Early recurrent hemorrhage after coil embolization in ruptured intracranial aneurysms

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Abstract

Introduction The authors present a series of patients in whom early rebleeding occurred after coiling for ruptured aneurysms. We investigated the incidence and possible mechanisms of early rebleeding.

Methods This study consisted of 1,167 consecutive patients who underwent coiling for a ruptured saccular aneurysm. Clinical and radiological data were collected retrospectively from three institutions. Early rebleeding was defined as occurrence of further bleeding within 30 days after coiling with worsening of the patient’s condition. We divided early rebleeding into hyperacute, subacute, and delay groups depending on the timing of rebleeding after coil embolization.

Results Incidence of early rebleeding after coiling of a ruptured saccular aneurysm was 1.1% (13 of 1,167), and mortality was 31% (4 of 13) in our series. Out of ten patients in hyperacute group, three (30%) had incomplete occlusion result and six patients (60%) underwent intra-arterial (IA) infusion of abciximab or tirofiban during the procedures. Seven patients (70%) had an intracerebral hemorrhage (ICH) on initial computed tomography. Four patients died, another four sustained severe disabilities, and the others had good recovery. All three patients in subacute and delay group showed recanalization on post-rebleeding angiography and made an excellent recovery.

Conclusion Early rebleeding was associated with high mortality and morbidity. IA abciximab infusion or thrombolytic interventions during the procedure, maintenance of anticoagulation after the procedure, incomplete treatment of the aneurysms, and presence of ICH seemed to be related to hyperacute early rebleeding after coiling. Increased aneurysmal size and coil compaction could induce subacute and delayed early rebleeding.

Keywords Aneurysm · Rebleeding · Coiling · Embolization · Ruptured aneurysm

Introduction

Since the International Subarachnoid Aneurysm Trial study, endovascular coil embolization has been proven as a safe and effective treatment for intracranial aneurysm. Early rebleeding before treatment is often fatal or disabling; thus, the goal of early treatment of a ruptured aneurysm is prevention of rebleeding [1]. The long-term risk of rebleeding in coil embolization is reported to be low and not significantly different from surgery [2]. However, late
recanalization and retreatment are also known to be more common in the endovascular treatment group than in the clipping group. A few of these cases may present with late rebleeding. While there have been many reports on the low rebleeding rate and the relatively high late-recanalization rate after coiling, investigations of early rebleeding after coiling are few possibly due to very low incidence. Therefore, the authors present a series of patients in whom early rebleeding occurred after coiling for ruptured aneurysms.

Patients and methods

Study population

Clinical and radiological data were collected retrospectively from three institutions. This study consisted of 1,167 consecutive patients who underwent coiling for a ruptured saccular aneurysm during the time period from August 1996 to July 2011 in one institution, from May 2003 in another one, and from July 2008 in the other one. All of the patients presented with subarachnoid hemorrhage (SAH) confirmed by CT, MRI, or lumbar puncture. The ruptured aneurysms were identified by conventional angiography, and coiling was performed in the acute stage. Clinical aneurysms were identified by conventional angiography, and at the time of treatment, the H–H grade [3]. Early rebleeding was defined as occurrence of further bleeding within 30 days after coiling with worsening of the patient’s condition. Diagnostic confirmation was made by CT when it showed an increased amount of hemorrhage compared with immediate postprocedural CT. Those who showed delayed deterioration after recovery from anesthesia were also included if the bleeding amount increased on follow-up brain CT compared to initial brain CT. We excluded cases where hemorrhage increased on immediate postprocedural brain CT compared to initial brain CT. We also excluded patients with dissecting, fusiform, blood blister-like, or false aneurysms. CT images before coiling and after rebleeding were analyzed by an experienced neuroradiologist. We divided early rebleeding into hyperacute (within 3 days), subacute (4–14 days), and delay (15–30 days) groups depending on the timing of rebleeding after coil embolization. The outcome of the patients was measured using the Glasgow Outcome Scale (GOS) [4].

Endovascular treatment procedure

All treatments were performed under general anesthesia, and the patients were not heparinized systemically before proper protection of the ruptured aneurysm. The aim of coiling was to obtain a packing of the aneurysms that was as attenuated as possible. Unless the thromboembolic complication occurred or a stent was used, further antiplatelet or anticoagulant medications were not administered. In the case of intraprocedural thromboembolic complication, various strategies for thrombolysis were applied, such as mechanical thrombolysis and intraarterial (IA) or intravenous (IV) abciximab, tirofiban, urokinase, or heparin infusion during or after the procedure. Degree of the aneurysmal occlusion was assessed by completion angiographies: total occlusion (no residual filling of contrast medium in the aneurysms), near-total occlusion (a small residual contrast filling at the base of the aneurysm), and subtotal occlusion (any contrast filling in the aneurysm sac).

