Subarachnoid hemorrhage after surgical treatment of unruptured intracranial aneurysms

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OBJECTIVE Only a few previous studies have investigated subarachnoid hemorrhage (SAH) after surgical treatment in patients with unruptured intracranial aneurysms (UIAs). Given the improvement in long-term outcomes of embolization, more extensive data are needed concerning the true rupture rates after microsurgery in order to provide reliable information for treatment decisions. The purpose of this study was to investigate the incidence of and risk factors for postoperative SAH in patients with surgically treated UIAs.

METHODS Data from 702 consecutive patients harboring 852 surgically treated UIAs were evaluated. Surgical treatments included neck clipping (complete or incomplete), coating/wrapping, trapping, proximal occlusion, and bypass surgery. Clippable UIAs were defined as UIAs treated by complete neck clipping. The annual incidence of postoperative SAH and risk factors for SAH were studied using Kaplan-Meier survival analysis and Cox proportional hazards regression models.

RESULTS The patients' median age was 64 years (interquartile range [IQR] 56–71 years). Of 852 UIAs, 767 were clip-pable and 85 were not. The mean duration of follow-up was 731 days (SD 380 days). During 1708 aneurysm years, there were 4 episodes of SAH, giving an overall average annual incidence rate of 0.23% (95% CI 0.12%–0.59%) and an average annual incidence rate of 0.065% (95% CI 0.0017%–0.37%) for clippable UIAs (1 episode of SAH, 1552 aneurysm-years). Basilar artery location (adjusted hazard ratio [HR] 23, 95% CI 2.0–255, $p = 0.0012$) and unclippable UIA status (adjusted HR 15, 95% CI 1.1–215, $p = 0.046$) were significantly related to postoperative SAH. An excellent outcome (modified Rankin Scale score of 0 or 1) was achieved in 816 (95.7%) of 852 cases overall and in 748 (98%) of 767 clip-pable UIAs at 12 months.

CONCLUSIONS In this large case series, microsurgical treatment of UIAs was found to be safe and effective. Aneurysm location and unclippable morphologies were related to postoperative SAH in patients with surgically treated UIAs.

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KEY WORDS intracranial aneurysm; neurosurgical procedures; risk factors; subarachnoid hemorrhage; vascular disorders

THE prevalence of unruptured intracranial aneurysms (UIAs) has been estimated at 3.2%, and in follow-up studies, the overall risk of subarachnoid hemorrhage (SAH) for patients with these lesions has been reported to be approximately 1% per year.^{35,42} Patients with UIAs are informed that they are at a risk of SAH, and this knowledge often creates anxiety for both patients and

doctors, leading to a desire in both parties to attempt to control the risk of SAH with preventive treatments. Treatment decisions, however, should be based on comparisons between the results of preventive treatment and the natural course of UIAs, not on comparisons between the results of preventive treatment and outcome after SAH.

Although clip ligation is believed to be the most durable

ABBREVIATIONS IQR = interquartile range; mRS = modified Rankin Scale; SAH = subarachnoid hemorrhage; UIA = unruptured intracranial aneurysm.

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TABLE 1. Summary of mRS scores in 852 surgical cases

Assessment	mRS Score						
	0	1	2	3	4	5	6
Overall							
Preop (n = 852)	775 (91)	49 (5.8)	23 (2.7)	3 (0.4)	2 (0.2)		
At discharge (n = 852)	621 (73)	151 (18)	56 (6.6)	10 (1.2)	2 (0.2)	10 (1.2)	2 (0.2)
6 mos postop (n = 852)	749 (88)	50 (5.9)	33 (3.9)	8 (0.9)	2 (0.2)	8 (0.9)	2 (0.2)
12 mos postop (n = 851)*	776 (91)	40 (4.7)	16 (1.9)	7 (0.8)	2 (0.2)	8 (0.9)	2 (0.2)
Clippable UIAs							
Preop (n = 767)	728 (95)	24 (3.1)	13 (1.7)	2 (0.3)			
At discharge (n = 767)	585 (76)	128 (17)	46 (6.0)	7 (0.9)	1 (0.1)		
6 mos postop (n = 767)	697 (91)	38 (5.0)	27 (3.5)	5 (0.7)			
12 mos postop (n = 766)*	717 (94)	31 (4.0)	14 (1.8)	4 (0.5)			

Data expressed as number of cases (%). Patients with multiple aneurysms underwent clipping of separate aneurysms at different times; these aneurysms are therefore presented as separate surgical cases.

