

# A Single Center Experience with Coil Embolization for Cerebral Aneurysms Greater than 10 mm in the Internal Carotid Artery

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## Abstract

We investigated endovascular treatment for 10 mm or larger aneurysms in the internal carotid artery (IC), including the cavernous portion, the paraclinoid portion, and the posterior communication artery (PC). Between 2011 and 2014 at our hospital, there were 35 cases of aneurysms that were 10 mm or larger in the carotid artery. We analyzed these 35 cases retrospectively based on the size and location of the aneurysms, method of treatment, number of coils implanted, use of a stent, complications, rupture after treatment, ophthalmologic symptoms, and need for re-treatment. There was no bleeding after treatment. Of the 35 cases, four cases (11%) had permanent complications. Re-treatment was indicated in 11 cases (31%), including eight cases localized in the paraclinoid portion, two cases in the IC-PC, and one case in the cavernous portion. Among these re-treatment cases, two cases required a third treatment. Of the 16 cases with paraclinoid aneurysms, half required re-treatment. Of the 12 cases with ophthalmologic symptoms prior to treatment, 9 (75%) improved or had no change and 3 (25%) became worse. There were no complications in the 13 re-treatment procedures. Re-treatment is not uncommon, and a scheduled follow-up is needed. Coil embolization has been one of the main options for aneurysms that are 10 mm or larger in the IC. In the future, these large aneurysms will be treated with a flow diverter stent (FD).

Key words: coil embolization, large aneurysm, re-treatment

## Introduction

Aneurysms in the carotid artery cause subarachnoid hemorrhage and ophthalmologic symptoms, including double vision, ptosis, and visual acuity disturbances depending on the dysfunction of either the oculomotor, the abducens, or the optic nerves. Large aneurysms have been treated by either surgery or endovascular treatment. Based on the excellent success with the endovascular treatment for aneurysms,<sup>1)</sup> this method has become more popular in Japan. Large aneurysms have a high risk of subarachnoid hemorrhage and are difficult to treat. Generally, neck clipping, parent artery occlusion (PAO) with/without bypass, and endovascular treatment are used for large aneurysms. Although PAO with a high flow bypass has been the gold standard therapy for these aneurysms,<sup>2)</sup> some problems remain, including the invasiveness, long

surgical time, ischemic events, hyperperfusion, and other complications. Also in Japan, the use of a flow diverter stent (FD) has become more common. In this study, we analyzed the results for the use of coil embolization for large aneurysms.

## Materials and Methods

Among the 343 cases of cerebral aneurysms treated in our institute between 2011 and 2014, we focused on 35 cases of internal carotid aneurysms that were 10 mm and larger in size. The average age of the patients in these 35 cases was 64 years (40–82), and the male/female was 7/28. There were eight cases of ruptured aneurysms and 27 cases with no rupture. Twelve of the 35 cases had pre-treatment ophthalmologic symptoms, including visual impairment and eye movement. Among the 35 cases, 12 patients had hypertension, one had diabetes, and one smoked. Only one patient had multiple

aneurysms. The average follow-up period was 3.5 years (1.5–5.0). We analyzed the size and location of the aneurysms, dome and neck ratio (D/N), aspect ratio, method of treatment, Raymond score, complications, need for re-treatment, and rupture after treatment. Statistical analyses were performed by the student's *t*-test, chi-square test, and Fisher's exact test using Microsoft Excel™. A *P* value less than 0.05 was considered statistically significant.

