

Timing of retreatment for patients with previously coiled or clipped intracranial aneurysms: Analysis of 156 patients with multiple treatments

Takeshi Okada, Tatsuya Ishikawa, Junta Moroi, Akifumi Suzuki

Department of Surgical Neurology, Research Institute for Brain and Blood Vessels Akita, Akita, Japan

E-mail: Takeshi Okada - takeshi-okada@mic-gmc.jp; *Tatsuya Ishikawa - teddyish@akita-noken.jp; Junta Moroi - moroi@akita-noken.jp; Akifumi Suzuki - akifumi@akita-noken.jp

*Corresponding author

Received: 01 August 15 Accepted: 27 October 15 Published: 07 January 16

Abstract

Background: Some patients require a second surgical intervention for recurrence of treated aneurysms, untreated aneurysms in patients with multiple lesions, or *de novo* aneurysm. This retrospective review of the data was undertaken to evaluate when retreatment is necessary after initial aneurysm treatment.

Methods: Cerebral aneurysms in 1755 patients were treated via clipping or coiling between January 1995 and September 2012. Postoperative follow-up was performed at 6 months after treatment and was repeated every 12 months (or longer) after treatment using three-dimensional computed tomography angiography or magnetic resonance angiography.

Results: A cumulative total of 156 patients (8.9%) (117 women, 39 men; mean age: 55.0 years; range: 25–79 years) needed retreatment for rupture or regrowth of aneurysm ($n = 31$; ruptured (R)/remaining unruptured (U), 26/5), formation of *de novo* aneurysm ($n = 45$; R/U, 23/22), known untreated aneurysm in patients with multiple lesions ($n = 78$; R/U, 5/73), and hemorrhage from undetected aneurysm ($n = 2$). The regrowth risk is higher after endovascular treatment than after craniotomy and clipping. Median time to retreatment was 187 months (range: 11–280 months) for regrowth, 165 months (range: 22–330 months) for *de novo*, and 24 months (range: 2.8–417 months) for known untreated aneurysm. Regrowth or known with subarachnoid hemorrhage were frequently treated within 2 years from initial treatment.

Conclusions: Aneurysms with residua or untreated aneurysms in patients with multiple lesions carry a risk of bleeding during a relatively short period, whereas there is a small but significant risk of *de novo* formation and subsequent hemorrhage at over 10 years after previous treatment.

Key Words: *De novo* aneurysm, follow-up, intracranial aneurysm, regrown aneurysm, retreatment

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Website:

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DOI:

10.4103/2152-7806.173570

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How to cite this article: Okada T, Ishikawa T, Moroi J, Suzuki A. Timing of retreatment for patients with previously coiled or clipped intracranial aneurysms: Analysis of 156 patients with multiple treatments. *Surg Neurol Int* 2016;7:540-8.
<http://surgicalneurologyint.com/Timing-of-retreatment-for-patients-with-previously-coiled-or-clipped-intracranial-aneurysms:-Analysis-of-156-patients-with-multiple-treatments/>

INTRODUCTION

Aneurysm clipping and coil embolization have provided robust treatments for preventing rupture of intracranial aneurysm. However, some patients must undergo retreatment due to recurrent aneurysm at the originally treated site, *de novo* aneurysm at a remote location, or aneurysms left untreated at initial treatment in cases of multiple aneurysms. Several case series have suggested that the risk of intracranial aneurysm formation is relatively high after surgical treatment.^[1,8] However, those studies have generally involved small-scale investigations, and the characteristics and clinical courses regarding retreatment after initial treatment of aneurysm remain unclear. We therefore retrospectively examined our data set of clinical records regarding the characteristics of patients who were admitted for treatment of intracranial aneurysm on two or more occasions.

MATERIALS AND METHODS

Patients and data collection

The Institutional Medical Review Board of the Research Institute for Brain and Blood Vessels–Akita approved the study protocol. From January 1995 to December 2012, a total of 1755 patients were admitted to the hospital for treatment of ruptured or unruptured intracranial aneurysms. Of those, we retrospectively identified those patients who had previously been admitted for surgical or endovascular obliteration treatments for intracranial aneurysms. In those patients, retreatment had been performed for the following reasons: Aneurysm located at the same site as the originally treated one, representing regrowth and/or rupture (regrown aneurysm); aneurysm located at a site completely remote from the originally treated one, is identified and/or ruptures (*de novo* aneurysm); aneurysm that had been visible at initial treatment, but had been left untreated (known untreated aneurysm); or subarachnoid hemorrhage (SAH) of unknown cause (occult aneurysm). We obtained information from medical records and operation records to assess clinical characteristics, the interval between initial treatment and retreatment, and outcomes for patients according to the type of retreatment. Clinical outcomes for patients with ruptured aneurysm were defined using modified Rankin scale (mRS) score at discharge.