* During the follow-up period, 1 female patient died due to oral anticoagulant-related intracerebral hemorrhage.

means of excluding an aneurysm from the circulation,²² some UIAs are not suitable for this treatment approach because of the surrounding vascular anatomy or dysplasia and branching or perforating arteries.⁵ In addition, published data suggest the risk of aneurysm recurrence, growth of the residual lesion, or SAH cannot be fully eliminated by endovascular or surgical treatment.^{7–9,16,34,37} Even in cases in which complete obliteration of the aneurysm is confirmed, patients may still be at risk for SAH. Therefore, SAH after initial treatment is an important issue in UIA management.

Reliable data on rupture rates of treated UIAs are needed in order to allow patients and health care providers to compare risks of endovascular and microsurgical treatment and arrive at the most appropriate decision on a case-by-case basis. To the best of our knowledge, only a few previous studies have investigated the rate of SAH after surgical treatment of UIAs. The aim of this study was to investigate the risk factors of postoperative SAH in patients with surgically treated UIAs.

Methods

This study is reported based on criteria from the STROBE (Strengthening the Reporting of Observational Study in Epidemiology) statement.⁴³ The study protocol was approved by the ethics committee of Teishinkai Hospital. Patient consent was obtained in each case. Surgical indications for UIAs were described recently.²⁵ We retrospectively reviewed 702 consecutive patients who were harboring 852 UIAs that were treated with direct surgery at our institutions between April 2012 and August 2015. Mycotic and traumatic UIAs were not included in this study.

We collected the following data: age, sex, smoking history (current vs former/never), history of SAH from other aneurysm, previous treatment of aneurysms, aneurysm location and side, type of surgical treatment, aneurysm size, whether UIAs were thrombosed, whether UIAs were symptomatic, multiple UIAs, whether UIAs needed bypass surgery, findings of postoperative diffusion-weight-

ed imaging (DWI), and intra- and postoperative rupture. Clippable UIAs were defined as UIAs treated by clip ligation along the ideal closure line. As described by Ishikawa et al., the closure line is considered ideal if it “restores the original vascular configuration present before the aneurysm developed” and “the maximum of the pathological wall of the aneurysm is included within the clips.”¹³ Aneurysm sizes were categorized as small (< 15 mm), large (15–24 mm), and giant (≥ 25 mm). The surgical technique of extracranial to intracranial high-flow bypass was described previously.^{26,27} The patients’ clinical status was evaluated by means of the modified Rankin Scale (mRS) preoperatively, at discharge, and at 6- and 12-month follow-up examinations or the last hospital visit,⁴⁰ either via telephone interviews with the patient or family members or during a physical examination in cases in which patients were able to visit our hospital. For patients without symptoms, a poor outcome was defined as an mRS score of 2–6. In patients with an mRS score greater than 1 due to UIA-related symptoms or other comorbidities, a poor outcome is defined as an increase in the mRS score of 1 or more points.

Statistical Analysis

Statistical analysis was performed using SPSS for Mac (version 21.0; IBM) and Stata software (StataCorp). Variables are expressed as mean (with standard deviation), median (with interquartile range [IQR]: 25th–75th percentile), or number of cases (%), as appropriate. Fisher exact tests were performed for nominal variables. Pearson chi-square tests were used to assess associations between categorical variables, complemented by adjusted residual analysis. The normality of the data was evaluated using the Shapiro-Wilk test. Normally distributed continuous variables were compared using the Student t-test and non-normally distributed variables using the Mann-Whitney U-test.