All of these aneurysm cases were treated by an endovascular procedure in our institute between 2011 and 2014. None of these cases was treated by open surgery. Endovascular treatment was performed under general anesthesia. The method of treatment depended on the size of the aneurysm and on the length of the neck. In our institute, we used a balloon assist coil embolization for all cases. For large aneurysms, multi-catheter procedures that included a stent-assist, balloon in stent technique, and double catheter technique were needed. We usually used a 7Fr Shuttle sheath™ (Cook Medical, Bloomington, IN, USA) and a 7Fr FUBUKI™ (ASAHI-INTECC, Nagoya, Japan) for a triple coaxial guiding system. For the cases with an intracranial stent, we prescribed two antiplatelet drugs 1 week before treatment. For the patients with a subarachnoid hemorrhage, a single antiplatelet drug was given just after embolization using a nasal-gastric tube. After femoral artery puncture under general anesthesia, we used 5000 U of heparin to extend the activated whole blood clotting time (ACT) by about 300 sec. We usually chose specific balloons, Scepter XC™ (TERUMO, Tokyo, Japan) or Hyperform™ (COVIDIEN, Minneapolis, MN, USA), and stents, Enterprise™ (CODMAN, Raynham, MA, USA) or Neuroform™ (STRYKER, Natick, MA, USA). Although the surgeons selected the micro-catheters and coils individually, 0.018 inch coils are recommended as the first coil for large and giant aneurysms.

Just after treatment, computed tomography (CT) was performed. Magnetic resonance imaging (MRI) with a diffusion-weighted image (DWI) was indicated to check for ischemic complications the day after treatment. Thereafter, a skull X-ray and MRI were scheduled every six months. If we saw coil compaction or re-canalization of the aneurysm, cerebral angiography was performed. Re-canalization revealed by angiography indicated the need for re-treatment. In all 11 cases requiring re-treatment, more coils were inserted into the residual aneurysms with or without stent and balloon-assist. In the cases with a stent-assist for the first treatment, a micro-catheter was inserted into the aneurysms via a trans-cell for the re-treatment.

## Results

Among the 35 cases, 12 cases presented with the ophthalmologic symptoms, including either a visual acuity or eye movement disturbance. The average size of the 12 aneurysms was 20 mm. These 12 aneurysms were significantly larger than that of the other 23 cases (average: 13.1mm,  $P = 0.0012$ , *t*-test). The locations of these 12 aneurysms were 4 (33%) in the IC-cavernous portion, 6 (50%) in the IC-paraclinoid portion, and 2 (18%) in the IC-posterior communication artery (PC) (Table 1). The ophthalmologic symptoms improved in 6 cases, did not change in three cases, and worsened in three cases. Two cases without pre-treatment ophthalmologic symptoms had a transient disturbance of eye movement due to oculomotor palsy after the treatment. Finally, permanent complications were found in 4 (11.4%) of the 35 cases, including one case of ischemic stroke with mild hemiparesis and three cases of aggravation of eye movement due to oculomotor palsy. There was no bleeding from the treated aneurysms during the follow-up period (3.5 years). For the first treatment, we used an average of 14.7 of the coils and required an average of 141 minutes for the procedure. In eight subarachnoid hemorrhage patients, the average diameter of the aneurysms was 11.6 mm which was significantly smaller than that of the un-ruptured aneurysms ( $P < 0.047$ , Table 1). These ruptured aneurysms needed a smaller number of coils to be embolized ( $P < 0.0057$ , Table 1).

Eleven (31%) of the 35 cases required re-treatment due to re-canalization. All of the 11 cases involved a second embolization within one year of the first treatment (average:  $10.0 \pm 1.3$  months). Among these, two cases required a third treatment. All of the re-treatment cases were performed within 1 year after the first treatment. Only one patient refused re-treatment due to her advanced age. In our institute, 308 cases of cerebral aneurysms, excluding the 35 large IC aneurysms, were treated by an endovascular procedure, and among these 308 cases, 17 cases (5.5%) required a second treatment. IC aneurysms that are 10 mm or larger had a higher risk of re-canalization than that of small aneurysms ( $P < 0.01$ , chi-square test). Re-treatment in these 11 cases had no relationship with the Raymond scale, the size of the aneurysm, number of coils, volume embolization ratio (VER), surgical time, and age of the patients (Table. 2). The D/N ratios were  $3.05 \pm 1.64$  in the re-treatment cases and  $2.54 \pm 0.65$  in the no re-treatment cases ( $P = 0.20$ , *t*-test). The aspect ratios were  $1.33 \pm 0.18$  in the re-treatment cases and  $1.25 \pm 0.20$  in the no-retreatment cases ( $P = 0.32$ , *t*-test).

