Aspect ratio is associated with recanalization after coiling of unruptured intracranial aneurysms

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Abstract

Background

The rate of recanalization after coil embolization for unruptured intracranial aneurysms (UIAs) is reported to occur around 11.3-49%. Aim of this study is to investigated the factors that influence the recanalization after coil embolization for unruptured intracranial aneurysms (UIAs) in our institution.

Methods

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 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.

Results

The mean follow-up period ranged from 6 to 172 months (mean: 79.0±39.8 months). Recanalization was noted in 87 (28.3%) 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 ($p = 0.002$), AR ($p = 0.003$), and VER ($p = 0.027$) 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.

Conclusions

In our study, AR and VER were significant predictors of recanalization after coil embolization for UIAs.

Background

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, recanalization rate following coil embolization has been reported to occur in 11.3–49% [1-3] of unruptured intracranial aneurysms (UIAs). Although 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 of 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.

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 trans-femoral approach was used. 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. 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 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 time-of-flight (TOF) MRA and 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 procedure, if recanalization of aneurysms were suspected with above evaluations.

We designed a 3D TOF MRA technique to depict embolized aneurysms that employed a short TE (1.54–1.60 ms) and high spatial resolution (0.3 × 0.3 × 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 aneurysm volume, the aneurysm was manually segmented from the parent artery on a 3D reconstruction, and the volume was calculated using a 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 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) in order to assess angiographic outcomes, which are shown in Table 1. In this study, we used the CGS and defined recanalization as a 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. Significance of intergroup differences was assessed using a chi-square test for categorical variables and a t-test for continuous variables. Furthermore, multivariate analysis was performed using aneurysm size, neck width, aspect ratio (AR), aneurysm type, and VER. Significance was signified by $p < 0.05$.

The protocol of this study was approved by our Institutional Review Board (Approval #M30-013-2).

Results

Patient characteristics and aneurysm profiles are provided in Table 2. Mean age of patients was 61.6 years (range, 27–83 years), and 73.3% (225/307) of patients were women. Mean follow-up period was 79.0 ± 39.8 months (range, 6–172 months). Mean aneurysm size was found to be 7.0 ± 2.7 mm. 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. Mean AR was 1.48 ± 0.59.

The locations of aneurysms are shown in Table 3. 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).

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 Grades 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 were asymptomatic, and the other two patients had gastrointestinal hemorrhage. Ischemic events occurred in 10 patients (3.3%). Eight patients (2.6%) suffered from a transient ischemic attack (defined as new neurological symptoms lasting less than 24 hours), and the remaining two patients (0.7%) had a stroke (defined as new neurological deficits lasting over 24 hours). All strokes were minor (National Institutes of Health Stroke Scale < 4 and mRS $\leq$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. Total mortality rate was 0 %, and morbidity rate was 0.7%.

Recanalization and retreatment

Recanalization, according to the definition above, was observed in 28.3% (87/307) 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 4. 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 worsening 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 5. Aneurysm size (p < 0.001), neck width (p = 0.002), AR (p = 0.003), and VER (p = 0.027) were found to be associated with occurrence of recanalization. Patient age, sex, anterior/posterior circulation, or 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, $p = 0.004$) and VER (OR: 0.94, 95% CI: 0.90, 0.99, $p = 0.015$) were significant predictors of recanalization (Table 6).

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, 15-17].

Recanalization rate after coil embolization has been reported to occur in 11.3–49% [1, 2] or 11.3–38.0% [1, 3] of UIAs. 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 [12] and recommended the use of a 6-point CGS for the evaluation of recanalization. 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]. Therefore, in our study, recanalization was defined as a worsening of 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 aneurysm depth by 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 dome-to-neck ratio <1.2 usually require adjunctive techniques. Furthermore, AR was an independent predictor of the need for adjunctive techniques[20)]. In this study, the ROC curve analysis showed that an AR of 1.5 was the cut-off value for recanalization after coiling (sensitivity, 56%; specificity, 65%). Therefore, all aneurysms were divided into two groups: group L (AR < 1.5) and group H (AR ≥ 1.5). Mean VERs of group H and L were 25.27% ± 6.06% and 25.74% ± 5.08%, respectively. No significant difference was observed between the two groups ($p = 0.713$). Our data demonstrated that a high AR is a risk factor of recanalization, whereas VER was equivalent across groups.

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 [21]. Mitsos et al. have also performed hemodynamic simulation of aneurysm coiling using an anatomically accurate computational fluid dynamics (CFD) model[22]. On completion of coiling, 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 a 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.

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[23][24]. 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[25] and angulation change of the parent artery due to the straightening effect of the stent [26], 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. In our study, the SAC cases were excluded to enable verification of the relationship between aneurysm morphology, geometry, and coil embolization.

AR has been reported as a predictor of aneurysm rupture[27-31]. There have been several reports on the correlation between parent vessel geometry and risk of aneurysm rupture and growth. Hassan et al. reported a correlation between aneurysm depth and both neck width and caliber of draining arteries[32]. Furthermore, the incidence of rupture of aneurysms with an AR exceeding 1.6 was 100% in the categories of side wall and 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[33]. 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.

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. Direct correlations between AR and recanalization after coil embolization of UIAs have not yet been reported. Further CFD studies investigating the correlation between AR and recanalization are required.

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 is different across institutions.

Conclusions

AR and VER were significant predictors of recanalization after coil embolization of UIAs.

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List Of 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

Tables

Tables 1-6 are in the supplementary files section.

Supplementary Files

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