Results

Early rebleeding occurred in 13 consecutive patients after coiling for ruptured aneurysms. There were ten patients in the hyperacute group, two patients in the subacute group, and the other one patient in the delay group. Patients’ ages ranged in age from 37 to 85 years (mean age, 55.3 years), and the male to female ratio was 4–9. At the time of treatment, the H–H grades of the patients were as follows: grade I in one, grade II in nine, grade III in two, and grade IV in one. The aneurysms were located in the following areas: anterior communicating artery (ACoA) in six, middle cerebral artery (MCA) in four, posterior communicating artery (PCoA) in one, distal anterior cerebral artery in one, and anterior choroidal artery (AChA) in one. Single catheter technique and multiple catheter technique were applied in six cases each. In the other case, catheter protection technique was used. Relevant clinical and radiologic data of the 13 patients are summarized in Table 1.

Incidence of early rebleeding after coiling of a ruptured saccular aneurysm was 1.1% (13 of 1,167), and mortality rate was 31% (4 of 13) in our series. Of these, 12 aneurysms (92%) had blebs and 11 aneurysms (85%) had wide neck, which dome-to-neck ratio was less than 2. The aneurysm sizes ranged from 2.0 to 11.2 mm (mean 6.4±2.4 mm), and the average aneurysm neck size was 3.8±1.6 mm. Two patients (15%) suffered intraprocedural leakage.

In the hyperacute group, degrees of initial aneurysmal occlusion were total occlusion in two (20%), near-total occlusion in five (50%), and subtotal occlusion in the other three patients (30%). Three patients (30%) underwent IA infusion of abciximab, and another three patients (30%) received IA tirofiban infusion during the procedures. Seven patients (70%) had an intracerebral hemorrhage (ICH) on initial CT, and the volume of the ICH increased significantly on rebleeding. Cerebral angiography was performed
after rebleeding in six patients, and there were no changes in coil configurations and aneurysmal occlusion status (Fig. 1). One patient underwent additional coiling for subtotally occluded aneurysms. Cerebral angiography was not performed after rebleeding in four patients, and three patients underwent surgical clipping among them. At operation, there was no active aneurysmal bleeding in these patients in spite of rehemorrhage. Six patients in the hyperacute group underwent decompressive surgery and/or hematoma removal. At the time of the discharge, four patients (40%) died, another four patients sustained severe disabilities (GOS of 2 to 3), and the other two patients had a good recovery (GOS 5).

In the subacute and delay groups, all three aneurysms were initially occluded with coils successfully. Cerebral angiography at the time of rebleeding revealed significant changes in the coil configurations, increased aneurysmal size, and recanalization. Therefore, all three patients underwent additional coiling (Fig. 2). The outcome of these groups was excellent, and all three patients made a good recovery (GOS 5).

### Discussion

Although endovascular embolization is a popular treatment modality for unruptured and ruptured aneurysms, a high percentage of aneurysmal remnants, possible long-term instability, and potential rehemorrhage are current concerns [3]. In particular, coil embolization is associated with a relatively high risk of late rerupture of the aneurysms and retreatment due to aneurysmal recanalization, which is caused by coil compaction and/or aneurysmal growth. Recently, there have been a few reports on early rebleeding after coiling for a ruptured aneurysm. According to the literatures, the incidence of early rebleeding was 1.0–3.6% [1, 6, 7]. In our series which included larger number of cases than previous studies, the incidence was 1.1%. This rate was similar to those of previous results.

According to our study, the factors related to early rebleeding and outcomes appeared to be different between the hyperacute and subacute/delay groups. In the hyperacute group, unsatisfactory aneurysmal occlusion results, IA infusion of abciximab or tirofiban, and the presence of ICH on initial CT seemed to be related to rebleeding, and notably, the outcome of the patients was poor. Meanwhile, in the subacute/delay group, aneurysmal recanalization seemed to induce rebleeding, and the outcome of the patients was excellent.

