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Aspect Ratio Is Associated with Recanalization after Coiling of Unruptured Intracranial Aneurysms

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Abstract

The rate of recanalization after coil embolization for unruptured intracranial aneurysms (UIAs) is reported to occur around 11.3%-49%. This study aims to investigate the factors that influence the recanalization after coil embolization for UIAs in our institution. We retrospectively investigated 307 UIAs in 296 patients treated at our institution between April 2004 and December 2016. The stent-used cases were excluded. Cerebral angiography and 3D time-of-flight magnetic resonance angiography (TOF MRA) were used for evaluation of the postoperative occlusion status. Volume embolization ratio (VER), aneurysmal size, neck width, and aspect ratio (AR) were compared between the recanalized and non-recanalized groups. The mean follow-up period ranged from 6 to 172 months (mean: 79.0 ± 39.8 months). Recanalization was noted in 78 (25.4%) aneurysms, and 19 (6.2%) aneurysms required retreatment. There was no aneurysmal rupture during the follow-up period. Univariate analysis showed that the aneurysm size ($p < 0.001$), neck width ($p < 0.001$), AR ($p = 0.003$), and VER ($p = 0.012$) were associated with recanalization. Multivariate logistic regression analysis showed that the AR ($p = 0.004$) and VER ($p = 0.015$) were significant predictors of recanalization. To summarize, a higher AR and a lower VER could lead to recanalization after coil embolization of UIAs. Careful follow-up is required for coiled aneurysms with these features.

Keywords: unruptured intracranial aneurysms, aspect ratio, coil embolization, recanalization

Introduction

Coil embolization is an established treatment for both unruptured and ruptured intracranial aneurysms. To prevent rupture, long-term durability after coil embolization is required. Despite developments in techniques and devices, the recanalization rate following coil embolization has been reported to occur in 11.3%-49%[1-3] of unruptured intracranial aneurysms (UIAs). Although the aneurysm size,[3-8] neck width,[7,8] volume embolization ratio (VER),[3,6,8] and patient age[4] have been recognized as risk factors for recanalization,[4,5] few studies have reported that morphological factors are related to recurrence. Thus, this study aimed to evaluate the factors that might influence recanalization following coil embolization of UIAs.

Materials and Methods

Patient population

Between April 2004 and December 2016, 307 unruptured intracranial saccular aneurysms in 296 patients were treated with coil embolization at our institution. Patients who were treated with stent-assisted coil embolization were excluded. All patients who were available for postoperative or MR angiography 6 months after treatment were included.

Endovascular treatment

All procedures were performed with patients under general anesthesia, and a transfemoral approach was used.

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Heparin (initial dose of 4,000 IU) was provided for anticoagulation after arterial access was obtained via the femoral artery. Coil insertion was initiated after confirmation of an activated clotting time (ACT) of over 250 seconds, with continuous administration of heparin to maintain an ACT of 250-300 seconds. Techniques for the endovascular procedure (i.e., simple technique, double-catheter technique, balloon-assisted technique, or double-catheter with balloon-assisted technique) and selection of coils were decided along with each aneurysm's location and morphology, such as volume, neck width, and maximum diameter. After completing coil placement, systemic heparinization was stopped but not reversed. Patients were then transferred to a neurosurgical intensive care unit, and intravenous argatroban (120 mg/day) was administered for 2 days.

Regimen for antiplatelet therapy and anticoagulation

All patients received antiplatelet therapy during the perioperative period. Administration of antiplatelet drugs was started 4 days to 2 weeks before the procedure. A single antiplatelet agent was given to patients who had narrow neck aneurysms (<4 mm), which was 81-200 mg/day of aspirin. Dual antiplatelet drugs were given to patients who had wide-neck aneurysms (≥4 mm) which comprised 100-200 mg/day of cilostazol, 100-200 mg/day of ticlopidine, or 75 mg/day of clopidogrel, added to aspirin. For dual therapy regimens, aspirin was the first-line drug, whereas cilostazol or thienopyridine (ticlopidine/clopidogrel) was used as an adjuvant. In the single therapy group, administration of antiplatelets was completed within 1-6 months of the procedure. In the dual therapy group, antiplatelet drugs were reduced to one drug (aspirin in most cases) 1 week to 3 months after the procedure, and administration was completed within 3-6 months.