Follow-up interval and acquisition of diagnostic images

Follow-up diagnosis of aneurysm for patients who underwent surgical clipping was based on images obtained using three-dimensional computed tomography angiography (3D-CTA) at least once within 6 months of the initial treatment. Magnetic resonance angiography

(MRA) was performed every 12 months thereafter until 2 years after surgery. Patients were also repeatedly examined with 3D-CTA or MRA every 1–5 years. Particularly in patients with suspicious residua or regrowth of the treated aneurysm, 3D-CTA was repeated frequently. Diagnostic images for patients who underwent endovascular coiling were obtained using plain skull X-ray to evaluate the formation of coils at least once within 1 month of initial treatment, plain skull X-ray and MRA once within 6 months, digital subtraction angiography (DSA) once around 12 months, and plain skull X-ray and MRA once every 12 months thereafter. If these patients were admitted for retreatment of the intracranial aneurysm, diagnostic imaging was performed on admission and postoperatively using 3D-CTA, MRA, and/or DSA depending on the treatments that had been performed initially and at retreatment.

Indications for surgical or endovascular intervention of intracranial aneurysms

Regardless of the treatment either the 1st time or on retreatment, we treated all patients with ruptured aneurysms defined as the World Federation of Neurosurgical Societies (WFNS) Grades I–IV, as well as selected patients with WFNS Grade V, who should have at least one of the following conditions: Glasgow Coma Scale score > 6; improving neurology; or large hematoma formation associated with SAH. We recommended surgical or endovascular treatment for patients with *de novo* or known untreated aneurysms that remained unruptured, when they had a history of another ruptured aneurysm, aneurysm larger than 5 mm, irregularly shaped, or that transformed in shape during follow-up. We took both age and activities of daily living (ADL) of the patient into consideration for treatment. We offered treatment to patients with regrown aneurysm, unless a significant contraindication was present.

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 21.0 (SPSS Japan, Tokyo, Japan). Categorical variables, except for the method of surgical or endovascular intervention at retreatment and location of the aneurysm at retreatment, were compared between the target group and other groups using Fisher's exact test or the Pearson Chi-square test. Methods of surgical or endovascular intervention at retreatment and locations of aneurysm at retreatment were compared to those at initial treatment using Fisher's exact test. Continuous variables were compared between the target group and other groups using the Mann–Whitney *U*-test or Student's *t*-test. Missing data were omitted and analyses of the available data were performed. Two-sided values of $P < 0.05$ were considered statistically significant.

RESULTS

Figure 1 shows the study profile. A cumulative total of 156 patients (117 women, 39 men; mean age: 55.0 ± 10.8 years) were identified from previous treatment of intracranial aneurysms. A total of 122 patients received treatment twice, 14 patients received treatment three times, and 2 patients received treatment four times. Patients who received clipping treatment for ruptured aneurysms were more frequent on initial treatment than on second or later treatment. The subsequent rupture risk of treated unruptured aneurysm is quite low, compared to treated ruptured aneurysm.

Table 1 shows the relationship between disease severity on admission and clinical outcome at discharge in patients with ruptured aneurysm. Among patients with ruptured

aneurysm, patients with better SAH grade at initial treatment predominated over those with better SAH grade at second treatment or later. Clinical outcome (mRS score at discharge) was thus better in patients at initial treatment than at second treatment or later. The size of aneurysm by aneurysm location is shown in Table 2. With ruptured aneurysms, no significant differences in aneurysm size were seen among aneurysm locations.

Table 3 shows aneurysm characteristics according to the type of retreatment for aneurysm. Thirty-one aneurysms were classified as regrown aneurysm, 45 as *de novo* aneurysm, 78 as known untreated aneurysm, and we have repeated angiography on 2 patients but any aneurysms could not be detected. Therefore, we considered that they had perimesencephalic SAH as occult aneurysm. Regrown aneurysms had been treated with coil embolization at initial treatment (54.8%) more frequently than other types of retreatment ($P < 0.01$). The regrowth risk is higher after endovascular treatment than after craniotomy and clipping regrown aneurysm tended to appear more frequently in the internal carotid (IC) artery or internal carotid-posterior communicating (ICPC) artery (54.8%), and less frequently in the middle cerebral artery (MCA) (19.4%), irrespective of first treatment modality, although no significant differences in distribution of aneurysm locations were seen among types of retreatment for aneurysm ($P = 0.096$). In patients with regrown aneurysm (excluding 1 patient in whom