From the published articles, we collected cases that fulfilled the criteria of early rebleeding after coiling defined in this study. We included the cases where separate information on patients was available, and there were 32 patients in nine articles who suffered early rebleeding after coiling [1, 5–12]. We investigated the characteristics of each group in the population of 45 patients, including our own 13 cases. Overall, there were 34 patients in the hyperacute, six in subacute, and five in delay group. The patients’ age ranged from 24 to 85 (mean age, 54.1 years), and there were 19 men and 26 women. At the time of treatment, the H–H grades of the patients were as follows: I in 3, II in 14, III in 15, IV in 8, and V in 5. The locations of the aneurysms were ACoA in 22, MCA in 11, PCoA in 5,
AChA in 2, paraclinoid in 2, A2–A3 segment of the anterior cerebral artery in 2, and basilar tip in 1.

In the hyperacute group, the ruptured aneurysms were initially occluded subtotally in eight patients (24%), near-totally in 14 (41%), and totally in 12 (35%). In this group, information on intraprocedural and postprocedural anticoagulant/fibrinolytic/antiplatelet medication was valid in 23 patients. Among them, 16 patients (70%) suffered thrombolytic intervention due to procedural thromboembolic complication. IA or IV abciximab infusion was performed during and/or after the procedures in four patients. Postprocedural systemic heparinization was maintained in five patients. IA or IV infusion of tPA or urokinase was done in three patients. IA tirofiban during the procedure was infused in three patients. A patient suffered rebleeding after tPA irrigation via the ventriculostomy catheter to resolve intraventricular hematoma. Among these 16 patients, 14 patients had successful occlusion results, which were near-total or total occlusion on the postembolization angiography. In the hyperacute group, 29 patients had useful information for ICH. Twenty patients (69%) initially presented with ICH combined with subarachnoid hemorrhage and increased volume of the ICH was noted on rebleeding. After rebleeding, cerebral angiography was performed in ten patients. Two patients among them had subtotal occlusion and eight patients had successful occlusion results. Among the latter patients, no one showed recanalization of the aneurysm on the angiography. Finally, 15 patients (44%) died after rebleeding, 8 patients (24%) sustained severe disability (GOS 2 to 3), and only 11 patients (32%) had good recovery (GOS 4 to 5).

In the subacute and delay groups, the ruptured aneurysms were initially occluded near-totally in five (45%) and totally in...
six (55%). After rebleeding, cerebral angiography was performed in seven patients. In all of them, cerebral angiography at the time of rebleeding showed recanalization of the aneurysms due to increase of aneurysmal size and/or coil compaction. No one in these groups suffered thrombolytic intervention or antithrombotic medication during or after the procedure. Valid information on the presence of ICH at the moment of initial presentation was available in five in six patients of the subacute group, and initial CT showed in three patients among them. Initial H–H grades were as follows: I in one, II in one, III in one, IV in two, and V in one. Eventual clinical outcomes of this group were as follows: GOS 1 in three, GOS 4 in one, and GOS 5 in two. In five patients of the delay group, useful information for ICH was obtained from four patients. Of these, initial CT showed ICH in only one patient. Initial H–H grades were as follows: II in three and III in two. Two patients died after rebleeding, one remained minor sequelae (GOS 4), and two patients made excellent recovery (GOS 5) (Table 2).

Overall, the most common site was ACoA (49%), followed by MCA (24%) and PCoA (11%). In a series [6], all of the cases with early rebleeding occurred on ACoA aneurysms, and the location was an independent risk factor (odds ratio 11.1). Twelve (92%) out of 13 aneurysms in our series had blebs. In aneurysms with blebs, the interventionist attempted to avoid insertion of the coil into the bleb for fear of procedural rupture, and thus, the risk of coil compaction may be high. When the bleb is filled with coils, migration of coils into the extra-aneurysmal space through the ruptured point may induce rebleeding. In our series, there were two patients (15%) of aneurysmal perforation during the procedure, and both the patients had aneurysms with blebs. We suggest the coil compaction and migration via perforation site as a possible mechanism of rebleeding.

An initial incomplete occlusion grade is known to be a strong predictor for rehemorrhage [1, 13, 14]. Eight out of 34 patients in the hyperacute group had unsatisfactory...
initial occlusion results, and this would be a cause of early rebleeding for them. Thrombolytic interventions and anticoagulant medications during and/or after the procedure are another common characteristic in the hyperacute group. In our series, six patients in hyperacute group suffered IA abciximab or tirofiban infusion for thromboembolic complication during the procedure. It is noticeable that some patients who underwent successful occlusion and did not suffer thrombolytic intervention in the hyperacute group had ICH on initial CT and cerebral angiography performed after hyperacute rebleeding demonstrated no recanalization (n=6). Sluzewski and van Rooij [6] and Jartti et al. [1] insisted that initial ICH was an independent risk factor. They suggested that the presence of a thrombosed pseudoaneurysm in the ICH may undergo early reopening and result in rehemorrhage.