Follow-up regimen

During hospitalization, a 3D TOF MRA and a craniogram were obtained 2 days after the procedure for comparison with immediate angiographic outcomes. Following discharge, 3D TOF MRAs and craniograms were obtained at 6, 12, and 24 months and annually thereafter. Angiography was the procedure, if recanalization of aneurysms was suspected with the above evaluations.

We designed a 3D TOF-MRA technique to depict embolized aneurysms that employed a short TE (1.54-1.60 ms) and a high spatial resolution ($0.3 \times 0.3 \times 0.3$ mm^3 with zero-filling) to reduce spin dephasing. To reduce spin saturation, the image volume was carefully positioned so that the neck of the targeted aneurysm was within 2 cm of the inflow portion along the direction of blood flow.[9]

Measurement of VER

To measure the aneurysm volume, the aneurysm was manually segmented from the parent artery on a 3D reconstruction, and the volume was calculated using machine software (3D-DSA workstation, Philips Medical Systems, Best, The Netherlands). To eliminate potential bias in the threshold setting, we used gradient edge detection as described by Bescos et al.[10]

Definition of recanalization

The Raymond scale is a commonly used outcome grading scale,[11] which divides angiographic outcomes of embolized aneurysms into three categories, that is, (1) complete occlusion, (2) neck remnant, and (3) residual aneurysm. Because of its simplicity, a detailed morphological evaluation can be difficult. For example, significant changes in the aneurysm morphology and occlusion may occur within the same category using the three-category scale. Recently, Meyers et al. have highlighted the importance of consensus recommendations for reporting standards, terminology, and written definitions when reporting radiological evaluations and endovascular treatments of intracranial cerebral aneurysms.[12] In their report, they proposed a 6-point consensus grading system (CGS) to assess angiographic outcomes which are shown in Supplementary Table 1. In this study, we used the CGS and defined recanalization as worsening of CGS by 1 point.

Statistical analysis

Data were analyzed using JMP version 9.02 (SAS Institute, Cary, NC). We analyzed multiple clinical and anatomical factors that are thought to influence recanalization, i.e., patient age, sex, aneurysm size, neck width, aspect ratio (AR; height to neck width), and VER. The significance of intergroup differences was assessed using a chi-squared test for categorical variables and a t-test for continuous variables. Furthermore, multivariate analysis was performed using the aneurysm size, neck width, AR, and VER. Statistical significance was taken as $p < 0.05$.

This study was conducted according to the principles expressed in the Declaration of Helsinki (1964) and was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center (Approval no. M30-013-2). Informed consent was waived because of its retrospective design, and the opportunity to opt out of the study was approved through the website.

Results

Patient characteristics and aneurysm profiles are provided in Table 1. The mean age of patients was 61.6 years (range, 27-83 years), and 73.3% (225/307) of patients were women. The mean follow-up period was 79.0 ± 39.8 months (range, 6-172 months). The mean aneurysm size was found to be 7.0 ± 2.7 mm. The mean neck width was 4.0 ± 1.7 mm. As per our findings, it was determined that 144 patients had small-neck (<4 mm) and 163 had wide-neck (≥4 mm) aneurysms. The mean AR was 1.48 ± 0.59.