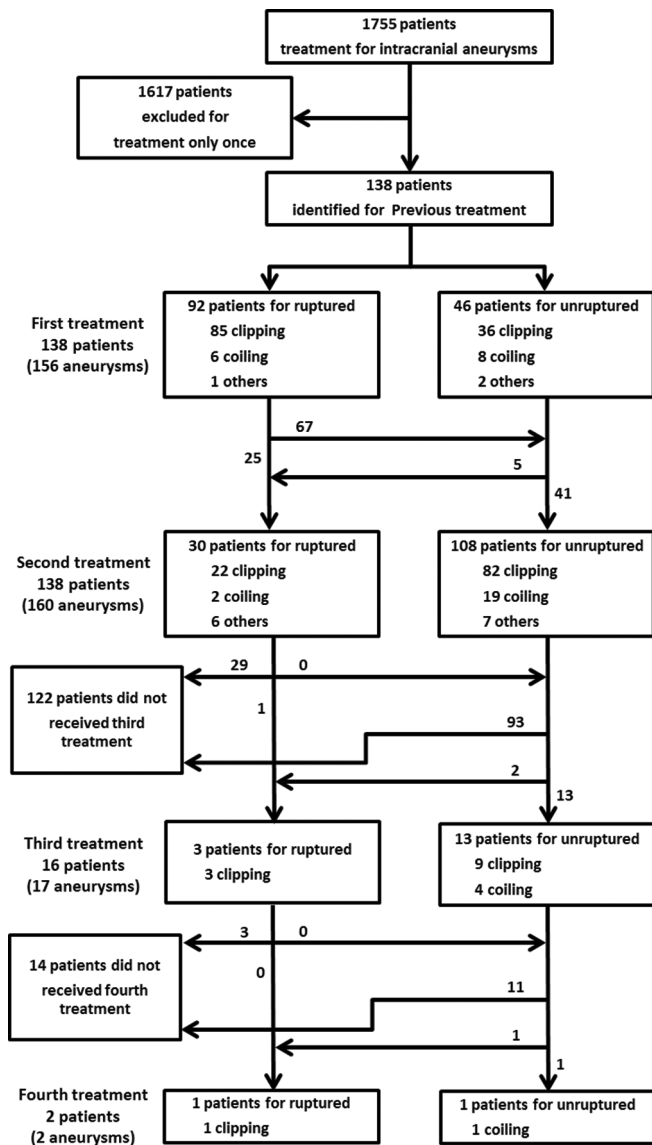


Figure 1: Flow diagram of the identification of enrolled patients and the number of patients at first treatment and retreatment

Table 1: Relationship between WFNS grade on admission and clinical outcome at discharge in patients with ruptured aneurysms

	WFNS on admission					
	I	II	III	IV	V	Unknown
First treatment with SAH (n=92)						
mRS at discharge						
0	38	8	4	7	1	8
1	7	1				1
2	3	1	2	2		1
3	1	2	1			
4	2		1			
5					1	
Second treatment or later with SAH (n=34)						
mRS at discharge						
0	6	1	1	1		1
1	4	2				
2		1	1			
3		1	2	2		
4	2	1				
5						1
6			2	1	3	

mRS: Modified Rankin Scale, SAH: Subarachnoid hemorrhage, WFNS: World Federation of Neurosurgical Societies

Table 2: Aneurysm characteristics on location of aneurysm at the initial treatment

Variable	ACA (n=17)	P	Acom (n=33)	P	MCA (n=119)	P	ICPC (n=72)	P	IC (n=56)	P	BA (n=20)	P	VA (n=14)	P	AICA (n=1)	PCA (n=1)
Number, unruptured/ruptured	12/5	0.49	16/17	0.074	76/43	0.76	44/28	0.74	39/17	0.24	13/7	0.83	8/6	0.66	0/1	1/0
Unruptured aneurysm																
Size of aneurysm, mm (mean±SD)																
Dome	4.0±2.1	0.040	5.8±2.9	0.35	6.8±4.8	0.85	6.5±3.8	0.55	8.5±6.0	0.022	8.4±6.7	0.24	5.9±3.2	0.61	-	5.4
Neck	2.8±0.8	0.021	4.2±1.7	0.47	4.9±2.6	0.44	4.4±2.4	0.42	5.3±3.5	0.17	5.2±2.7	0.52	4.9±2.2	0.85	-	2.5
Ruptured aneurysm																
Size of aneurysm, mm (mean±SD)																
Dome	7.1±4.0	0.55	7.2±4.5	0.31	9.0±4.3	0.30	8.9±5.1	0.41	7.4±3.0	0.50	8.9±5.5	0.72	5.7±3.5	0.14	4.5	-
Neck	3.5±1.3	0.18	4.4±2.3	0.27	5.9±3.3	0.15	5.6±3.8	0.52	4.3±1.1	0.26	6.0±2.6	0.51	4.6±1.6	0.55	1.7	-

ACA: Anterior cerebral artery, ACom: Anterior communicating artery, AICA: Anterior inferior cerebellar artery, BA: Basilar artery, IC: Internal carotid artery, ICPC: Internal carotid - posterior communicating artery, MCA: Middle cerebral artery, PCA: Posterior cerebral artery, SD: Standard deviation, VA: Vertebral artery

