | 　 |
| NeckArea (mm2) | 1.030  | 0.999  | 1.060  | 0.055† | 1.355  |
| ICA | (yes vs. no) | 0.609  | 0.247  | 1.500  | 0.280  | 　 |
| MCA | (yes vs. no) | 2.280  | 0.654  | 7.940  | 0.196  | 　 |
| ACA | (yes vs. no) | 0.674  | 0.174  | 2.610  | 0.567  | 　 |
| VABA | (yes vs. no) | 1.720  | 0.519  | 5.700  | 0.375  | 　 |
| Sex | (males vs. females) | 2.460  | 0.953  | 6.350  | 0.063† | 1.341  |
| History of alcohol consumption (yes vs.no) | 3.134 | 0.724 | 13.57 | 0.127 | 　 |
| Bleb | (yes vs. no) | 1.550  | 0.515  | 4.670  | 0.436  | 　 |
| DM | (yes vs. no) | 1.202 | 0.135 | 10.70 | 0.869 | 　 |
| HT | (yes vs. no) | 2.630  | 1.050  | 6.590  | 0.039† | 1.324  |
| Hyperlipidemia | (yes vs. no) | 2.090  | 0.748  | 5.820  | 0.160  | 　 |
| Family history of SAH | (yes vs. no) | 1.764 | 0.536 | 5.813 | 0.351 | 　 |
| Age (years) | 1.010  | 0.976  | 1.050  | 0.500  | 　 |

†*P*<0.1

OR, Odds ratio; CI, Confidence interval; VIF, Variance inflation factor; Ane., Aneurysm; V, Velocity; MF, Mass flow; PD, Pressure difference; Embo., Embolization; Reduc., Reduction; Incre., Increase.; VER, Volume embolization ratio; ICA, Internal carotid artery; MCA, Middle cerebral artery; ACA, Anterior communicating artery; VABA, Vertebral artery and basilar artery; DM, Diabetes mellitus; HT, Hypertension; SAH, Subarachnoid hemorrhage

### **References**

[1] Suzuki T, Takao H, Suzuki T, et al. Determining the Presence of Thin-Walled Regions at High-Pressure Areas in Unruptured Cerebral Aneurysms by Using Computational Fluid Dynamics. *Neurosurgery* 2016;79:589-95.

[2] Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. *Biom J*. 2005 Aug;47(4):458-72.

[3] Perkins NJ, Schisterman EF. The inconsistency of “optimal” cutpoints obtained using two criteria based on the receiver operating characteristic curve. *Am J Epidemiol*. 2006 Apr 1;163(7):670-5.