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Original Article

Evaluation of the Safety and Effectiveness of Coil Embolization for Anterior Communicating and Anterior Cerebral Artery Aneurysms

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Objective: Endovascular coil embolization for anterior communicating artery (ACoA) and anterior cerebral artery (ACA) aneurysms is associated with high total and near-total occlusion rates, but the complication rate is high. The development of newer endovascular technologies may improve the clinical outcomes. This study investigated the status of endovascular treatment of ACoA and ACA aneurysms by comparing our results with past reports.
Methods: Between January 2006 and December 2018, we investigated 50 patients who were followed for 12 months or longer to clarify the outcomes of coil embolization. The outcomes of embolization were evaluated using time-of-flight MRA. The safety was evaluated based on procedure-related complications that affected clinical outcomes.
Results: Initial assessments demonstrated complete obliteration in 84% (42 of 50 patients) and a residual neck in 14% (7 of 50 patients). Procedure-related complications developed in 12% (6 of 50 patients). The procedure-related morbidity rate was 2% (1 of 50 patients) and there was no procedure-related death. Recanalization was noted in 14% (7 of 50 patients, median follow-up period, 57 months). The recanalized aneurysms were significantly smaller than the stable aneurysms in maximum size (4.3 mm vs. 5.8 mm; $p = 0.017$) and height (3.7 mm vs. 4.3 mm; $p = 0.035$).
Conclusion: We demonstrated the safety and effectiveness of endovascular coil embolization for ACoA and ACA aneurysms. The small size of aneurysms may be related to recanalization.

Keywords ▶ anterior cerebral artery, anterior communicating artery, coil embolization, recanalization, small size

Introduction

According to a literature review of cerebral aneurysms, the morbidity and mortality rates of craniotomy and coil embolization are 3%–12% and 3%–9%, respectively.[1] The complication rate in craniotomy for patients with unruptured anterior communicating artery (ACoA) aneurysms is high at 4.4 and 5.8%.[2,3] Coil embolization of ACoA and anterior cerebral artery (ACA) aneurysms is technically difficult compared with that of aneurysms at other sites because of the small vascular diameter, the presence of important penetrating arteries, and meandering of the access route due to their location in the median region. In a meta-analysis of 14 studies of coil embolization for ruptured and unruptured ACoA aneurysms reported between 1994 and 2012,[4] the incidences of procedure-related permanent morbidity and mortality rates were 6% and 3%, respectively. Moreover, they did not differ between ruptured and unruptured aneurysms, and comparison of therapeutic outcomes between before and after 2007 revealed no difference in the embolization rate or procedure-related complication rate. However, the permanent morbidity and mortality rates were reported to decrease after 2007. A systematic review of coil embolization for distal ACA aneurysms demonstrated a high procedure-related complication rate of 12%, with iatrogenic rupture being observed in 7% and a permanent morbidity rate of 8%.[5] ACoA and ACA aneurysms were

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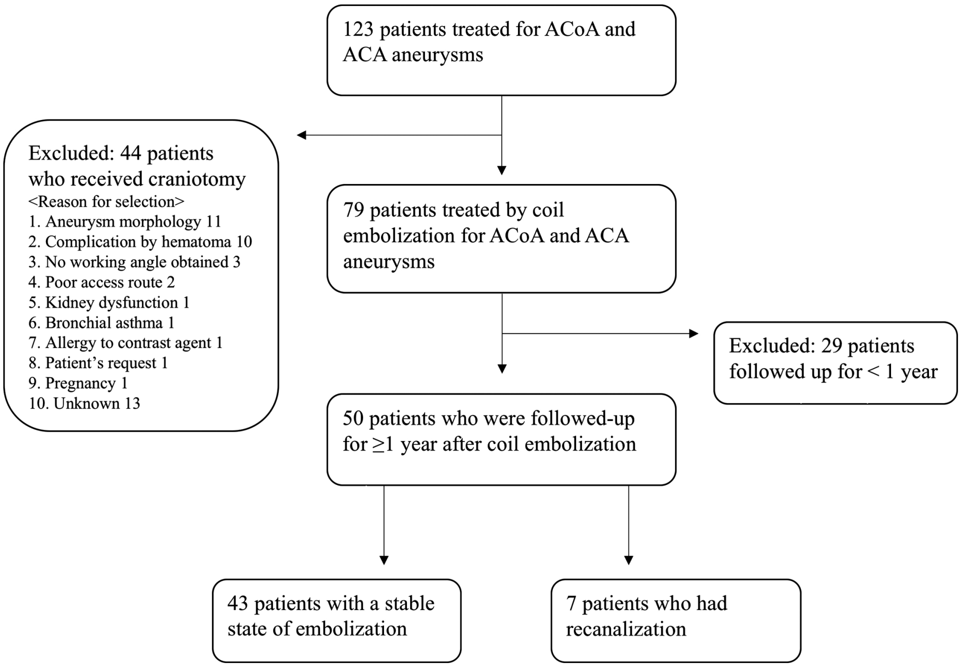