Table 3: Aneurysm characteristics on type of retreatment

Variable	Regrown aneurysms			P	De novo aneurysms	P	Known untreated aneurysm	P	Occult aneurysms
	All	Clipping/ wrapping	Coiling						
Number of retreatments	31	14	17		45		78		2
Aneurysm at initial treatment									
Unruptured/ruptured	15/16	4/10	11/6	0.31	17/28	0.67	31/47	0.87	0/2
Treatment, n (%)				<0.001		0.0013		<0.001	
Clipping	13 (41.9)	-	-		44 (97.8)		75 (96.2)		2 (100)
Coiling	17 (54.8)	-	-		0 (0)		2 (2.6)		0 (0)
Wrapping	1 (3.2)	-	-		1 (2.2)		0 (0)		0 (0)
Trapping	0 (0)	-	-		0 (0)		1 (1.3)		0 (0)
Conservative treatments	0 (0)	-	-		0 (0)		0 (0)		0 (0)
Location, n (%)				0.096		0.63		0.029	
ACA	0 (0)	0 (0)	0 (0)		2 (3.8)		3 (3.3)		0 (0)
ACom	3 (9.7)	2 (14.3)	1 (5.9)		4 (7.7)		15 (16.7)		0 (0)
MCA	6 (19.4)	4 (28.6)	2 (11.8)		17 (32.7)		38 (42.2)		1 (50.0)
ICPC/IC	18 (54.8)	8 (57.1)	10 (58.8)		23 (44.2)		25 (27.8)		1 (50.0)
BA/VA/AICA/PCA	4 (12.9)	0 (0)	4 (23.5)		5 (9.6)		9 (10.0)		0 (0)
Unknown	0 (0)	0 (0)	0 (0)		0 (0)		0 (0)		0 (0)
Aneurysm at retreatment									
Unruptured/ruptured	26/5	10/4	16/1	0.39	23/22	<0.001	73/5	<0.001	0/2
Treatment, n (%)				0.37*		0.040*		0.017*	
Clipping	12 (40.0)	8 (57.1)	4 (23.5)		39 (86.7)		66 (84.6)		0 (0)
Coiling	14 (46.7)	1 (7.1)	13 (76.5)		5 (11.1)		7 (9.0)		0 (0)
Wrapping	3 (10.0)	3 (21.2)	0 (0)		0 (1)		4 (5.1)		0 (0)
Trapping	0 (0)	0 (0)	0 (0)		0 (0)		0 (0)		0 (0)
Conservative treatments	2 (6.7)	2 (14.3)	0 (0)		1 (2.2)		1 (1.3)		2 (100)
Location, n (%)						0.51*		0.061*	
ACA	-	-	-		4 (7.3)		7 (8.0)		-
ACom	-	-	-		5 (9.1)		4 (4.5)		-
MCA	-	-	-		21 (38.2)		37 (42.0)		-
ICPC/IC	-	-	-		16 (29.1)		32 (36.4)		-
BA/VA/AICA/PCA	-	-	-		9 (16.4)		8 (9.1)		-
Unknown	-	-	-		-		-		2 (100)
Time to re-treatment of aneurysm									

Contd...

Table 3: Contd...

Variable	Regrown aneurysms			P	De novo aneurysms	P	Known untreated aneurysm	P	Occult aneurysms
	All	Clipping/wrapping	Coiling						
All, months (median, range)	20.8 (2.5-370)	185 (2.5-370)	9.3 (3.4-200)	0.068	177 (22-330)	<0.001	4.1 (0.7-417)	<0.001	115 (14-215)
Unruptured, months (median, range)	16.2 (2.5-370)	175 (2.5-370)	8.8 (3.4-200)	0.011	186 (32-294)	<0.001	4.1 (0.7-268)	<0.001	-
Ruptured, months (median, range)	187 (11-280)	194 (128-280)	11	0.90	165 (22-330)	0.12	24 (2.8-417)	0.065	115 (14-215)

*P value for the comparison of initial treatment versus re-treatment. ACA: Anterior cerebral artery, ACom: Anterior communicating artery, AICA: Anterior inferior cerebellar artery, BA: Basilar artery, IC: Internal carotid artery, ICPC: Internal carotid - posterior communicating artery, MCA: Middle cerebral artery, mRS: Modified Rankin Scale, PCA: Posterior cerebral artery, SD: Standard deviation, VA: Vertebral artery, WFNS: World Federation of Neurosurgical Societies

degree of obliteration was unidentified), 9 (69%) of the 13 aneurysms after clipping or wrapping and 14 (82%) of the 17 after coiling showed incomplete obliteration radiographically (e.g. residual neck by clipping or loose packing of coils, etc.) during the perioperative period of initial treatment. These incomplete obliterations and development of regrown aneurysm were frequently seen in IC or ICPC, accounting for 7 (50%) of 14 aneurysms after clipping or wrapping, and 8 (47%) of 17 after coiling [Figure 2]. For patients who received clipping or wrapping for aneurysm that had ruptured at initial treatment, incomplete obliteration was found frequently. Initial extent of occlusion with coiling treatment showed a similar trend between ruptured and unruptured aneurysms [Table 4]. The *de novo* aneurysms were likely to be found by rupture as compared to regrown or known untreated aneurysms ($P < 0.001$), appearing in 22 (48.9%) of 45 retreatments for *de novo* aneurysm, 5 (16.1%) of 31 for regrown aneurysm, and 5 (6.4%) of 78 for known untreated aneurysm [Table 3].

