Risk Factors for Recurrence after Endovascular Treatment of Saccular Cerebral Aneurysms

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Abstract

Background and Purpose: Endovascular coiling is the established standard treatment for managing both unruptured and ruptured cerebral aneurysms worldwide, but long-term durability remains inferior to surgical clipping. We investigated the risk factors for recurrence after endovascular treatment of cerebral aneurysms.

Materials and Methods: Between April 2012 and Aug 2016, we treated 92 patients with 95 saccular cerebral aneurysms. Aneurysms were categorized as side-wall or bifurcation type based on their morphology.

Results: We included 72 patients; 31 aneurysms were classified as side-wall aneurysms, and two had an axis parallel to the parent artery. Forty-one bifurcation aneurysms had an axis either perpendicular (n=23) or parallel (n=18) to the parent artery. Twelve recurrences (16.7%) were observed during follow-up, and nine underwent retreatment after 3–25 months. All retreatments were performed endovascularly without subsequent neurological complications. In univariate analysis, aneurysm dome size, neck width, cerebral aneurysms with an axis parallel to the parent artery, and incomplete occlusion showed statistically significant associations with recurrence. In multivariate Cox regression analysis, dome size (hazard ratio: 1.38; 95% CI: 1.06–1.97; p=0.013); branch incorporation (hazard ratio: 5.76; 95% CI: 1.05–35.66; p=0.042); and axis parallel to the parent artery (hazard ratio: 33.04; 95% CI: 4.47–430.36; p=0.0004) remained risk factors for recurrence.

Conclusion: Dome size, cerebral aneurysms with an axis parallel to the parent artery, and branch incorporation were significant factors for recurrence after endovascular coiling. More meticulous embolization and follow-up or alternative methods of changing blood flow into the aneurysm are necessary in this subgroup of patients.

Abbreviations

CI = Confidence Interval

Introduction

Since the publication of the International Subarachnoid Aneurysm Trial [1], endovascular coiling has been the accepted standard treatment to manage both ruptured and unruptured cerebral aneurysms. Advancements in endovascular technology and techniques have increased the safety of endovascular treatment for the majority of cerebral aneurysms [2,3]. However, the major drawback of endovascular treatment compared with surgical clipping is that long-term durability is inferior especially for large aneurysms [4-6]. A meta-analysis by Ferns et al. [6] showed that aneurysms recurred in 20.8% of patients, and retreatment was performed in 10.3%. In contrast, the reported recurrence rate after surgical clipping was less than 5% [7]. Both coil compaction and aneurysm sac growth are considered the principal mechanisms of recanalization after coil embolization [8]. We prospectively collected data for all patients treated by endovascular treatment between 2012 and 2016, at Kyoto Medical Center. We investigated the incidence of recurrence in clinical practice and identified the risk factors significantly associated with angiographic recurrence after endovascular treatment of cerebral aneurysms.
Variable selection in the model was performed by backward selection [13]. All P-values are two-sided, and the level of statistical significance was defined as p<0.05. All statistical analyses were performed using JMP software for Mac, version 11 (SAS software, Cary, NC).

### Results

#### Study population

Our study included 24 men and 48 women, with ages ranging from 20–86 years (median, 66 years). Thirty-one patients had unruptured aneurysms, and 41 patients presented with subarachnoid hemorrhage, including one who experienced subarachnoid hemorrhage several years earlier and was initially treated conservatively.

#### Procedure outcomes

Patients’ demographic and clinical characteristics and the treatment results are summarized in Table 1. Aneurysms were located on the internal carotid artery in 34 (47%) patients, middle
cerebral artery in 8 (11%), anterior cerebral artery in 19 (26%), and vertebrobasilar system in 11 (15%). Postembolization angiography revealed complete occlusion in 31 (43%) aneurysms, neck remnant in 32 (44%), and incomplete occlusion in 8 (13%). No patients with unruptured aneurysms had a change in modified Rankin scale score after treatment. Thirty-four of 41 (83%) patients with ruptured aneurysms had favorable outcomes. Overall, 64 patients (89%) had favorable outcomes (modified Rankin scale, 0–2) at 90 days after treatment. However, one patient died after 6 months because of multiple organ failure secondary to sepsis unrelated to the procedure or the cerebral aneurysm.

Recurrences

Recurrences occurred in 12 (15.7%) of the treated aneurysms, as shown in Table 2. Recurrent aneurysms were located on the internal carotid-posterior communicating artery in seven cases, middle cerebral artery in one, anterior communicating artery in two, and basilar artery in two. Nine recurrent patients were retreated

<table>
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<tr>
<td>Sex</td>
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<td>Male</td>
<td>24 (33.3%)</td>
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<td>Age</td>
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<td>&lt;50</td>
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<td>60-69</td>
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<tr>
<td>Internal carotid artery</td>
<td>34 (47.2%)</td>
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<tr>
<td>Anterior cerebral artery</td>
<td>19 (26.4%)</td>
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<tr>
<td>Middle cerebral artery</td>
<td>8 (11.1%)</td>
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<td>Vertebrobasilar system</td>
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The reported incidence of recanalization in a large prospective study was 5.5% to 33% [7,14-17]. Large aneurysmal size, posterior circulation endovascularly with no neurological sequelae. The timing of retreatment ranged from 3–25 months after the first procedure. In 5/9 repeat procedures, embolization was performed using a stent-assisted technique as shown in Figure 2. One of these patients experienced a second and third recurrence after retreatment with coils because of enlargement of the aneurysmal wall, and was eventually treated using a stent-assisted technique at 19 months. In one patient with a major recurrence, retreatment was suspended because of the patient’s advanced age and concomitant chronic kidney disease. No patient experienced a bleeding episode during follow-up.