Fig. 1 Flow chart of patient selection. ACA: anterior cerebral artery; ACoA: anterior communicating artery

reported to be smaller and have a higher risk of rupture in surgery than aneurysms at other sites.[6] However, in consideration of the recent improvements in treatment devices and examination techniques, the clinical outcomes of coil embolization for ACoA and ACA aneurysms may have improved. The objective of this study was to review the clinical outcomes of coil embolization for ACoA and ACA aneurysms at our facility, and evaluate whether they have improved compared with past reports.

Materials and Methods

This was an exploratory single center retrospective case series study carried out after approval by the Institutional Review Board of Kindai University Nara Hospital (approval No. 584). Of the 123 patients surgically treated for ACoA or ACA aneurysms between January 2006 and December 2018, 79 underwent coil embolization. The clinical records were reviewed in 50 patients who were followed up for at least 1 year after the treatment (**Fig. 1**). The site of aneurysm was classified into the proximal segment of the ACA (A1A), ACoA, and A2 or more distal segment of the ACA (DACA). The morphology of aneurysms was analyzed using 3D digital subtraction angiography performed during coil embolization. The angiography systems were the Innova 4100-IQ system (GE Healthcare, Chicago, IL, USA), BRANSIST safire system (Shimadzu, Kyoto, Japan), and Innova IGS 630 system (GE Healthcare), which were used in combination with Advantage Workstation (AW) VS2 (GE Healthcare), 3D-Angio option V4.0 (Shimadzu), and AW VS5 (GE Healthcare), respectively. Regarding the morphology of aneurysms, the maximum diameter, neck diameter, height, presence of blebs, dome and neck ratio, and aspect ratio were evaluated.

Therapeutic procedures

For unruptured aneurysms, dual-antiplatelet therapy using 100 mg/day of aspirin and 75 mg/day of clopidogrel was performed for at least 7 days before surgery, in principle. For ruptured aneurysms, if procedures, such as balloon-assisted and double catheter techniques, were used, 100 mg of aspirin was administered intraoperatively, and if stents were used, 300 mg of clopidogrel was additionally administered. Oral antiplatelet therapy was stopped 4–8 weeks after surgery. If stents were used, antiplatelet therapy was converted 6 months after surgery to single-drug therapy, which was continued thereafter. In all patients, surgery was performed via the femoral artery after the induction of general anesthesia. The patients were heparinized after sheath insertion and the activated clotting time was maintained at twice the control level. In general, embolization was performed by the simple technique, but advanced techniques, such as balloon-assisted, double-catheter, and stent-assisted techniques, were used depending on the morphology of the aneurysm.