In patients with retreatment performed for aneurysmal bleeding, median time from initial treatment to retreatment was 165 months (range: 22–330 months) for *de novo* aneurysm, 187 months (range: 11–280 months) for regrown aneurysm, and 24 months (range: 2.8–417 months) for known untreated aneurysm [Table 3]. Figure 3 shows the interval between initial treatment and retreatment. Irrespective of the presence of residuals after initial clipping, many regrown aneurysms after clipping needed to be retreated after an interval of over 120 months because of regrowth or rupture. However, most regrown aneurysms after coiling were treated within 2 years from initial treatment [Figure 3a and b]. On the other hand, time to retreatment for *de novo* aneurysm showed a wide distribution from 24 to 330 months. However, retreatment for rupture of *de novo* aneurysm consistently occurred after 120 months, with the exception of only 2 aneurysms [Figure 3c]. In one, the distal anterior inferior cerebellar aneurysm had ruptured and was trapped through craniotomy at initial treatment. Twenty-three months later, *de novo* aneurysm was detected at the right MCA by MRA and ruptured 1 month later [Figure 4]. The other was a *de novo* distal posterior inferior cerebellar

Table 4: Comparison of regrown aneurysms treated by clipping/wrapping or coiling with initial extent of occlusion and rupture state

	Clipping/wrapping			Coiling	
	Complete	Incomplete	Unidentified	Complete	Incomplete
Ruptured	2	7	1	1	5
Unruptured	2	2	0	2	9

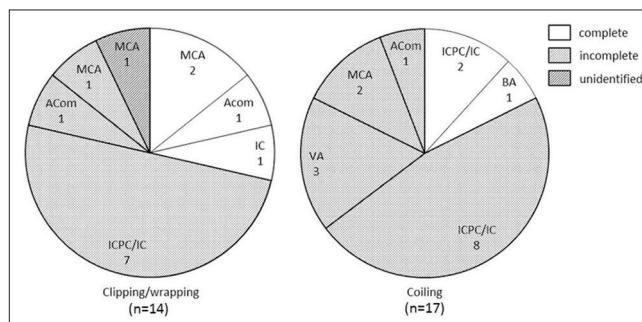


Figure 2: Pie graphs showing the proportion of regrown aneurysm locations by degree of occlusion at initial treatment. ACom: Anterior communicating artery, BA: Basilar artery, IC: Internal carotid artery, ICPC: Internal carotid-posterior communicating artery, MCA: Middle cerebral artery, and VA: Vertebral artery

aneurysm that had ruptured 22 months after clipping surgery for ruptured right MCA aneurysm. Most known untreated aneurysms were treated within 2 years. We considered that most known untreated aneurysms should be considered an indication for intervention because of the high risk of rupture, irrespective of the presence of growing aneurysm. Eleven known untreated aneurysms developed growth during the observation period. Six showed growth in size and were treated within 2 years from initial treatment, but the other 5 (31.3%) grew in size and were treated only after 4 years [Figure 3d]. Clinical profiles of the 5 known untreated aneurysms that resulted in rupture are shown in Table 5. Of these 5 patients, 4 (80%) experienced SAH at the initial treatment and were found to have another aneurysm. Moreover in these 5 patients, one aneurysm showed growth during observation, excluding 1 patient for whom data were lacking. The case in which SAH from known untreated aneurysm developed within the shortest period from