Table 1 Profiles of Patients and Aneurysms

Patient characteristics	
Age, mean (yrs) ± SD	61.6 ± 11.4
Female, *n* (%)	225 (73.3)
Follow-up period, mean ± SD (range)	79.0 ± 39.8 (6-172)
Aneurysm characteristics	
Maximum size, mean (mm) ± SD	7.0 ± 2.7
Neck size, mean (mm) ± SD	4.0 ± 1.7
Small neck (<4 mm), *n* (%)	144 (46.9)
Wide neck (≥4 mm), *n* (%)	163 (53.1)
Aspect ratio, mean ± SD	1.48 ± 0.59

Table 2 Aneurysm Location

Location	Number (%)
Anterior circulation	221 (72)
Paraclinoid	106 (34.5)
ICA-PCom	33 (10.7)
ICA-AChA	5 (1.6)
ACoA	54 (17.6)
DACA	7 (2.3)
MCA	2 (0.6)
Other	14 (4.6)
Posterior circulation	86 (28%)
BA bifurcation	51 (16.6)
BA-SCA	12 (3.9)
VA-PICA	9 (2.9)
Other	14 (4.6)
Total	307

Abbreviations:
ICA: internal carotid artery, PCom: posterior communicating artery, AChA: anterior choroidal artery, BA: basilar artery, VA: vertebral artery, SCA: superior cerebellar artery, and PICA: posterior inferior cerebellar artery.

The locations of aneurysms are shown in Table 2. In total, 72.0% (221/307) of aneurysms were located in the anterior circulation (106 in the paraclinoid; 54 in the anterior communicating artery; 33 in the posterior communicating artery; 10 in the carotid terminus; 7 in the pericallosal artery; 2 in the middle cerebral artery; 5 in the anterior choroidal artery; and 4 in the ophthalmic artery). Meanwhile, 28.0% (86/307) were located in the posterior circulation (51 in the basilar bifurcation; 12 in the superior cerebellar artery; 9 in the vertebral artery; 9 in the posterior inferior cerebellar artery; and 5 in the posterior cerebral artery).

Technical methods performed in this study are as follows: 101 cases with the simple technique, 176 cases with the balloon-assisted technique, 18 cases with the double-catheter technique, and 12 cases with a combination of double-catheter and balloon-assisted techniques.

Immediate results and procedure-related complications

Initial occlusion statuses achieved were Grade 0 in 25.4% (78/307), Grade 1 in 65.5% (201/307), Grade 2 in 6.2% (19/307), and Grade 3 in 2.9% (9/307). None of the aneurysms resulted in Grade 4 or 5. Procedure-related complications were noted in 5.5% (17/307) of all procedures. Hemorrhagic events occurred in three patients (1.0%). One of the three patients had extravasation which was asymptomatic, and the other two patients had a gastrointestinal hemorrhage. Ischemic events occurred in 10 patients (3.3%). Eight patients (2.6%) suffered from a transient ischemic attack (defined as a new neurological symptom lasting less than 24 hours), and the remaining two patients (0.7%) had a stroke (defined as a new neurological deficit lasting over 24 hours). All strokes were minor (National Institutes of Health Stroke Scale < 4 and mRS ≤ 2). Two patients had a femoral hematoma related to an arterial puncture, which required blood transfusion or repair. One patient had transient oculomotor nerve palsy and one patient had visual impairment, which was due to a mass effect of the coils. An asymptomatic carotid-cavernous fistula occurred in one patient. The total mortality rate was 0 %, and the morbidity rate was 0.7%.

Recanalization and retreatment

Recanalization, according to the definition above, was observed in 25.4% (78/307) of all aneurysms, and retreatment was required in 6.2% (19/307) of all aneurysms.

The worsening of grades and follow-up periods are shown in Table 3. Six months after the procedure, 13.4% (41/307) of aneurysms showed recanalization. A 1-point worsening of grade was noted in 38 aneurysms, and a 2-point worsening was observed in three aneurysms. None of the patients required retreatment during this term.

Between 6 and 12 months after the procedure, new recanalization was noted in 6.8% (21/307) of aneurysms. A 1-point worsening of grade was noted in 19 aneurysms, whereas a 2-point worsening was noted in two aneurysms. Three patients required retreatment during this term (range 9-10 months).