Receiver operating characteristic curve analysis was performed for age and the binary endpoint of poor outcome and postoperative SAH, and the cutoff points for these variables that optimized sensitivity and specificity

TABLE 2. Analysis of factors related to poor outcome at 12 months

Variable	Total (n = 852)	Outcome		p Value
		Poor (n = 29)	Not Poor (n = 823)	
Age				
Median in yrs	64	56	61	
IQR in yrs	56–71	22–57	52–69	
No. of cases w/ pt age ≥65 yrs*	420 (49)	21 (72)	399 (49)	0.011
Male sex*	181 (21)	12 (41)	169 (21)	0.007
Current smoking	271 (32)	10 (35)	261 (32)	0.75
History of SAH	24 (2.8)	1 (3.4)	23 (2.8)	0.83
Laterality				0.81
Midline	139 (16)	6 (21)	133 (16)	
Left side	371 (44)	12 (41)	359 (44)	
Right side	342 (40)	11 (38)	331 (40)	
Surgical treatment*				<0.0001
Neck clipping	768 (90)	13 (45)	755 (92)	
Proximal clipping	43 (5.0)	9 (31)	34 (4.1)	
Trapping	31 (3.6)	5 (18)	26 (3.2)	
Partial clipping	10 (1.2)	2 (6.9)	8 (1.0)	
Aneurysm size in mm				<0.0001
Median	4.7	19	4.6	
IQR	3.4–6.7	7.1–27	3.4–6.5	
Size				<0.0001
Normal	779 (91)	12 (41)	767 (93)	
Large*	45 (5.3)	8 (28)	37 (4.5)	
Giant*	28 (3.3)	9 (31)	19 (2.3)	
Location*				<0.0001
MCA	216 (25)	2 (6.9)	214 (26)	NS
Paraclinoid ICA	175 (21)	4 (14)	171 (21)	NS
ICA-PCoA	136 (16)	4 (14)	132 (16)	NS
ACoA	117 (14)	2 (6.9)	115 (14)	NS
Basilar top†	60 (7.0)	11 (38)	49 (6.0)	<0.01
AChA	43 (5.0)	0	43 (5.2)	NS
VA	39 (4.6)	3 (10)	36 (4.4)	NS
ACA	28 (3.3)	0	28 (3.4)	NS
ICA top	24 (2.8)	0	24 (2.9)	NS
PCA	8 (0.9)	0	8 (1.0)	NS
Basilar trunk†	5 (0.6)	3 (10)	2 (0.2)	<0.01
PICA	1 (0.1)	0	1 (0.1)	NS
Thrombosed UIA*	22 (2.6)	7 (24)	15 (1.8)	<0.0001
Nonsaccular UIA*	34 (4.0)	6 (21)	28 (3.4)	<0.0001
Symptomatic UIA*	34 (4.0)	4 (14)	30 (3.6)	0.006
Preop mRS score ≥1*	77 (9.0)	13 (45)	64 (7.8)	<0.0001
Multiple aneurysms	167 (20)	3 (10)	164 (20)	0.20
PTI*	53 (6.2)	11 (38)	42 (5.1)	<0.0001
Previously treated UIA*	34 (4.0)	8 (28)	26 (3.2)	<0.0001
Bypass surgery*	109 (13)	20 (69)	89 (11)	<0.0001
Intraop rupture	10 (1.2)	1 (3.4)	9 (1.1)	0.25
Postop rupture*	4 (0.5)	3 (10)	1 (0.1)	<0.0001

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TABLE 2. Analysis of factors related to poor outcome at 12 months

ACA = anterior cerebral artery; AChA = anterior choroidal artery; ACoA = anterior communicating artery; ICA = internal carotid artery; MCA = middle cerebral artery; NS = not significant; PCA = posterior cerebral artery; PCoA = posterior communicating artery; PICA = posterior inferior cerebellar artery; pt = patient; PTI = perforator territory infarction; VA = vertebral artery.

Data expressed as number of cases (%), unless otherwise indicated.

* Variables significantly related to poor outcome in univariate analysis.

† Variables significantly related to poor outcome by adjusted residual analysis.

were selected. First, variables were compared between patients with and without poor outcome at 12 months by univariate analysis. A multivariate logistic regression analysis was performed using variables that were significantly associated with poor outcome in the univariate analysis. Second, we compared the clinical and radiological characteristics of patients with and without postoperative SAH by means of the log-rank test and performed multivariate analysis by means of a Cox proportional hazards model using variables that were significantly associated with the postoperative SAH on the log-rank test. Differences were considered significant at $p < 0.05$.

