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Causes of early rebleeding after coil embolization of ruptured cerebral aneurysms

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ABSTRACT

Objective: Early rebleeding after coil embolization of a ruptured cerebral aneurysm is rare but may cause severe disability or death. We present a case series of early rebleeding after coil embolization of ruptured cerebral aneurysms and investigate the incidence, clinical outcome and possible mechanism through retrospective analysis of angiographic and surgical findings.

Patients and methods: This study included 347 consecutive patients who had undergone successful coil embolization of 347 ruptured cerebral saccular aneurysms. Clinical and angiographic data and findings from emergent surgery were analyzed retrospectively.

Results: Early rebleeding occurred in eight aneurysms (2.3%) and was especially frequent among anterior communicating artery lesions (6 out of 122, 4.9%). The other two events involved posterior communication artery lesions. The maximum diameter of the aneurysms that developed early rebleeding was 4.89 ± 0.65 mm, ranging from 3.9 to 5.7 mm. In seven out of eight patients, the immediate radiologically determined occlusion status was a residual neck, and the remaining patient had a residual sac. The coil packing density was between 21% and 34%. Six cases of rebleeding were detected within 48 h, 1 case was detected on the 5th day, and 1 case was detected on the 10th day. Coil compaction was not detected by follow-up angiography after early rebleeding. We performed surgical clipping as a rescue procedure in 5 cases and additional coil embolization in 1 case. During follow-up angiography and rescue clipping, inflow of blood to the aneurysm was detected in 6 cases. Three patients died, and the other 3 patients were severely disabled. The mechanisms of early rebleeding were divided into two types. First, blood may flow into the rupture site through a gap between the coil mesh and the aneurysm neck. Second, blood may enter the rupture site through the coil mesh due to insufficient thrombus formation.

Conclusions: The early rebleeding rate after coil embolization of ruptured cerebral aneurysms in our study was 2.3%. The ruptured aneurysms were small in size (< 6 mm), and rupture frequently occurred in the anterior communicating artery. In most cases, inflow of blood to the aneurysm was detected by follow-up angiography or during rescue surgery.

1. Introduction

In 1991, coil embolization was introduced as a new treatment option for cerebral aneurysms [1]. After the International Subarachnoid Aneurysm Trial (ISAT), coil embolization became one of the main treatment options for ruptured cerebral aneurysms [2]. This procedure is now the preferred treatment option for ruptured cerebral aneurysms in the acute stage [3,4]. Nevertheless, coil embolization has limitations. In particular, it has a high recurrence rate of up to 30% [5,6]. Therefore, several technologies, such as flow diverters, hybrid coils, liquid embolics, shape memory polymer foams, and magnetic microparticles, have been investigated as solutions for the drawbacks of coil embolization [7–9]. However, these investigations focused on the long-term durability of aneurysm treatments, and the new treatments have not yet been established as superior to coil embolization of ruptured cerebral saccular aneurysms using bare metal coils.

Early rebleeding after coil embolization of ruptured cerebral aneurysms is rare but does sometimes occur. Its incidence has been

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reported to be from 1% to 3.6%, and the prognosis is generally poor [2,10–16]. However, there has not yet been any active research on ways to overcome this problem, and there have been only scattered reports about this issue [2,10–16]. Considering these facts, we should attempt to understand the status of cerebral aneurysms that have undergone coil embolization, identify the problems that may cause rebleeding, and devise a strategy to reduce early rebleeding after coil embolization. For this purpose, it is necessary to analyze each early rebleeding case in detail. Herein, we present a case series of early rebleeding after coil embolization of ruptured cerebral aneurysms and investigate the incidence, clinical outcome and possible mechanisms through retrospective analysis of angiographic and surgical findings.

2. Patients and methods

This study is a two-center retrospective study of early rebleeding after coil embolization of ruptured cerebral saccular aneurysms. We reviewed the aneurysm databases of two hospitals and collected information on the patients who met the inclusion criteria. Between January 2011 and July 2017, 1072 cases of cerebral aneurysm were treated using coil embolization. Among them, we treated 380 cases of ruptured cerebral aneurysm. We excluded cases of failed coil embolization, blood-blister-like aneurysm, dissecting aneurysm, pseudoaneurysm and any aneurysm that required occlusion of the parent artery. Ultimately, this study included 347 consecutive patients who underwent successful coil embolization of 347 ruptured saccular cerebral aneurysms.