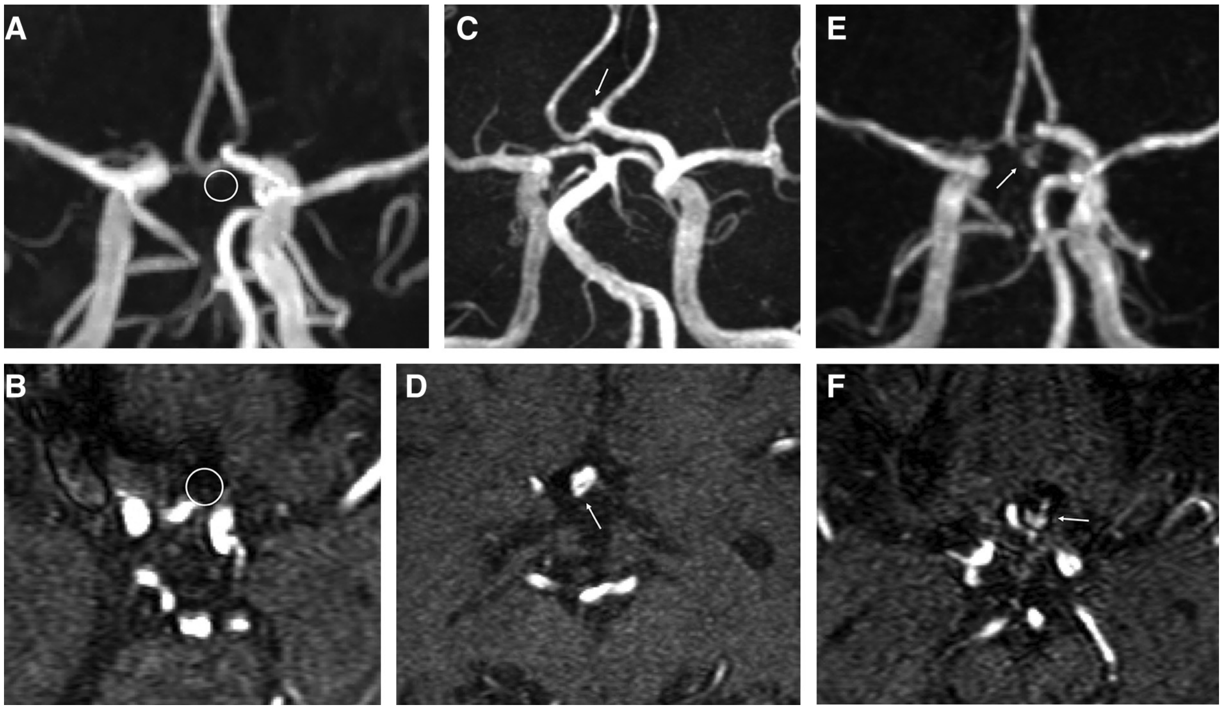

Fig. 2 Classification of state of embolization by MRA (Top: MIP images, bottom: original MRA images). (**A** and **B**) Images of complete obliteration. (**C** and **D**) Images of residual neck. (**E** and **F**) Images of residual aneurysm. The circles (**A** and **B**) show the position of the coil mass. The arrows (**C**–**F**) indicate blood flow signals. MIP: maximum intensity projection

Assessment of embolization

The endovascular procedures were classified into simple and advanced (balloon-assisted, double-catheter, or stent-assisted) techniques. For the safety evaluation, procedure-related complications, complications that affected the outcome, and death were reviewed. The state of embolization was evaluated by time-of-flight (TOF) MRA within 5 days, 6 months, and 1 year after treatment, and every 6 months to 1 year thereafter. MRA was performed using 1.5-T (Signa HDxt; GE Heathcare and Intera; Phillips Healthcare, Best, The Netherlands) and 3-T (Achieva-QD, Philips Healthcare) systems. TOF-MRA was performed using sequences formulated at our hospital, in which the TE was 3.1, 6.9, and 3.45 s, and TR was 21, 21, and 23 s, respectively. The flip angle was set at 20° in all cases. The state of embolization was defined as complete obliteration (CO) when there was no signal in the aneurysm, residual neck (RN) when signals were noted in the neck, and residual aneurysm (RA) when signals were observed in the coils (**Fig. 2**).

Patients who exhibited improvement or no change compared with TOF-MRA after the initial treatment were classified into the stable group and those with aggravation were classified into the recanalization group. The imaging diagnoses were confirmed by checking the diagnoses of the radiologists and records of the neurosurgeons in charge at our hospital, and by the author's own review.