Results

The median age of the 702 patients included in this study was 64 years (IQR 56–71 years). A total of 852 aneurysms were treated (each considered a single surgical case), with 167 (20%) of these lesions occurring in patients with multiple UIAs. Six hundred seventy-one (79%) of the 852 aneurysms were in women. The mean follow-up period was 731 days (SD 380 days) and no patient was lost to follow-up. The distribution of mRS scores is shown in Table 1. Among 77 cases in which the patients' postoperative mRS scores were greater than 1, the causes of mRS score decrease were other comorbidities (in 34 cases [4.0%]),

TABLE 3. Multivariate analysis of factors related to poor outcome at 12 months

Variable	OR	95% CI	p Value
Age >65 yrs	2.3	0.73–7.3	0.15
Male sex	2.6	0.84–8.3	0.096
Thrombosed UIA	2.9	0.50–18	0.23
Nonclippable UIA	1.5	0.32–6.7	0.63
Large or giant UIA	3.8	0.71–20	0.12
BA aneurysm*	11	3.4–34	<0.0001
Symptomatic UIA	0.22	0.018–2.7	0.24
Preop mRS score >1	1.3	0.19–8.2	0.80
PTI*	4.0	1.2–14	0.029
Previously treated UIA	4.2	0.81–21	0.088
Bypass surgery	4.5	0.98–21	0.053
Postop rupture	13	0.049–3502	0.37

BA = basilar artery.

* Variables significantly related to poor outcome.

TABLE 4. Summary of cases of postoperative SAH

Case	Age (yrs), Sex	Aneurysm Location	Aneurysm Size (mm)	Previous Treatment	Treatment	Bypass	Time Btwn Op & SAH (days)	mRS Score
1	70, M	BA trunk	30.6	None	BA occlusion	V ₃ -SVG-P _{2a} , STA-SCA, STA-AICA	32	6
2	70, F	ACoA	4.1	None	Neck clipping	A ₃ -A ₃	11	0
3	66, F	BA-SCA	42.2	None	BA occlusion	STA-SCA, STA-PCA	29	6
4	70, F	BA top	9.6	Coil	Partial clipping		23	4

AICA = anterior inferior cerebellar artery; A₃ = A₃ portion of anterior cerebral artery; P_{2a} = P_{2a} portion of posterior cerebral artery; SCA = superior cerebellar artery; STA = superficial temporal artery; SVG = saphenous vein graft; V₃ = V₃ portion of vertebral artery.

symptomatic UIA (in 34 cases [4.0%]), and morbidities due to previous UIA treatment (in 12 cases [1.4%]). Bypass surgery was performed in 109 cases (13%). Among these cases, low-flow bypasses were performed in 55 (6.5%) and combinations of low-flow and high-flow bypasses in 59 cases (6.9%).

A summary of clinical and radiological characteristics is shown in Table 2. Age $\geq$ 65 years, male sex, unclippable aneurysm morphology, large or giant aneurysm size, basilar top and basilar trunk artery aneurysms, thrombosed aneurysms, nonsaccular aneurysms, symptomatic UIAs, preoperative mRS score $\geq$ 1, perforator territory infarction on postoperative diffusion-weighted MRI, treatment with bypass surgery, and postoperative SAH were significantly related to poor outcome at 12 months after surgery (29 cases [3.4%]) by univariate analysis (Table 2). In multivariate analysis, perforator territory infarction and basilar artery location were significantly related to poor 12-month outcome (Table 3). Other variables showed no significant association with poor 12-month outcome. Median aneurysm size in UIAs with perforator territory infarction was 8.0 mm (IQR 3.6–13 mm) and it was significantly larger than those without perforator territory infarction (4.6 mm [IQR 3.4–6.5 mm]), $p < 0.0001$.

One patient died due to anticoagulant-related intracerebral hemorrhage (international normalization ratio > 10) 10 months after aneurysm treatment. The overall follow-up time for the 852 UIAs was 1708 aneurysm-years. During follow-up, postoperative SAH was observed in 4 cases, yielding an overall annual rupture rate of 0.23% (95% CI 0.12%–0.59%) (Table 4). The log-rank test revealed that basilar artery location, giant aneurysm size, and unclippable status were significantly related to postoperative SAH (Table 5). Even in multivariate analysis, basilar artery location and unclippable status remained significantly related to postoperative SAH (Table 5). Other variables

showed no significant association with postoperative SAH. In regard to clippable UIAs, during the follow-up period (1552 aneurysm-years) postoperative SAH was observed in 1 case (Table 4). Therefore, the annual rupture rate for clippable UIAs was 0.066% (95% CI 0.017%–0.37%).