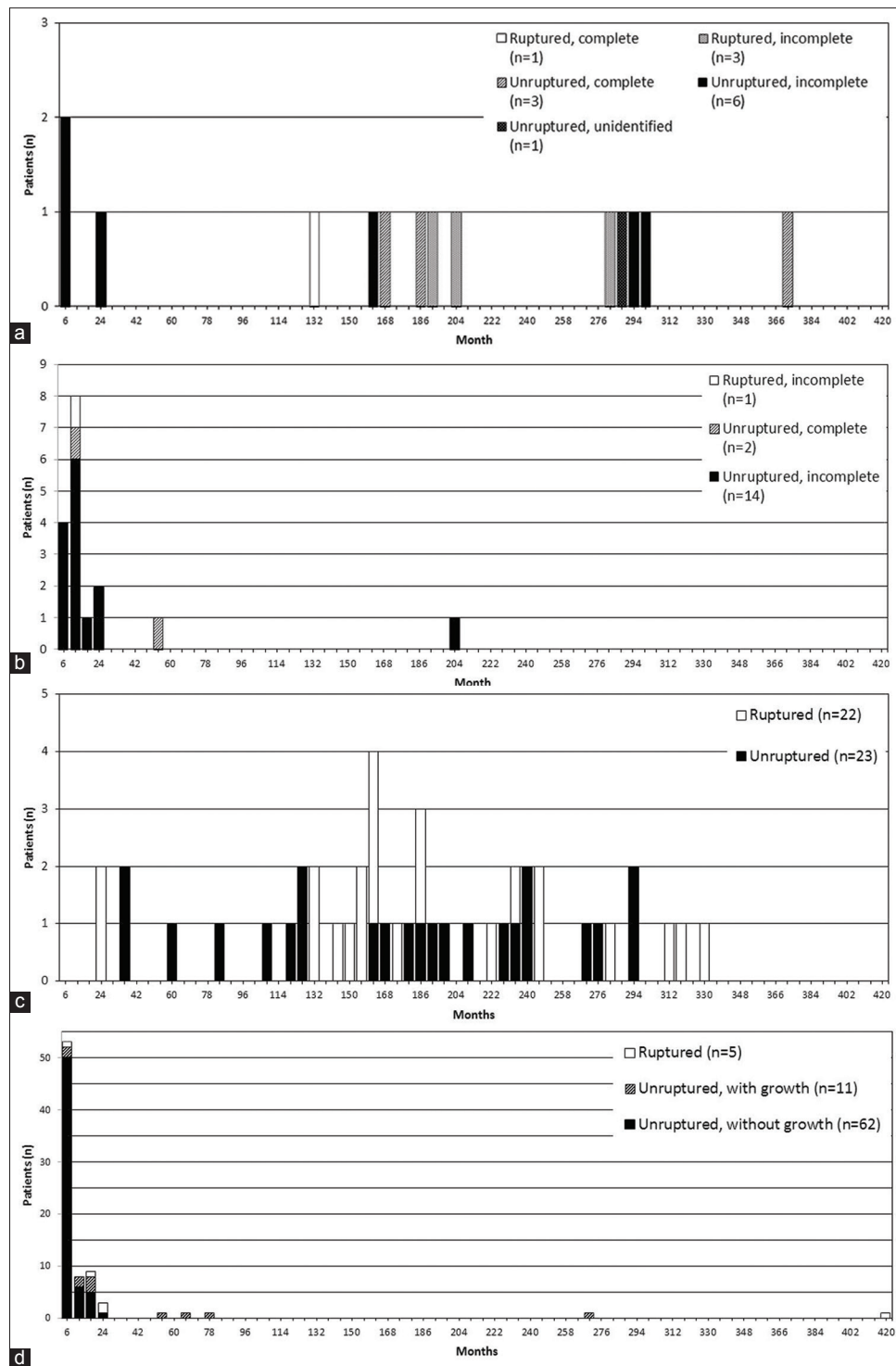


Figure 3: Bar graphs showing interval between initial treatment and retreatment by type of recurrence. (a and b) Regrown aneurysms treated by clipping (a) and coil embolization (b) at initial treatment according to aneurysms with and without rupture at retreatment, and aneurysms with and without incomplete obliteration at initial treatment. (c) De novo aneurysms according to aneurysms with and without rupture at retreatment. (d) Known untreated aneurysms according to aneurysms with and without rupture at retreatment, and change in size

initial treatment is shown in Figure 5. This 74-year-old female underwent clipping of vertebral artery-posterior inferior cerebellar artery aneurysm for SAH. Although an aneurysm at the anterior communicating artery with

20 mm in size was shown at the initial hospitalization and we considered perform intervention, she refused to undergo any treatment. This aneurysm has ruptured in 2.8 months after initial treatment.

In terms of clinical outcomes, patients with ruptured regrown aneurysm showed the worst results at discharge, with an mRS score ≥ 4 in all cases ($P = 0.003$) [Table 6]. All the patients with SAH for occult reasons resulted in mRS score 0 at discharge.

DISCUSSION

The known risk factors for formation of a new aneurysm are female sex, young age, smoking, hypertension, and multiple aneurysms.^[3,6,10,11,13,15] Patients who receive retreatment may originally possess more high-risk factors than those receiving treatment only once. The Natural Course of Unruptured Cerebral Aneurysms in a Japanese Cohort (UCAS Japan) was a cohort study that evaluated the risk of cerebral aneurysm onset in Japan, showing that mean age at aneurysm treatment was about 63 years and that 67% of patients were female.^[3] The present study found that patients at initial treatment were relatively

younger (55.0 ± 10.0 years), and females (75%) were more prevalent than in data from the UCAS Japan.

Our study agrees with previous studies that have revealed regrown aneurysms commonly develops when aneurysms are clipped incompletely at initial treatment, as well as obstructed with coils,^[1,2,8,16] and are commonly found in the ICPC or IC (30–89%), but less frequently in the MCA (2.7%) in not only patients who received endovascular coiling but also patients who received surgical clipping at initial treatment.^[6,7] The following points may be given as reasons. Coiling treatment is applied to IC or ICPC aneurysms more frequently than to MCA aneurysms. In patients who undergo clipping treatment, residua behind the aneurysm is sometimes left because observation of the back of the neck is not always easy in IC or ICPC aneurysms. In addition, hidden neck, overly broad neck, thrombosed sac, and branching from the sac are considered to impede complete neck clipping.^[5,15,16] Detailed surgical records that can be referred to afterward are thus crucial to discern whether a treated aneurysm has a residual neck after clipping or coiling. *De novo* and known untreated aneurysm were distributed equally among common sites for aneurysms in our study and previous studies.^[9,14,16]

To the best of our knowledge, the interval between initial treatment and retreatment, including for unruptured aneurysms, has not been reported. Some studies