Statistical analysis

The stable and recanalization groups were compared by univariate analysis. Continuous variables were compared by the Mann–Whitney test and categorical variables were compared by Fisher's exact test. $p < 0.05$ was regarded as significant. Statistical analyses were performed using EZR of R commander software (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

Results

Patient background

The patient background is presented in **Table 1**. The median age was 65 years and females accounted for 54% (27) of the patients. The site of the aneurysm was ACoA in 42 (84%), DACA in 6 (12%), and A1A in 2 (4%). The median maximum aneurysm diameter was 5.3 mm, median neck diameter was 3.0 mm, and median height was 4.3 mm. The median dome and neck ratio was 1.8 and the median aspect ratio was 1.5. The aneurysms were unruptured in 35 (70%) and irregularly shaped in 28 (56%).

Table 1 Patient background (n = 50)

Characteristics	
Age (median), years	65
Females, n (%)	27 (54.0)
Unruptured, n (%)	35 (70.0)
Site of aneurysm	
ACoA, n (%)	42 (84.0)
A1A, n (%)	2 (4.0)
DACA, n (%)	6 (12.0)
Maximum aneurysm diameter (median) (mm)	5.3
Aneurysm neck diameter (median) (mm)	3.0
Aneurysm height (median) (mm)	4.3
Dome and neck ratio (median)	1.8
Aspect ratio (median)	1.5
Irregular shape and blebs, n (%)	28 (56.0)
Treatment procedure	
Simple, n (%)	30 (60.0)
Balloon-assisted, n (%)	10 (20.0)
Double-catheter, n (%)	8 (16.0)
Stent-assisted, n (%)	2 (4.0)
Procedure-related complications, n (%)	6 (12.0)
Thrombosis, n (%)	2 (4.0)
Intracranial hemorrhage, n (%)	3 (6.0)
Device-related, n (%)	1 (2.0)
Complication that affected the outcome, n (%)	1 (2.0)
Results of first embolization	
CO	42 (84.0)
RN	7 (14.0)
RA	1 (2.0)
Re-treatment, n (%)	2 (4.0)

A1A: proximal segment of the anterior cerebral artery; ACoA: anterior communicating artery; CO: complete obliteration; DACA: distal segment of the anterior cerebral artery; RA: residual aneurysm; RN: residual neck

Results and embolic effects of the initial treatment

The embolization procedure was simple in 30 (60%), balloon-assisted in 10 (20%), double-catheter in 8 (16%), and stent-assisted in 2 (4%). The outcome of the first embolization was CO in 42 (84%), RN in 7 (14%), and RA in 1 (2%). Procedure-related complications were observed in 6 (12%) and thromboembolic complications were observed in 2 (4%), all developing in the ACoA. A ruptured and unruptured aneurysm was present in one patient each. All complications were due to intraoperative thrombus formation, but thrombi were resolved in all patients by the additional administration of antithrombotic agents. Hemorrhagic complications were observed in three patients (6%), all of whom had ACoA aneurysms, and the hemorrhage was due to intraoperative rupture in two and perforation of a penetrating artery by the wire in one. The remaining patient had coil-related trouble. As the coil unraveled during embolization of an unruptured DACA aneurysm, it was fixed using a stent. The complications affected the treatment outcome in only 1 (2%) who had a thrombotic complication of a ruptured ACoA aneurysm. Both patients (4%) who were re-treated during the follow-up period had ruptured ACoA aneurysms.

Concerning the embolic effects, the median follow-up period was 57 months. In the 43 patients (85%) classified into the stable group, 40 had no change and 3 exhibited improvement. Of the three patients with improvement, the improvement was from RN to CO in two and from RA to CO in one. Recanalization was observed in seven, and the state of embolization decreased from CO to RN in all. The stable and recanalization groups are compared in **Table 2**. In the recanalization group, the maximum aneurysm diameter (4.3 mm vs. 5.8 mm, respectively; p = 0.017) and height (3.7 mm vs. 4.3 mm, respectively; p = 0.035) were significantly smaller.