In 11 cases, including three re-current and eight non-recurrent cases, HydroCoil™ (TERMO Tokyo, Japan), which self-expands, was chosen, and the VER was calculated based on the expanded volume.

Eight cases required re-treatment in the IC-paraclinoid portion, one in the IC-cavernous portion, and two in the IC-PC (Table 3). Although half of the IC-paraclinoid aneurysms needed re-treatment, there was no significant difference. For the first treatment of these 35 cases, 22 cases (62.8%) involved a stent-assisted coil embolization and 26 cases (74.3%) involved a double catheter technique (Table 4). In three of eight cases with subarachnoid hemorrhage, stent replacement was performed to prevent coil migration into the internal carotid artery because of the wide neck of the aneurysms. These three cases received a double dose of platelet therapy just after the treatment.

The second treatments were performed with a balloon in stent technique in eight cases and with a stent replacement in four cases. In the cases with stenting used in the first treatment, we put a micro-catheter into the aneurysm via a trans-cell and added the coils. The average time of re-treatment was 140 minutes, which is the same as that of the first treatment. Only two cases required a third treatment. There were no complications with the 11 procedures for the second treatment and with the two procedures for the third treatment.

## Discussion

In this decade, the treatment for cerebral aneurysms has changed dramatically. Endovascular treatment has improved due to the availability of many devices.<sup>1,3)</sup> However, very large aneurysms are still difficult to treat. Because we know that the larger aneurysms have a risk of hemorrhage<sup>4)</sup>, the successful treatment of these aneurysms is a challenge. Some cases where it is impossible to clip directly, parent artery occlusion (PAO) with high-flow bypass is indicated and is usually successful.<sup>2)</sup> However, invasiveness, ischemic complications, and hyperperfusion remain as problems. Depending on the balloon occlusion test (BOT), PAO could be indicated either with a low flow bypass or without a bypass. In fact, a 4.7–25% risk of ischemic complications has been reported.<sup>5)</sup> In the history of the treatment for large and giant aneurysms, coil embolization with preservation of the parent artery is the most suitable procedure for cerebral blood flow. Thus, the use of stent-assisted coil embolization has been increasing for large and giant aneurysms. However, the re-canalization rate is increased, and re-treatment is usually required with coil embolization, especially for large and giant aneurysms. This study was designed to analyze the effectiveness of coil embolization for aneurysms that were 10 mm or larger in the carotid artery before the introduction of FD.

**Table 1** Result of the first treatment

Symptom	Number of case	Size (mm. average)	Location			First treatment		Raymond scale		
			Paraclinoid	IC-cavernous	IC-PC	Number of coils (average)	with stent	CO	NR	BF
All cases	35	15.5	16	8	11	15.5	22	18	9	8
With pre-operative visual symptom	12	20*	6	4	2	17.5	9	3	4	5
Post-the first treatment										
better	6	22.7	3	2	1	18.2	5	1	2	3
no change	3	19	2	1	0	17	3	1	1	1
worse	3	15.7	1	1	1	16.7	1	1	1	1
Without visual symptom post-the first treatment	23	13.1*	10	4	9	14.4	13	15	5	3
no change	21	12.4	10	2	9	14.1	11	14	4	3
transient visual worsening	2	21	0	2	0	18	2	1	1	0
SAH										
yes	8	11.6**	1	0	7	10.76***	3	3	2	3
no	27	16.6**	15	8	4	16.9***	18	15	7	5

\* $P = 0.0012$ , \*\* $P < 0.047$ , \*\*\* $P < 0.0057$  ( $t$ -test). BF: body filling Statistical analysis by the  $t$ -test, CO: complete occlusion, IC: internal carotid artery, NR: neck remnant, PC: posterior communicating artery, SAH: subarachnoid hemorrhage.