### Factors associated with recurrences

The associations between potential clinical risk factors and recurrence after embolization are summarized in Table 2. In the Cox regression analysis, the variables aneurysm dome size (hazard ratio: 1.47; 95% confidence interval: 1.21–1.87; p=0.0001), neck width (hazard ratio: 2.09; 95% confidence interval: 1.30–3.29; p<0.0001), cerebral aneurysm with an axis parallel to the parent artery (hazard ratio: 2.09; 95% confidence interval: 1.30–3.29; p=0.035), dome size (hazard ratio: 1.38; 95% confidence interval: 1.21–1.87; p<0.0001), neck width (hazard ratio: 1.47; 95% confidence interval: 1.21–1.87; p<0.0001), cerebral aneurysm with an axis parallel to the parent artery (hazard ratio: 3.73; 95% confidence interval: 1.16–12.04; p=0.029), and incomplete occlusion (hazard ratio: 5.56; 95% confidence interval: 1.47–17.96; p=0.035) showed statistical significance (Table 3). Multivariate analysis revealed that cerebral aneurysm with an axis parallel to the parent artery (hazard ratio: 3.34; 95% confidence interval: 4.47–430.36; p=0.0004), dome size (hazard ratio: 1.38; 95% confidence interval: 1.06–1.97; p=0.013), and branch incorporation (hazard ratio: 5.76; 95% confidence interval: 1.05–35.66; p=0.042) remained statistically significant risk factors (Table 4).

### Discussion

Endovascular coiling is the established standard treatment in managing both unruptured and ruptured cerebral aneurysms worldwide. However, most authors agree that the durability of endovascular treatment is inferior to that of surgical clipping [7,14]. The reported incidence of recanalization in a large prospective study was 5.5% to 33% [7,14-17]. Large aneurysmal size, posterior circulation...
aneurysms, wide neck, incomplete occlusion, low packing density, and ruptured aneurysms are reported risk factors for recurrence [4,6,12,18-20]. Although some clinical studies have included advanced technologies to gain more stability or packing density, including stent-assisted embolization [21,22], hydrogel-coated coils [23], and large-diameter coils [24], less durability remains the major drawback of endovascular coiling. In our series, the recanalization rate after coil embolization of ruptured and unruptured aneurysms was 16%, which was compatible with previous reports. In our univariate analysis, larger size, wider neck, and incomplete occlusion were associated with recanalization, as in previous studies.

Branch incorporation
Because of remarkable advances in endovascular techniques and technology, aneurysms with a branch incorporated into the aneurysmal wall can now be embolized without occluding the incorporated branch [25], which was considered difficult in the past. However, although it is now easier to preserve an incorporated branch, it remains difficult to balance the patency of the incorporated branch and treatment durability to prevent bleeding. Also, few data are available regarding long-term durability of endovascular coiling in this subgroup of cerebral aneurysms. To our knowledge, branch incorporation has not been investigated previously as a factor in recanalization after endovascular coiling.

Axis to the parent artery
It is well known that cerebral aneurysms at the tip of the basilar artery are likely to recur after embolization [26,27]. Basilar tip aneurysms are classified as bifurcation aneurysms and usually have an axis parallel to the parent artery. In our series, an axis parallel to the parent artery was the most significant predictor of recanalization, possibly because of a jet-pattern inflow for these aneurysms. Szikora et al. [9] reported that aneurysms with a main axis parallel to the parent artery have a tendency to have a jet-flow pattern and uneven distribution of unsteady pressure. We are currently conducting a clinical study to clarify the association between disturbed flow in the aneurysm and recurrence after embolization using computational flow-dynamic techniques [28]. We hypothesize that high-magnitude wall-shear stress and strong disturbed flow may be involved in aneurysm recurrence. However, our findings and hypothesis require confirmation in larger future studies.

Size
In our series, univariate analysis showed that aneurysm size was highly associated with recurrence, similar to previous studies [6,26]. Recurrence was observed in 3/6 (50%) aneurysms larger than 10 mm, which was compatible with previous studies reporting an incidence of recanalization after embolization of large or giant aneurysms as high as 39% [29]. Therefore, although a flow-diverting stent can be a promising option [30,31], further study is needed to establish the best method to treat large and giant aneurysms.

Limitations
There are certain limitations in our study. First, because of the retrospective nature, selection bias may be present. However, this bias may have been minimized by prospectively recording the data for aneurysms treated endovascularly into a database. A second limitation is the limited number of cases; our findings should be confirmed in a larger prospective study. A third limitation is that the follow-up period was relatively short; the median follow-up period was 15 months. However, all of the patients in this series had follow-up magnetic resonance imaging at 6–12 months, and all recurrences were observed within 12 months. Reopening of cerebral aneurysms is rare when adequate occlusion is confirmed at 6 months after embolization [32]. We found that the risks of recurrence associated with axis to the parent artery and branch incorporation were significant, but a slight data bias may be present [33] because these aneurysms had large hazard ratios and/or very wide confidence intervals on multivariable Cox regression.

Conclusion
In our cohort, the recanalization rate after coil embolization of ruptured and unruptured aneurysms was 16%. In addition to dome size, cerebral aneurysms with an axis parallel to the parent artery and branch incorporation were significant predictors of recurrence after endovascular coiling. More meticulous embolization and follow-up or alternative methods of changing flow into the aneurysm are necessary in this subgroup of patients.

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References