Discussion

In this study, the embolic effects evaluated by TOF-MRA were excellent, being CO in 42 patients (84%) and RN in 7 (14%). Furthermore, concerning complications related to

Table 2 Comparisons between recanalization and stable groups

	Recanalization (n = 7)	Stable (n = 43)	p-value
Age (years)	50	65	0.294
Female	3	24	0.689
Unruptured	4	31	0.415
Site			0.685
ACoA	7	35	
A1A	0	2	
DACA	0	6	
Maximum diameter (mm)	4.3	5.8	0.017
Neck diameter (mm)	2.9	3.1	0.747
Height (mm)	3.7	4.3	0.035
Dome and neck ratio	1.7	1.7	0.25
Aspect ratio	1.5	1.4	0.643
Irregularity blebs	5	23	0.711
Simple procedure	3	27	0.26
Procedure-related complications	1	5	1
Result of initial embolization			0.431
CO	7	35	
RN	0	7	
RA	0	1	

A1A: proximal segment of the anterior cerebral artery; ACoA: anterior communicating artery; CO: complete obliteration; DACA: distal segment of the anterior cerebral artery; RA: residual aneurysm; RN: residual neck

the surgical procedures, thrombotic complications were observed in two (4%) and intraoperative hemorrhagic complications were observed in three (6%), but the complications only affected the outcome in one (2%) and no procedure-related death was noted. In systematic reviews of coil embolization for ACoA and DACA aneurysms, the initial embolic effects were high, with complete and near-complete occlusion being achieved in 86%–88% of the patients.[4,5] However, the permanent morbidity and mortality rates related to surgical procedures were high at 8%–9% compared with the treatment results of aneurysms at other sites. In particular, in coil embolization of DACA aneurysms, the frequencies of arterial dissection, intraoperative rupture, and incomplete occlusion are reportedly high.[7] Difficulties in coil embolization of ACoA and DACA aneurysms include a long distance of the access route because of their peripheral locations, meandering of the vessel, and small vascular diameter. In addition, in ACoA aneurysms, there are important penetrating branches and communication with the contralateral vessel, and close attention to their preservation is necessary. Poor access to the aneurysm increases the risk of arterial injury and intraoperative rupture of the aneurysm. In addition, the use of therapeutic devices is restricted by the small vascular diameter. Recently, however, coil embolization has become possible even in patients with marked meandering of the access route and broad neck aneurysms, which were previously untreatable, because of the development of therapeutic devices and techniques. In this study, procedure-related complications comprised thrombotic complications observed in 4% and hemorrhagic complications observed in 6%, and they affected the outcome in 2%, a lower rate than in previous studies. To prevent thrombotic complications, we heparinize patients after sheath placement regardless of whether the aneurysm is ruptured. In addition, as preoperative antiplatelet therapy, we perform DAPT, in principle, for unruptured aneurysms regardless of the therapeutic procedure. As the operability of the microcatheter is important for the prevention of hemorrhagic complications, we proactively employ a distal access catheter (DAC) in patients with a poor access route. In this study, DAC was used in half the patients; 20 were treated by simple coiling, 4 by balloon-assisted coiling, and 1 by stent-assisted coiling. Of the three patients with hemorrhagic complications, two were treated using DAC, but perforation occurred in both during coil insertion and there were no complications during microcatheter navigation. There was no mention of the use of DAC in previous reports, but we consider the use of DAC to have played a role in the decrease in complications during microcatheter navigation. According to a recent report of the therapeutic results of stent-assisted coil embolization for ACoA aneurysms by Choi et al.,[8] procedure-related complications were observed in 9.2%, thromboembolism in 7.6%, and hemorrhagic complications in 2.7% of the patients, but most patients recovered to a condition with no problem in daily activities within 6 months from the beginning of treatment. In coil embolization of DACA aneurysms, thrombotic complications associated with advanced procedures, such as balloon-assisted and double-catheter techniques, are of concern because of the small diameter of the parent artery. Recently, a series of seven cases of pericallosal artery aneurysm treated by flow diversion using the pipeline embolization device (PED) was reported.[9] Cerebral angiography demonstrated high embolic effects 6–12 months after treatment, with five achieving CO and two exhibiting reduced intra-aneurysmal contrast with no procedure-related complications. However, asymptomatic narrowing of the origins of branching vessels covered by PED was observed in two patients and long-term follow-up is considered necessary. Presently, PED is not indicated for aneurysms of this artery, but it is expected to become a useful treatment for aneurysms of peripheral arteries if high embolic effects and safety are established because the device is simple to use, and because anesthesia and radiation exposure can be reduced due to the short treatment time.