**Table 2 With or without re-treatment No. 1 D/N ratio: Dome and Neck ratio Statistical analysis by either the t-test or Fisher's exact test**

No	Size of aneurysm (mm. average)			First treatment				Raymond scale						
	Age (average)	D/N ratio	Aspect ratio	Stent	Double cath	SAH	Visual symptom	Number of coils (average)	VER (%)	Time of treatment (min. average)	CO*	NR*	BF	
Retreatment 11	63 ± 12.4	15.9 ± 6.0	3.05 ± 1.64	1.33 ± 0.18	8 (72.7%)	8 (72.7%)	1 (9%)	5 (45.5%)	17.9 ± 6.7	43.7 ± 17.7	142 ± 29.7	4 (36.4%)	4 (36.4%)	3 (27.3%)
No retreatment 24	65 ± 9.5	15.3 ± 6.3	2.54 ± 0.65	1.25 ± 0.20	14 (58.3%)	18 (75%)	7 (29.2%)	7 (29.2%)	14.3 ± 4.7	39.1 ± 20.6	140 ± 27	13 (54.2%)	6 (25%)	5 (20.8%)
P value	0.61*	0.72*	0.20*	0.32*	0.48**	1**	0.39**	0.45**	0.15*	0.55*	0.91*	0.47**		

\*t-test, \*\*Fisher's exact test.

In our institute, endovascular treatment has been the first choice for cerebral aneurysms, and all cases of aneurysms that were 10 mm or larger in the IC were treated by an endovascular procedure. Thus, based on the standard use at our hospital, there was no bias for the indication of the treatment. Our study period for large and giant aneurysms occurred in the stent-assisted era.

Some large and giant IC aneurysms presented with not only subarachnoid hemorrhage but also with the ophthalmologic symptoms, including oculomotor palsy, abducens palsy, and optic nerve disturbances. In the IC-cavernous aneurysms, coil embolization has a risk of such ophthalmologic symptoms.<sup>6)</sup> Alternatively, another study reported that the risk was low in the same situation.<sup>7)</sup> In our study, pre-treatment ophthalmologic symptoms were present in 12 cases with aneurysms that were significantly larger than that of the others (20 mm vs 13.1 mm). Among them, the ophthalmologic symptoms improved in 6 cases (50%), showed no change in three cases, and worsened in three cases. In the three cases that worsened, the aneurysms were smaller without a significant difference in size (average 15.7 mm, Table 1). This result shows that there is a risk for ophthalmologic symptoms after coil embolization even in the mid-sized aneurysms of 15 mm diameter. The two patients without pre-treatment ophthalmologic symptoms showed transient double vision after treatment, and the sizes of their aneurysms were 17 mm and 25 mm. In the literature, pre-treatment ophthalmologic symptoms improved in 56.6% of the patients by clipping and in 41.5% of the patients by coiling.<sup>8)</sup> However, direct clipping is not easy for large and giant aneurysms. On the other hand, FD was reported to improve the ophthalmologic symptoms in 75% of the cases.<sup>9)</sup> FD is recommended especially for large and giant IC aneurysms in patients with ophthalmologic symptoms.

One of the important results in coil embolization for large and giant aneurysms is whether re-canalization occurs and requires re-treatment.<sup>10-14)</sup> We found that 31.4% of the cases needed re-treatment due to re-canalization. A published study involving the same type of patients as our study reported that 35% of the patients required re-treatment.<sup>14)</sup>

**Table 3 With or without re-treatment No. 2. Location of aneurysms. Statistical analysis by the Fisher's exact test**

	Paraclinoid	Caverous*	IC-PC
Re-treatment	8	1	2
No re-treatment	8	7	9

\*P = 0.065 (Fisher's exact test).