![Image](a). The cerebral angiography of the patient who initially presented with SAH with ICH (a) showed the right MCA aneurysm with a bleb (b). The aneurysm was occluded with a neck remnant with coils (c). Because no problem occurred during the procedure, neither anticoagulant nor antiplatelet medication was used. After 26 h, the clinical condition of the patient had worsened and CT showed that the volume of ICH had increased (d). Without cerebral angiography, surgical clipping and hematoma removal were performed.

**Table 2** Summary of the patients’ characteristics according to timing of rebleeding

<table>
<thead>
<tr>
<th>Related factors</th>
<th>Hyperacute group (n=34)</th>
<th>Subacute group (n=6)</th>
<th>Delayed group (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete occlusion result (8/34)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Thrombolytic intervention (16/23)</td>
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<tr>
<td>Initial intracerebral hemorrhage (20/29)</td>
<td></td>
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<td>Thrombolytic intervention (16/23)</td>
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<tr>
<td>Initial intracerebral hemorrhage (20/29)</td>
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<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>15</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Severe disability</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Good recovery</td>
<td>11</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
Kang et al. [7], who reported on cases of hyperacute rebleeding after successful coil embolization, hypothesized a few mechanisms for those events, based on intraoperative findings. First, uneven distribution of the coil masses could possibly cause a channel of blood stream to the ruptured point of the aneurysm. Second, spontaneous resolution of the thrombi among the coil loops could permit free blood flow into the embolized aneurysm. However, absence of the reopening on the angiography after rebleeding in our study did not support these suggestions. We hypothesize another possibility that rebleeding with ICH may be caused by delayed hemorrhage or propagation of the initial ICH due to vulnerability of the parenchyma adjacent to the ICH, rather than by rerupture of the coiled aneurysm. This is based on the following: (1) Some patients who had successful occlusion results and did not undergo thrombolytic intervention had an ICH on initial CT and the volume of the ICH mainly increased on rebleeding (Fig. 3) and (2) six patients who underwent cerebral angiography revealed no evidence of recanalization.

In the subacute and delay groups of the literature population, recanalization of the aneurysm with coil compaction combined with aneurysm growth was the main cause, similar to our results. However, the mechanisms of early recanalization may be somewhat different from those of late recanalization. We suggest that early recanalization may be caused by the soft thrombus within the aneurysm on initial rupture, which was not shown on angiography. When the thrombus was lysed after coiling, an increase of aneurysmal size with coil migration could be shown on angiography. Migration or leakage of coils through the ruptured point within aneurysms may also cause early recanalization. We have routinely performed follow-up plain radiography within 1 month or before discharge in order to detect early change of coil masses. When changes were observed, cerebral angiography was performed.

When we reviewed the literature and our data, earlier rebleeding was associated with higher mortality and morbidity. In the hyperacute and subacute groups, 65% (26 of 40) of the patients had poor outcome (GOS; 1–3), and 35% had good recovery. In the delay group, 40% (two of five) died, and 60% had excellent recovery. Earlier rebleeding seemed to induce worse outcome. At time of initial rupture, the condition of brain would be unstable and have increased intracranial pressure. Earlier rebleeding under that condition might induce more severe deterioration. With passage of time over 2 weeks, the condition of the brain would become more stable and the adjacent environment of the aneurysm would change into a more protective direction, such as fibrosis.

There are some limitations in our study. This was a retrospective study. There would be selection bias and protocol deviations. The sample size was small and the statistical analysis estimation of the risk factors was not possible. Cerebral angiography was performed in a limited number of patients after rebleeding.

**Conclusion**

This study showed that the causes and outcome of early rebleeding are variable depending on the timing of the rebleeding. Intra-arterial abciximab/tirofiban infusion or thrombolytic interventions during the procedure, maintenance of anticoagulation after the procedure, incomplete treatment of the aneurysms, and presence of ICH seemed to be related to hyperacute early rebleeding after coiling. Increased aneurysm size and coil compaction could induce subacute and delayed early rebleeding. Early rebleeding was associated with high mortality and morbidity.

**Conflict of interest** We declare that we have no conflict of interest.

**References**