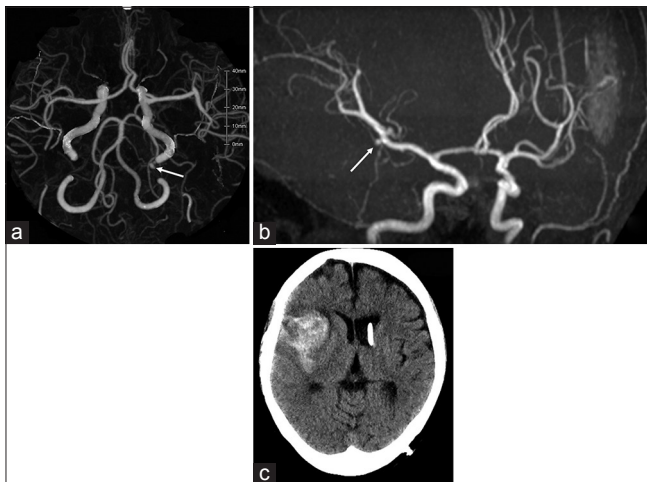


Figure 4: Three-dimensional computed tomography angiography on first admission (a) demonstrates distal anterior inferior cerebellar aneurysm (white arrow) as well as the absence of aneurysm of the right middle cerebral artery (MCA). Magnetic resonance angiography taken 23 months after initial treatment (b) shows *de novo* aneurysm of the right MCA (white arrow). One month later, the patient suffered subarachnoid hemorrhage in the right sylvian fissure by rupture of *de novo* aneurysm as shown by plain computed tomography on the second admission (c)

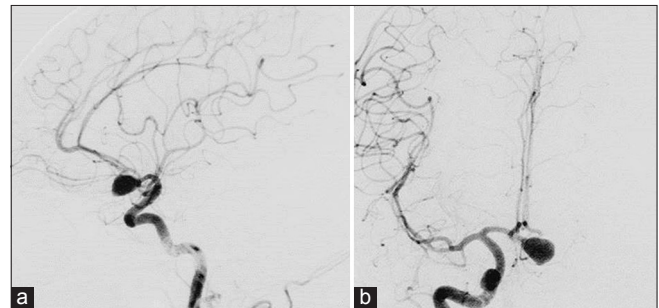


Figure 5: A case of known untreated aneurysm that resulted in subarachnoid hemorrhage within 3 months after initial treatment. Lateral view (a) and anteroposterior-view (b) right internal carotid angiography on initial treatment shows aneurysm of the anterior communicating artery, 20 mm in size

Table 5: Patients developed subarachnoid hemorrhage from known untreated aneurysm

Patient	Initial treatment				Interval (months)	Retreatment		
	Age/sex	Location	Size (dome/neck, mm)	SAH		Location	Size (dome/neck, mm)	Growth*
1	74/female	VA	7/5	Yes	3	ACom	20/10	No
2	66/female	ACA	3/3	Yes	14	VA	4/4	No
3	64/female	ICPC	19/11	No	24	BA	7/5	No
4	79/female	MCA	5/3	Yes	24	ICPC	12/4	Yes
5	54/female	MCA	10/9	Yes	417	MCA	-	-

*Growth of aneurysm in the interval between initial treatment and re-treatment. ACA: Anterior cerebral artery, ACom: Anterior communicating artery, BA: Basilar artery, ICPC: Internal carotid - posterior communicating artery, MCA: Middle cerebral artery, SAH: Subarachnoid hemorrhage, VA: Vertebral artery, -: Data not given

Table 6: Relationship between WFNS grade on admission and clinical outcome at discharge on type of retreatment (ruptured case only)

Variable	Regrown aneurysm	P	De novo aneurysm	P	Known untreated aneurysm	P	Occult aneurysm
Number of patients	5		22		5		2
WFNS grade on admission, n (%)							
I	0 (0)	0.009	10 (45.5)	0.024	1 (20.0)	0.28	1 (50.0)
II	0 (0)		4 (18.2)		0 (0)		1 (50.0)
III	2 (40.0)		3 (13.6)		2 (40.0)		0 (0)
IV	0 (0)		3 (13.6)		1 (20.0)		0 (0)
V	3 (60.0)		1 (4.5)		1 (20.0)		0 (0)
Unknown	0 (0)		1 (4.5)		0 (0)		0 (0)
mRS score at discharge, n (%)							
0	0 (0)	0.003	7 (31.8)	0.039	1 (20.0)	0.33	2 (100)
1	0 (0)		6 (27.3)		0 (0)		0 (0)
2	0 (0)		1 (4.5)		1 (20.0)		0 (0)
3	0 (0)		4 (18.2)		1 (20.0)		0 (0)
4	1 (20.0)		3 (13.6)		0 (0)		0 (0)
5	1 (20.0)		0 (0)		0 (0)		0 (0)
6	3 (60.0)		1 (4.5)		2 (40.0)		0 (0)

mRS: Modified Rankin Scale, WFNS: World Federation of Neurosurgical Societies

have shown a mean interval between initial SAH and retreatment with repeated SAH of 6.5–9.9 years.^[9,13,14,16] Those studies documented no recurrent bleeding from *de novo* or regrown aneurysms within the first 33 months after initial SAH.^[9,13,16] They therefore suggested that screening for new aneurysms after clipping of all detected aneurysms is useful, but should not begin earlier than 2.5 years after treatment.^[13] However, among patients who received retreatment for aneurysmal rupture, our study showed that the minimum interval from initial treatment to retreatment was only 2.8 months for known untreated aneurysms, 11 months for regrown aneurysm, and 22 months for *de novo* aneurysm. In particular, we should keep in mind that aneurysms with incomplete clipping or coiling and known untreated aneurysms continue to carry a risk of rupture after the initial treatment in a shorter period of time.