The distribution of mRS scores by case is shown for the 767 clippable UIAs in Table 1. Among clinical and radiological characteristics, large or giant aneurysm size, perforator territory infarction, and previously treated aneurysm were significantly related to poor outcome at 12 months ($n = 11$, 1.4%). After multivariate analysis, these 3 variables remained significant (Table 6). Other variables showed no significant association with poor 12-month outcome for clippable UIAs.

Details of 2 of the 4 cases in which postoperative SAH was observed are given below. For details of the other 2 cases, please refer to the recently published article by Matsukawa et al. on the treatment of unruptured basilar artery aneurysms.²⁴

Illustrative Cases of Postoperative SAH

Case 1

This 70-year-old man with a thrombosed giant basilar trunk aneurysm was referred to our hospital due to worsening symptoms of brainstem compression (Fig. 1A). He underwent saphenous vein V₃ to P_{2a} bypass (placement of a saphenous vein graft between the V₃ segment of the vertebral artery and the P_{2a} segment of the posterior cerebral artery), superficial temporal artery-to-superior cerebellar artery bypass, and superficial temporal artery-to-anterior inferior cerebellar artery bypass with basilar artery occlusion (Fig. 1B). Although he had no neurological worsening, he suddenly developed a subarachnoid hemorrhage due to rupture of the treated basilar trunk aneurysm and died 32 days after the operation (Fig. 1C).

TABLE 5. Multivariate analyses using the Cox proportional hazards model for postoperative SAH

Variable	Rupture		Univariate Analysis			Multivariate Analysis		
	Present (n = 4)	Absent (n = 848)	HR	95% CI	p Value	HR	95% CI	p Value
BA aneurysm*	3 (75)	62 (7.3)	37	3.8–352	0.002	23	2.0–255	0.0012
Giant	2 (50)	26 (3.1)	30	4.2–212	0.001	1.8	0.16–21	0.63
Nonclippable UIA*	3 (75)	81 (9.6)	28	2.9–267	0.004	15	1.1–215	0.046

Data expressed as number of cases (%), unless otherwise indicated. Multivariate analysis was performed using variables that were significantly related to postoperative aneurysm rupture by the log-rank test.

* Variables significantly related to postoperative SAH.

TABLE 6. Analysis of factors related to poor outcome at 12 months in patients with clipable UIAs

Variable	Total (n = 767)	Poor Outcome		Univariate Analysis			Multivariate Analysis		
		Present (n = 11)	Absent (n = 756)	OR	95% CI	p Value	OR	95% CI	p Value
Large or giant UIA*	28 (3.7)	3 (27)	25 (3.3)	11	2.7–44	0.0010	8.4	1.9–35	0.0040
Perforator infarction*	39 (5.1)	3 (27)	36 (4.8)	7.5	1.9–29	0.0040	5.4	1.3–23	0.020
Previously treated*	20 (2.6)	2 (18)	18 (2.4)	9.1	1.8–45	0.0070	6.7	1.2–36	0.027

Data expressed as number of cases (%), unless otherwise indicated. Multivariate analysis was performed using variables that were significantly related to poor outcome by the univariate analysis.

* Variables significantly related to poor outcome.

Case 2

This 70-year-old woman was referred to our hospital because she hoped to be treated surgically for an unruptured anterior communicating artery aneurysm (Fig. 2A). An interhemispheric approach was performed. During observation of the aneurysm and surrounding structures, the aneurysm ruptured. The rupture point was the aneurysm neck near the right A₁-A₂ junction. Complete neck clipping was performed (Fig. 2B). Immediately after the operation, the patient had no neurological deficits. However, 11 days postoperatively, she developed a subarachnoid hemorrhage due to rupture of the treated aneurysm (Fig. 2C). 3D CT angiography revealed no aneurysm recurrence. The rupture point was the aneurysm neck near the right A₁-A₂ junction. Aneurysm trapping was performed between the right A₁, anterior communicating artery, and right A₂ in combination with an A₃-A₃ side-to-side anastomosis. The patient was discharged to home without neurological deficits (mRS score of 0).