Early rebleeding was defined as the occurrence of further bleeding that was definitely related to the previously coiled aneurysm within 30 days after coil embolization, with any worsening of the patient's condition. In all cases, brain CT scans were routinely conducted after coil embolization. When worsening of a patient's condition was detected through clinical signs, including headache, a brain CT scan was immediately conducted, after which experienced neurosurgeons and neuroradiologists discussed the issue. The degree of occlusion was categorized as a complete occlusion, residual neck, or residual sac according to the 'Raymond-Roy Occlusion Classification' [17]. Two experienced neuroradiologists reviewed all brain CT and angiography images. We calculated the theoretical volume of the aneurysm and inserted coils according to the method previously used by other investigators [18–20]. The aneurysm was approximated as an ellipsoid shape, and its volume was calculated as follows: Aneurysm volume = $(4 / 3) \times \pi \times (A / 2) \times (B / 2) \times (C / 2)$, where A denotes the largest horizontal diameter on the anteroposterior view of the angiogram, B denotes the largest vertical diameter on the lateral view, and C denotes the largest horizontal diameter on the lateral view. The volume of each coil was calculated under the assumption that the coils were cylindrical: Coil volume = π (outer diameter / 2)^2 × length. The total volume of inserted coils was the sum of the volumes of the individual coils. The calculated coil density (%) was defined as the proportion of the total volume of inserted coils to the volume of the aneurysm. However, this mathematical equation has several substantial limitations under conditions in which the aneurysm is not ellipsoidal. Despite such limitations, the calculated coil density was used in this study, as it is the only available objective measurement for the estimation of whether the extent of coil embolization was acceptable.

When it was judged that rebleeding had occurred, we tried to apply all possible methods of confirmation and treatment, such as magnetic resonance angiography (MRA), follow-up angiograms, further coil embolization and surgical clipping. Clinical and angiographic data and findings upon rescue surgery were analyzed. In particular, we focused on clarifying the location and the possible mechanism of rebleeding by applying the findings from follow-up angiography and rescue clipping. This retrospective study was approved by the Institutional Review Board.

Table 1
Locations of all treated ruptured cerebral saccular aneurysms, the rate of using stent and the rate of early rebleeding.

Location (cases)		Use of stent (%)	Early rebleeding (%)
Anterior circulation (292)	A-com (122)	2 (1.6)	6 (4.9)
	Distal ACA (20)	1 (5)	
	A1 (7)	0 (0)	
	ICA-P-com (93)	6 (6.5)	2 (2.2)
	ICA-others (35)	5 (14.3)	
	MCA (15)	0 (0)	
Posterior circulation (55)	Basilar tip (21)	4 (19)	
	Others (34)	5 (14.7)	
Total (347)		23 (6.6)	8 (2.3)

ACA, anterior cerebral artery; A-com, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; and P-com, posterior communicating artery.

2.1. Endovascular strategies

Coil embolization procedures were performed under general anesthesia in most cases and local anesthesia in some cases. Three biplane angiographic units (an Integris Allura 12/12, Philips, Netherlands; an Artis Zee biplane system, Siemens, Germany; and a Trinias Digital Angiography System, Shimadzu, Japan) were used. In most cases, the right common femoral artery was accessed using a short sheath or a 6-Fr long sheath. A 6-Fr or 5-Fr guiding catheter was then placed in the middle of the internal carotid artery or vertebral artery. Before coil embolization of the ruptured aneurysms, we did not use any oral antiplatelet agents or IV anticoagulants to reduce thromboembolic complications. The typical dose of intravenous heparin based on the patient's weight (3000 IU to 4000 IU) was administered as a bolus as soon as the aneurysm was deemed to be secured safely with coils. All sheaths, guiding catheters, and microcatheters were continually flushed with normal saline. An Excelsior SL-10 (Stryker, Fremont, CA), Echelon 10 (Medtronic, Irvine, CA) or Headway 17 (Microvention, Tustin, CA) microcatheter was used for coil delivery. The detachable coils used were Target (Stryker, Fremont, CA), Axium (Medtronic, Irvine, CA) and Microplex (Microvention, Tustin, CA) coils. When stent-assisted coiling was needed, an Enterprise stent (Codman & Shurtleff, Raynham, MA) or a Neuroform stent (Stryker, Fremont, CA) was used. In addition, HyperGlide (Medtronic, Irvine, CA) and HyperForm (Medtronic, Irvine, CA) balloons were used in balloon-assisted coiling. When a thromboembolic event occurred, we occasionally gave intraarterial infusions (dose, 0.5 mg to 1.0 mg) of glycoprotein IIb/IIIa inhibitor (Tirofiban HCl, MERCK & CO, PA). After coil embolization, we administered 2850 IU of Fraxiparine subcutaneously twice per day for 1 or 2 days. If a thromboembolism was identified and subsequent intraarterial thrombolysis appeared to be insufficient, an intravenous infusion of heparin or glycoprotein IIb/IIIa inhibitor was administered. Beginning 24 h after coil embolization, a daily oral aspirin regimen (100 mg) was maintained for more than 6 months, unless there is any bleeding tendency or additional major operation. In the event of stent-assisted coiling, a regimen of dual antiplatelet agents (aspirin 100 mg and clopidogrel 75 mg) was maintained for more than 3 months.

3. Results

The mean age of the 347 patients was 59.3 ± 13.2 years, ranging from 13 to 89 years. The number of female patients was 243, and 292 aneurysms were located in the anterior circulation. The location of the aneurysm was the anterior communicating artery (A-com) in 122 cases,