Long-term follow-up is also recommended. Our study showed that regrown aneurysm and *de novo* aneurysm rupture again in about 10 years from initial treatment. This result was consistent with results of previous surveys.^[8-10] Tsutsumi *et al.*^[8] reported that, in a study of patients who survived >3 years after surgery, 8 of 11 patients developed aneurysm regrowth and formation of *de novo* aneurysm leading to SAH in ≥ 9 years after initial treatment. Long-term follow-up with diagnostic imaging would therefore be reasonable.

All patients who received retreatment for aneurysms that remained unruptured achieved good clinical outcomes in our study. For patients who received retreatment for aneurysm that had ruptured, clinical outcomes from our data consisting of second treatment or later showed a

similar trend according to WFNS grade on admission as compared to the Japanese stroke databank in 2009 (which included any occasions of SAH) (Fisher's exact test; $P = 0.14-0.99$) [Table 7].^[4] In a previous study, the mortality rate after second SAH was 33% and half of the patients died or were left disabled. Such outcomes were comparable to those from a series of patients with first SAH during the same study period in the same hospitals.^[4] This shows that clinical outcomes for patients who received retreatment for SAH correlate with severity on admission, with no difference from those for patients with first SAH. However, patients with ruptured regrown aneurysm displayed worse clinical outcomes at discharge. This poor prognosis may be due to difficulties in achieving complete clipping or re-exposure of the aneurysms with preservation of normal vasculature while avoiding brain damage, for the following reasons. First, aneurysms could originally be at deep locations or have complex shapes. Second, approach corridors to the aneurysm are narrow with the presence of scar tissue and adhesions resulting from previous treatments and present bleeding, as well as clip application and/or materials placed at previous surgeries. Earlier intervention before rupture may be recommended for retreatment of regrown aneurysms if the risk of surgical or endovascular intervention appears low.

This study had various limitations that need to be considered when interpreting the results. First, we do not know the total number of patients who received retreatment for intracranial aneurysms because this study only retrospectively identified patients who had been admitted to our hospital for aneurysm retreatment. Some patients might have been admitted to other hospitals for

Table 7: Comparison of clinical outcomes between present study and Japanese database result

Variable	Second SAH or later (n (%))		Japanese stroke databank ⁽¹⁾ (n (%))		P
	Favorable	Unfavorable	Favorable	Unfavorable	
Number of patients	17 (53.1)	15 (46.9)	1202 (58.7)	846 (41.3)	0.53
WFNS grade on admission					
I	10 (83.3)	2 (16.7)	556 (82.4)	119 (17.6)	>0.99
II	4 (80.0)	1 (20.0)	370 (72.0)	144 (28.0)	>0.99
III	2 (28.6)	5 (71.4)	102 (58.6)	72 (41.4)	0.13
IV	1 (25.0)	3 (75.0)	117 (33.5)	232 (66.5)	>0.99
V	0 (0)	4 (100)	57 (17.0)	279 (83.0)	0.59

WFNS: World Federation of Neurosurgical Societies, SAH: Subarachnoid hemorrhage

retreatment, and others might have died without precise diagnosis of SAH. Second, in this study, many known untreated aneurysms had been scheduled for retreatment in advance at the time of initial treatment, and therefore only a few aneurysms ruptured. In contrast, half of the retreatments for *de novo* aneurysms were for bleeding. This means that opportunities for appropriate diagnostic imaging and/or surgical or endovascular interventions may have been overlooked. The surgical and endovascular indications and intervals for follow-up diagnostic imaging also differ somewhat among surgeons, by patient age, and with patient ADL. As a result, the best solution on how to perform surgical or endovascular treatment in a timely manner for an individual patient remains unclear. Prospective trials using a large cohort after aneurysm treatment are needed to clarify these trends in our study. Third, this study only included Japanese patients. Risk of SAH is higher in Japanese populations, even though the incidence of unruptured aneurysm resembles that in Western populations.^[12] These data are therefore not directly applicable to other populations.

CONCLUSIONS

We need timely and long-standing follow-up regarding aneurysm status in patients who have once treated for aneurysm irrespective of treatment modality. For the first 2 years after initial treatment, regrown aneurysm at the originally treated site and known untreated aneurysms, in particular, show a high risk of rupture. Long-term follow-up is also needed to detect formation of *de novo* aneurysms from around 10 years after initial treatment.

Acknowledgments

We wish to thank Shotaro Yoshioka, M.D., Kentaro Hikichi, M.D., Keisho Sano, M.D., Yuka Sano, M.D., Shinya Kobayashi, M.D., Jun Tanabe, M.D., Hiroshi Saito, M.D., Masaki Maeda, M.D., Nobuharu Furuya, M.D., and Takuro Endo for their invaluable support in the acquisition of postoperative data and for intraoperative technical support.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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