Discussion

The present study showed the annual rupture rate after surgical treatment and risk factors of postoperative SAH in patients with UIAs. Despite the inclusion of complex and larger UIAs in this case series, there was a low incidence of surgical complications and a high proportion of good outcomes.

The annual rupture risk has been reported to be between 0.5% and 1.4% in the most recent relatively large (> 100 patients) cohort studies for natural history of UIAs, despite substantially different demographic characteristics, risk factor rates, and UIA characteristics in the groups studied

(Table 7).^{12,15,18,30,31,36,44} Larger aneurysm size, younger age, female sex, current smoking, history of SAH, daughter sac, and specific locations (anterior communicating artery, vertebrobasilar circulation, and internal carotid-posterior communicating artery junction) were significant predictive risk factors for rupture of UIAs.^{12,15,18,30,31,36,44} Because so-called preventive treatments of UIAs have become common, these current natural course studies are biased.¹⁷ Therefore, it has been speculated that the true natural course of UIAs will never be described,³³ and the annual rupture rates that have been reported might be relative underestimates.

As stated by Tsutsumi et al., “An optimistic assumption is that appropriate surgical treatment of aneurysms would eliminate the rupture risk or at least reduce it to the level of [the] normal population.”³⁸ To date, a few studies have investigated posttreatment rupture (Table 7).^{3,11,19,21,26,28} In the present study, posttreatment rupture was observed in 4 cases (0.57% of all UIAs) and annual rupture rates after surgical treatments were 0.23% overall and 0.065% for clipable UIAs. The risk factors were basilar artery aneurysm location and unclipable UIA status. Although these results should not be simply compared with the annual risks of SAH in the natural course studies, annual rupture rates in the present study were lower than those observed in the natural history. In spite of inclusion of symptomatic and complex UIAs, an excellent outcome (mRS score of 0 or 1) was achieved in 816 cases (95.7%) overall and in 748 cases (98%) of clipable UIAs. Our surgical results were comparable or superior to those reported in previous studies. Due to technical advances, microsurgery for UIAs can be performed more safely than previously and may be just-

FIG. 1. Case 1. Preoperative 3D CT angiography showed a giant basilar trunk aneurysm (A). Postoperative 3D CT angiography showed that the basilar artery was occluded by a clip and bypasses were patent (B). Subarachnoid hemorrhage was observed 32 days after the operation (C). Figure is available in color online only.

FIG. 2. Case 2. Postoperative 3D CT angiography showed the anterior communicating artery aneurysm (A). Although complete neck clipping was confirmed (B), subarachnoid hemorrhage was observed 11 days after the operation (C). Figure is available in color online only.

tified. However, the perforator territory infarction rate was still high (6.2%) in our study and was associated with poor outcome at 12 months. This is one of the problems that need to be solved in the surgical management of UIAs.

The PHASES score provides an estimate of the absolute risk of aneurysm rupture based on 6 factors (population, hypertension, age, size of aneurysm, earlier SAH from another aneurysm, site of aneurysm).¹⁰ This score has also been found useful for identifying aneurysms with a high relative risk of growth.² In addition to the PHASES score, older age, female sex, smoking history, hypertension, nonsaccular UIAs, multiplicity of UIAs, larger initial aneurysm size, and specific locations (cavernous internal carotid and basilar artery) have been thought to be associated with an increased risk of aneurysm growth.^{1,4,6,23,29,32,41} Korja et al.¹⁸ indicated that because even small UIAs can

rupture, treatment decisions should not be based solely on aneurysm size. As stated above, the size of UIAs with perforator territory infarction was larger than those without perforator territory infarction. Therefore, we suggest that curative microsurgery for small UIAs, especially basilar artery aneurysms, with risk factors for aneurysm growth might be one of the treatment options considered after discussion of the natural history of UIAs and the risk of morbidity and mortality associated with surgical treatment.

Although our results should not be simply compared with the annual risks of SAH from studies of the natural course of aneurysms, they do show that modern microsurgery for UIAs can safely reduce the incidence of SAH. Our study provides additional evidence to support clip ligation as a durable treatment modality for the management of UIAs.