Between 12 and 24 months after the procedure, new recanalization was observed in 5.9% (18/307) of aneurysms. A 1-point worsening of grade was noted in 18 aneurysms. Meanwhile, none of the patients showed a 2-point worsening during this term. Six patients required retreatment during this term (range 13-23 months).

At 24 months after the procedure, new recanalization was noted in seven (2.3%) aneurysms. A 1-point worsening of grade was noted in six aneurysms, while a 2-point wors-

Table 3 The Worsening Grade and Follow-up Period of Recanalization

Worsening grading scale	CGS grade	Follow-up period				Total (n, %)
		-6 m	6-12 m	12-24 m	24 m-	
1 point	0 to 1	8	2	2	1	13 (4.2)
	1 to 2	29	10	10	1	50 (16.3)
	2 to 3	1	5	5	3	14 (4.6)
	3 to 4	-	2	1	1	4 (1.3)
	4 to 5	-	-	-	-	-
2 point	0 to 2	2	-	-	-	2 (0.7)
	1 to 3	1	2	-	-	3 (1.0)
	2 to 4	-	-	-	1	1 (0.3)
	3 to 5	-	-	-	-	-
Total (n, %)		41 (13.4)	21 (6.8)	18 (5.9)	7 (2.3)	87 (28.3)

Table 4 Univariate Analysis for Risk Factor of Aneurysm Recanalization

	Recanalization (+)	Recanalization (-)	p-value
n (%)	78 (25.4)	229 (74.6)	
Age, mean (yrs) ± SD	60.2 ± 12.3	62.0 ± 11.1	0.382
Male, n (%)	20 (26.3)	61 (26.5)	0.961
Maximum size, mean (mm) ± SD	8.8 ± 3.7	6.5 ± 2.0	<0.001
Neck size, mean (mm) ± SD	4.8 ± 2.3	3.9 ± 1.3	<0.001
AR, mean ± SD	1.68 ± 0.66	1.42 ± 0.55	0.003
VER, mean ± SD	25.6 ± 5.6	27.3 ± 6.3	0.012
CO, n (%)	12 (15.8)	65 (28.1)	0.083

Abbreviations:
AR: aspect ratio, VER: volume embolization ratio, and CO: complete obliteration.

Table 5 Multivariate Analysis for Risk Factor of Aneurysm Recanalization

	Odds Ratio (95% CI)	p-value
Maximum size	1.27 (0.94-1.73)	0.119
Neck size	1.21 (0.74-1.96)	0.444
Aspect ratio	4.15 (1.57-11.00)	0.004
Volume embolization ratio (VER)	0.94 (0.90-0.99)	0.015
Complete obliteration	0.83 (0.18-3.83)	0.814

ening was noted in one aneurysm. Ten patients required retreatment during this term (range 25-160 months).

Results of the univariate analysis are shown in Table 4. The aneurysm size ($p < 0.001$), neck width ($p < 0.001$), AR ($p = 0.003$), and VER ($p = 0.012$) were found to be associated with the occurrence of recanalization. Patient age, sex, and complete occlusions on completion of the procedure were not associated with recanalization.

The multivariate logistic regression analysis showed that AR (odds ratio [OR]: 4.15, 95% confidence interval [CI]: 1.57, 11.00, $p < 0.01$) and VER (OR: 0.94, 95% CI: 0.90, 0.99, $p = 0.02$) were significant predictors of recanalization (Table 5). In this study, the ROC curve analysis showed that an AR of 1.6 was the cut-off value for recanalization after coiling (sensitivity, 51%; specificity, 31%). Therefore, all aneurysms were divided into two groups: group L (AR < 1.6) and group H (AR ≥ 1.6). The mean VERs of groups H and L were 27.51% ± 0.58% and 26.49% ± 0.44%, respectively. No significant difference between these two groups was observed ($p = 0.08$). Furthermore, when we classified each of these two groups according to the size (small (3 ≤ mm < 7), medium (7 ≤ mm < 10), or large (10 ≤ mm)), there was no significant difference between the aneurysm size and VER in each group (Supplementary Table 2).