In general, the embolic effects are evaluated and classified according to the state of embolization examined by cerebral angiography immediately after treatment.[10] However, repetition of cerebral angiography is invasive and burdens patients. Recently, there have been reports that embolic effects evaluated by MRI are not markedly different from those evaluated by cerebral angiography.[11] In the present study, the state of embolization was evaluated using TOF-MRA images after embolization as the baseline and comparing subsequent images. As additional treatments are evaluated after the development of recanalization space, MRA is considered sufficient for the judgment of their necessity. In this study, re-embolization was performed in two patients with ruptured aneurysms. No patient had rupture during the follow-up period and a satisfactory state of embolization was maintained with 85% of the patients in a stable state. Although there is no clear rule concerning the follow-up period, follow-up using imaging modalities is continued as much as possible because there was a case of exacerbation from CO after the first embolization to RN after 82 months.

In previous reports, a large aneurysm size (>10 mm) and incomplete occlusion were reported to be risk factors for recanalization after embolization.[12–15] Gonzalez et al. evaluated recanalization factors of ACoA aneurysms after coil embolization and reported that a dome diameter ≥10 mm, the presence of the neck on ACoA, posterior development of the dome, and incomplete occlusion are related to recanalization.[12] In the present study, the target lesions were small aneurysms with a median maximum diameter of 5.3 mm. Comparison between the stable and recanalization groups revealed significant differences in maximum diameter and height of the aneurysms, and both were notably smaller in the recanalization group (maximum diameter: 4.3 vs. 5.8 mm; $p = 0.017$, height: 3.7 vs. 4.3 mm; $p = 0.035$). Small cerebral aneurysms were reported to recur less frequently after embolization than average-sized aneurysms and to have more favorable outcomes.[6] Oishi et al. reviewed 500 cases of coil embolization of small unruptured cerebral aneurysms <10 mm in diameter and found that the recurrence rate was lower in those with a maximum diameter of <5 mm and a dome/neck ratio of ≥1.5.[16] Feng et al. reported the embolic effects in unruptured aneurysms <5 mm in diameter[17] and observed recanalization in 10 of the 174 patients evaluated by angiography. They also reported by evaluating recanalization factors in 56 patients with incomplete occlusion after the first embolization that a diameter of <3 mm was a factor related to recanalization. However, they did not mention four patients who had recanalization following complete occlusion after the first embolization. According to our results, recanalization was observed invariably in patients judged as achieving complete occlusion after the first embolization. However, this may have resulted from differences in the method of imaging evaluation. Some small aneurysms develop recanalization after complete occlusion and evaluation of factors related to recanalization of such aneurysms is necessary in the future. Feng et al. also suggested the use of stents as a reason for the high embolic effects. In the present study, consistent embolic effects were obtained even though stents were used in only 4% of the patients. Therefore, we considered the embolic effects to be within an acceptable range in ACoA and ACA aneurysms even without using stents. There is a possibility that improvements in balloons and coils played a role in the embolic effects, but the relationships of the embolic effects with the volume embolization ratio and the coils we used were unable to be evaluated due to insufficient data. Recently, small-diameter and flexible coils have been developed, and the increased coil options in the final stage of embolization is hypothesized to have improved the embolic effects.

This study has several limitations. It was a retrospective study, the number of patients was small, and patients with ruptured and unruptured aneurysms treated by different approaches were mixed. Craniotomy was selected for patients judged by prior examinations to be poor candidates for coil embolization. Regarding the aneurysm morphology, the growth direction was not analyzed. Comparative evaluation with DSA was not performed. TOF-MRA images evaluated were not obtained using the same device. The follow-up period was 1 year after surgery and long-term results have not been evaluated. The treatment outcomes were not evaluated. Only univariate analysis was performed and caution is needed in the interpretation of its results in consideration of the involvement of confounding factors. Blinding was not carried out in the evaluation of treatment. In the future, we will assess more cases and conduct more detailed evaluation of the aneurysm morphology in order to reduce the recanalization rate of ACoA and ACA aneurysms after coil embolization.

Conclusion

In our study, the complication rate in coil embolization of ACoA and ACA aneurysms was lower than that in previous reports, and consistent embolic effects were obtained. The maximum diameter and height of the aneurysm were notably smaller in the recanalization group.

Disclosure Statement

All authors have no conflicts of interest to declare.

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