TABLE 7. Natural history and posttreatment SAH in UIAs

Authors & Year	No. of Pts & UIAs	Follow-Up	SAH (no. of cases)	Size in mm*	Annual Rupture Rate†	Others
Natural history						
Murayama et al., 2016	1556 pts w/ 1960 UIAs	7388 aneurysm-yrs	56	3.4 ± 2.2	0.76 (0.58–0.98)	
Korja et al., 2014	118 pts	2782 aneurysm-yrs	34	4 (2–25)	1.2	
Juvela et al., 2013	142 pts w/ 181 UIAs	3064 pt-yrs	34	5.1 ± 3.7	1.1	
Morita et al., 2012	6697 UIAs	11,660 aneurysm-yrs	111	5.7 ± 3.6	0.95 (0.79–1.15)	
Sonobe et al., 2010	374 pts w/ 448 UIAs	1307 pt-yrs	7	3.3 ± 0.9	0.54	Small UIAs
Ishibashi et al., 2009	419 pts w/ 529 UIAs	1312 aneurysm-yrs	19	NA	1.4	
Wiebers et al., 2003	1692 pts w/ 2686 UIAs	6544 pt-yrs	51	7.4 ± 6.9	0.78	
Posttreatment rupture						
Direct surgery						
Hokari et al., 2013	144 pts	1137 pt-yrs	2	NA	0.18	Clipping
Matsumoto et al., 2003	110 pts w/ 132 UIAs	449 aneurysm-yrs	1	7.0 ± 5.5	0.22	Clipping, AC UIAs
Tsutsumi et al., 1998	115 pts	1012 pt-yrs	4	NA	0.39	Direct surgery
Endovascular treatment						
Lopes et al., 2014	410 pts w/ 464 UIAs	951 aneurysm-yrs	2	NA	0.21	Stent & coil
Brinjikji et al., 2013	1451 pts w/ 1654 UIAs	NA	66	NA	NA	FD
Kulcsár et al., 2011	NA	NA	13	22 ± 6	NA	FD

AC = anterior circulation; FD = flow diverter; NA = not available; Pts = patients.

* Data expressed as a mean ± SD or median (IQR).

† Values in parentheses are 95% CIs.

Limitations

Some limitations of this study should be mentioned. Our study had a retrospective design, with inherent limitations that may lead to ascertainment bias, and did not address the influence of endovascular therapy, which should be considered in any decision-making process involving the treatment of UIAs.^{14,20} Nevertheless, reliable comparison of the risks of endovascular and surgical treatment of aneurysms is difficult because of differences between individual patients and lesions. A treatment indication paradigm in which neurosurgeons decide about the preferred treatment for individual cases on a case-by-case basis inherently causes selection bias. Although our study reconfirmed the efficacy of microsurgery for UIAs in terms of postoperative SAH, the risk of de novo aneurysm formation was significant after 9 years, and in a previous study of the long-term results of clip ligation of ruptured and unruptured aneurysms, some patients who developed de novo aneurysms appeared to have SAH due to bleeding from these new lesions.³⁷ In light of the fatality rate of SAH, follow-up investigation may be indicated 9–10 years after surgery even for patients with completely clipped aneurysms, for whom the accumulated risk of aneurysm recurrence might exceed 10%.³⁷ The follow-up period of the present study was therefore relatively short. As noted by Tsutsumi et al., “surgery does not change the underlying vascular condition that contributed to aneurysm formation,”³⁸ thus longer follow-up is needed. As noted above, the results of the present study should be further clarified in a study design employing an independent cohort to lead to more concrete and revealing findings.

Conclusions

The present study showed that basilar artery location and unclippable morphologies were related to postoperative SAH, although surgical treatments were durable and could be performed safely in patients with UIAs.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Tanikawa, Matsukawa, Kamiyama. Acquisition of data: Matsukawa, Tsuboi, Noda, Ota, Miyata, Miyazaki, Kinoshita, Saito. Analysis and interpretation of data: Matsukawa. Drafting the article: Matsukawa. Critically revising the article: Tanikawa. Reviewed submitted version of manuscript: Tanikawa, Matsukawa. Statistical analysis: Matsukawa, Takahashi. Administrative/technical/material support: Tanikawa, Kamiyama, Tsuboi, Noda, Ota, Miyata, Miyazaki, Kinoshita, Saito, Takeda, Tokuda. Study supervision: Tanikawa, Kamiyama, Tsuboi, Noda, Ota, Miyata, Takeda, Tokuda.

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