Discussion

Coil embolization of intracranial aneurysms has become a common technique with recent developments in devices and adjunctive techniques. Although the overall outcome of coil embolization is deemed favorable, recanalization following treatment has become a greater concern compared with surgical clipping.[2,4,13-17)]

Recanalization rate after coil embolization has been reported to occur in 11.3%-49% or 11.3%-38.0% of UIAs.[1-3)] Recanalization rates vary widely across reports. This may be because of differences in the definition of recanalization, follow-up duration, image modality used for follow-up, and advances in imaging modalities. Meyers et al. highlighted the importance of consensus recommendations for reporting standards, terminology, and written definitions when reporting radiological evaluations and endovascular treatments of intracranial cerebral aneurysms and recommended the use of a 6-point CGS for the evaluation of recanalization.[12)] These definitions are thus helpful for making direct comparisons between studies. Digital subtraction angiography remains the gold standard modality for follow-up; however, the superiority of the less-invasive TOF MRA for follow-up evaluations for coiled aneurysms has been advocated in several reports.[9,18,19)] Since the past report suggested the similarity of very short TE TOF-MRA and DSA to visualization of residual neck flow after coiling aneurysms,[10)] we replaced DSA with MRA to evaluate this grading for long-term follow-up. After confirming the homology of MRA and DSA images with those performed after the procedure, the Meyer scale was judged by a neuroradiologist independent from treatment at each follow-up period. In our study, recanalization was defined as worsening of the CGS score by more than 1 point, and these patients were evaluated using 3D TOF MRA.

Several factors such as aneurysm size,[3-8)] neck width,[7,8)] VER,[3,6,8)] and patient age[4)] have been reported as risk factors for recanalization. In our study, we found that AR and VER were significant predictors of recanalization. To date, AR has not been reported as a factor influencing recanalization.

AR is a pre-interventional morphological feature of aneurysms that is calculated by dividing the aneurysm depth by the aneurysm neck width. Generally, aneurysms with a high AR are embolized with ease compared with those with a low AR. Brinjikji et al. have reported that aneurysms with an AR and a dome-to-neck ratio < 1.2 usually require adjunctive techniques. Furthermore, AR was an independent predictor of the need for adjunctive techniques.[20)]

Regarding AR and recurrence of coiled aneurysms, there was a Japanese report demonstrating that low AR was a factor for recurrence by analyzing a single-center experience although the number of cases was smaller than ours and detailed statistical data were not shown.[21)] On the other hand, a low VER was designated as a factor for recanalization in our study similar to previous studies listed above; the importance of VER should be well taken care of. Sadato et al. reported that dense packing was difficult to achieve in aneurysms with a low AR when stents were not used.[22)] Therefore, the recurrence in aneurysms with a low AR could be strongly affected by a low VER in these aneurysms. In our study, however, a comparison of groups H and L according to the size showed no significant difference between each group (Supplementary Table 2). This uniformity of VER regardless of the AR and aneurysmal size strongly influenced our result that a high AR was designated as a factor for recurrence.

Regarding the hemodynamic stress for coiled aneurysms, Bavinzski et al. investigated gross and microscopic histopathological findings of aneurysms treated with GDC obtained at autopsy. They discovered tiny open spaces between the coils and aneurysm neck on post-interventional angiographies, even when complete obliteration was achieved.[23)] Mitsos et al. have also performed hemodynamic simulation of aneurysm coiling using an anatomically accurate computational fluid dynamics (CFD) model.[24)] On completion of coiling, the flow at the coil mesh/parent vessel interface was detected (i.e., at the aneurysm neck area), even if packing densities over 24-25% were achieved. Moreover, gradual coil introduction resulted in a stepwise relief of wall pressure at the aneurysm dome, and redistribution of wall pressure was identified at the aneurysm inflow zone. These factors may have contributed to recanalization after coil embolization and may correlate with parent vessel geometry.