**Table 4** Methods of coil embolization cath: catheter

	No	Treatment			Number of coil (average)	Permanent complication
		Stent	Balloon in stent	double cath		
First coiling	35	22 (62.8%)	26 (74.3%)	8 (22.9%)	14.3 ± 4.7	4(11.4%)
Second coiling	11	5 (45.5%)	8 (72.7%)	1 (9%)	15.5 ± 8.0	0
Third coiling	2	0	1 (50%)	1 (50%)	19.5 ± 2.5	0

In our study, the average of follow-up period was 3.5 years, and it is possible that additional patients after this period may require a re-treatment. There were no ruptures after the treatment, and all re-treatments were performed within 1 year after the first treatment. Rupture of coiled large aneurysms was reported to be about 1.9% per year.<sup>14)</sup> In the follow-up, digital subtraction angiography (DSA) at 6 months after the treatment was recommended to check for re-canalization.<sup>15,16)</sup> Re-canalization or rupture have been reported even at a long time after treatment.<sup>10,11,13)</sup> Thus, some cases in our study may have had re-canalization after the 3.5 year follow-up. We conclude that long-term follow-up is necessary to check for re-canalization.

The risk factor for re-canalization was reported as a larger aneurysm size.<sup>11,13)</sup> In this study, half (8 of the 16 cases) of the IC-paraclinoid aneurysms required re-treatment. Wang et al. reported that large paraclinoid aneurysms had a high rate of recurrence.<sup>17)</sup>

The reason why the paraclinoid aneurysms recur is not known. However, some published studies suggest that the influence of hemodynamic stress on the paraclinoid aneurysms may be a cause.<sup>18)</sup> Although only one IC-cavernous aneurysm required re-treatment in our study, another report showed a high re-canalization rate for IC-cavernous aneurysms.<sup>7)</sup> Ogilvy reported that the risk factors for re-canalization were aneurysm over 10 mm in size, ruptured aneurysm, lack of a stent, lack of a FD, presence of a thrombus, and Raymond Roy scale.<sup>12)</sup> Another paper reported that re-canalization could occur in 10 mm and larger aneurysms despite the use of a stent.<sup>13)</sup>

Some papers have reported on the use of a FD. When comparing FD and coil embolization, complete obliteration was found in 86% of the cases with FD and in 41% of the cases with coiling.<sup>19)</sup> In addition, FD was superior in terms of cost relative to that of the usual coil embolization.<sup>20)</sup> In our study, we used 14 coils (average) per one treatment. Our findings also showed the superiority of FD. However, after FD placement, hemorrhagic or ischemic events were reported.<sup>19)</sup>

So, additional studies on FD are needed to determine its superiority in Japanese institutes.

One study showed the safety of the second coil embolization<sup>21)</sup> and another study reported a different result with 11% peri-treatment complications.<sup>22)</sup> In our experience, 11 of the second treatments and two of the third treatments were all safe. We added a stent in five cases, used a stent on balloon technique in eight cases, and added over 15 coils for re-canalization. We confirmed that the second treatment was safer than the first treatment. Thus, we do not hesitate if a second treatment is required. Furthermore, the second treatment with FD was found to be effective.<sup>23)</sup> Another report showed a low effectiveness of FD for the second treatment in re-canalization after stent-assisted coil embolization.<sup>24)</sup> Therefore, a staged flow diversion strategy was designed.<sup>25)</sup>

For large and giant IC aneurysms, we can also perform PAO with or without extracranial-intracranial (EC-IC) bypass. There have been problems with ischemic events after PAO.<sup>26)</sup> BOT has been refined, has 1.6% complications,<sup>5)</sup> and false-negative results can occur. High-flow bypass is sophisticated, and Ishishita et al. had excellent results with high-flow bypass and PAO without BOT.<sup>2)</sup> However, invasiveness, low level of evidence, and limitation of the operator remain as the barriers for standard treatment. In the future, we will select the suitable treatment for the patient, including either coil embolization with or without stent, PAO with or without EC-IC bypass, or FD placement.

## Limitation

This study had some limitations as follows: single center experience, mid-term follow-up, and no randomization. We analyzed our results for the next FD era indication.

## Conclusion

Coil embolization for aneurysms that are 10 mm or larger in the internal carotid artery are safe, effective, and do not rupture. However, re-treatment is



required in 31% of these cases. The ophthalmologic symptoms are improved in 50% of the cases by coil embolization. Coil embolization with or without stent-assisted has been one of the main options for large and giant aneurysms.

### Conflicts of Interest Disclosure

The authors declare no conflict of interest.

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