We excluded the stent-used cases in this study. Stent-assisted coiling (SAC) of intracranial aneurysms has been proposed for the treatment of fusiform or wide-neck aneurysms when other conventional endovascular techniques are not feasible. Several studies have reported that SAC decreases recanalization after coiling.[25,26)] The coverage of the aneurysm neck prevents coil migration to the parent artery, which then contributes to the increase in packing density. Moreover, the flow-diversion effect, which causes progressive occlusion and angulation change of the parent artery due to the straightening effect of the stent,[27,28)] was also shown to decrease recanalization after coiling. Conversely, these hemodynamic and morphological changes of the aneurysm and parent artery caused by stent deployment may affect original anatomical features. Thus, the SAC cases were excluded to enable verification of the relationship among aneurysm morphology, geometry, and coil embolization.

AR has been reported as a predictor of aneurysm rupture.[29-33)] There have been several reports on the correlation between parent vessel geometry and the risk of aneurysm rupture and growth. Hassan et al. reported a correlation between aneurysm depth and both neck width and caliber of draining arteries.[34)] Furthermore, the incidence of rupture of aneurysms with an AR exceeding 1.6 was 100% in the categories of a side wall and a side wall with branching vessels. Hoi et al. studied the hemodynamics of 3D saccular aneurysms arising from the lateral wall of arteries with varying arterial curves (starting with a straight vessel model) and neck width using CFD analysis.[35] They reported that as the degree of arterial curvature increased, flow impingement on the distal side of the neck has also intensified, which led to the enlargement of the impact zone at the distal side of the aneurysm neck, and the large impact zone at the distal side of the aneurysm neck correlated with aneurysm growth and regrowth of treated lesions.

Another recent report regarding the recurrence of ophthalmic segment aneurysms listed high AR as an independent factor for recanalization.[36] Based on these reports, aneurysms with a high AR may occur in regions of higher hemodynamic stress, and this may lead to recanalization after coil embolization. Further CFD studies investigating the correlation between AR and recanalization are required.

In addition, the use of CGS or Meyers' scale, which is a more detailed grading, and the definition of recanalization as the one point worsening in our study may also affect the results. The commonly used Raymond and Roy scale is a 3-point grading (complete obliteration, residual neck, and residual aneurysm). If there was a change of aneurysm occlusion status from 1 to 2 in CGS, was judged as no recurrence in the studies which applied Raymond and Roy classification.

To sum up, aneurysms with a high AR may have high hemodynamic stress, and we consider that it emerged as a factor for the recurrence of coiled aneurysms by eliminating the influence of VER, another major factor for recanalization, and adopting CGS.

There are several limitations of this study. This was a single-center retrospective study. There was also a degree of selection bias. Therefore, the patients in this study are not representative of all patients with UIAs. Furthermore, the general indications and choice of treatment method are different across institutions. Optimal coil selection and adjunctive techniques (including neck bridging stent) may be required to aim for a high VER when the coil embolization was considered in aneurysms with high AR.

Recently, the treatment without inserting a coil in an aneurysm, such as a flow-diverter device, is being actively performed. In these cases, a morphological factor of AR and a treatment factor of VER are considered to be less important. However, coil embolization is still prioritized in ruptured cases, there may be some values for predicting the aneurysms recurrence after coiling and the selection of endovascular treatment strategies.

Conclusion

AR and VER were significant predictors of recanalization after coil embolization of UIAs. Coiled aneurysms with a high AR and a low VER should be carefully observed with appropriate imaging.

Supplementary Material

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Acknowledgments

Not applicable.

Abbreviations

UIAs: unruptured intracranial aneurysms, VER: volume embolization ratio, ACT: activated clotting time, TOF: time-of-flight, CGS: consensus grading system, AR: aspect ratio, CFD: computational fluid dynamics, SAC: stent-assisted coiling

Conflicts of Interest Disclosure

Dr. Hara, Dr. Hamano, Dr. Hashimura, Dr. Sumi, Dr. Ikedo, Dr. Ohta, Dr. Takahashi, and Dr. Kataoka declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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