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Aneurysm remnant after clipping: the risks and consequences

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OBJECTIVE The complete clipping of a cerebral aneurysm usually warrants its sustained occlusion, while clip remnants may have far-reaching consequences. The aim of this study is to identify the risk factors for clip remnants requiring retreatment and/or exhibiting growth.

METHODS All consecutive patients with primary aneurysm clipping performed at University Hospital of Essen between January 1, 2003, and December 31, 2013, were eligible for this study. Aneurysm occlusion was judged on obligatory postoperative digital subtraction angiography and the need for repeated vascular control. The identified clip remnants were correlated with various demographic and clinical characteristics of the patients, aneurysm features, and surgery-related aspects.

RESULTS Of 616 primarily clipped aneurysms, postoperative angiography revealed 112 aneurysms (18%) with clip remnants requiring further control (n = 91) or direct retreatment (n = 21). Seven remnants exhibited growth during follow-up, whereas 2 cases were associated with aneurysmal bleeding. Therefore, a total of 28 aneurysms (4.5%) were retreated as clip remnants (range 1 day to 67 months after clipping). In the multivariate analysis, the need for retreatment of clip remnant was correlated with the aneurysm's initial size (> 12 mm; OR 3.22; p = 0.035) and location (anterior cerebral artery > internal carotid artery > posterior circulation > middle cerebral artery; OR 1.85; p = 0.003). Younger age with a cutoff at 45 years (OR 33.31; p = 0.004) was the only independent predictor for remnant growth.

CONCLUSIONS The size and location of the aneurysm are the main risk factors for clip remnants requiring retreatment. Because of the risk for growth, younger individuals (< 45 years old) with clip remnants require a long-term (> 5 years) vascular follow-up.

Clinical trial registration no: DRKS00008749 (Deutsches Register Klinischer Studien)

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KEY WORDS intracranial aneurysm; clipping; remnant; rest; residuum; retreatment; risk factor; predictor; angiographic control; vascular disorders

First described by Walter Dandy in 1938,[5] microsurgical clipping of cerebral aneurysms has been regarded for many decades as the only treatment option for potentially fatal aneurysm sacs.[11] Although endovascular coiling of cerebral aneurysms increasingly displaces clipping at the present time,[13] clipping is still superior with regard to occlusion rates and rebleeding risk.[12]

Nevertheless, the complete microsurgical closure of an aneurysm cannot be achieved in all cases. The reported rate of clip remnants varies between 1.6% and 42%[2,7,10,16,18,21] and basically depends on the sensitivity of the imaging modality used for postoperative visualization.[2] However, the presence of a clip remnant on postoperative angiography may have far-reaching clinical consequences, with a risk of rebleeding of 1.9% per year.[6] That is why many authors recommend late angiographic follow-up review for incompletely obliterated aneurysms.[6,22]

The risk factors for aneurysm residuals after clipping are poorly investigated and mainly limited to univariate correlations with aneurysm location.[7,11,15,16] Large to giant aneurysms with complex morphology were also shown to be prone to clip remnants.[11] Even less is known about the predictors of the growth of clip remnants.

The goal of this study was to identify independent pre-

ABBREVIATIONS ACA = anterior cerebral artery; AUC = area under the curve; CTA = CT angiography; DSA = digital subtraction angiography; ICA = internal carotid artery; ICG = indocyanine green; MCA = middle cerebral artery; PC = posterior circulation; ROC = receiver operating characteristic; SAH = subarachnoid hemorrhage.

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dictors for clip remnants that require retreatment and/or show remnant growth. In this large single-center series, we evaluated the demographic and clinical data of the patients and the radiographic characteristics of the clipped aneurysms. We also assessed the impact of various surgery-related aspects on the success of aneurysm clipping.

Methods

Patient Population

The study was based on the database that contains all consecutive patients with cerebral aneurysm(s) treated at the University Hospital of Essen. The approval of the institutional ethics committee was obtained prior to data collection. All persons or their relatives gave their informed consent using the written treatment contract, which was signed on admission to our institution. The study was registered in the German clinical trial register (DRKS unique identifier: DRKS00008749).

The inclusion criteria for the current study were: 1) primary treatment of the (ruptured and unruptured) aneurysm(s) by microsurgical clipping performed between January 2003 and December 2013; and 2) the patient underwent postoperative digital subtraction angiography (DSA) that documented aneurysm occlusion. Patients with wrapped or coagulated aneurysms, i.e., without use of any clip, were excluded from the final analysis.

Perioperative and Later Postoperative Management of Clipped Patients

All patients with subarachnoid hemorrhage (SAH) were initially admitted to our intensive care unit. The management of SAH patients was performed according to the latest guidelines.[3,14,17,19] After the clipping of unruptured aneurysms, the patients were routinely admitted to the intensive care unit for 1 day, unless a longer stay was clinically required.

The choice of the treatment modality was made after interdisciplinary assessment. The following clips were used in the observed time: MIZUHO Sugita Titanium and Elgiloy (Nikolai), LAZIC (Peter Lazic), and YASARGIL (Aesculap).

Micro-Doppler ultrasound is routinely used during aneurysm surgery. Furthermore, intraoperative indocyanine green (ICG) videoangiography has been increasingly used (n = 298; 48.4%) since its implementation in our clinic in 2008. Intraoperative electrophysiological monitoring has also been selectively applied in recent years (n = 183; 29.7%). Intraoperative catheter angiography was not used during aneurysm clipping at our center.

All patients underwent early postoperative CT scanning within 24 hours after surgery. In addition, postoperative DSA using a dedicated biplane neuroangiography unit was routinely performed during the first week after clipping to prove complete aneurysm occlusion.

According to the hospital's standards, the identified clip remnants were stratified and thereafter managed using the Sindou classification.[18] Sindou Grade IV and V aneurysm residuals (see Fig. 1) were considered to be directly retreated, whereas the Sindou Grade I to III remnants were considered to be controlled with at least 1 additional DSA study. Further postoperative controls were usually performed using CT angiography (CTA), unless additional DSA was required for the proper visualization of the clip remnant or the treatment of other aneurysms. In cases of any remnant growth, the patients were subjected to retreatment. Due to poor outcome or incompliance, some patients, despite the identification of the aneurysm remnants on the first postoperative DSA, did not undergo repeated postoperative vascular controls. These patients were included in the "drop-out" group.

Data Management

All recorded variables were recorded in a unique database (Microsoft Access 2013, Microsoft Corp.). The following demographic and clinical variables were recorded: age, sex, presence of an acute SAH (0–21 days after bleeding), previous history of SAH (> 21 days after the bleeding event), presence of multiple aneurysms, occurrence of rebleeding from the clip remnant, and the duration of postoperative vascular follow-up.

Among the characteristics of the clipped aneurysms, their location(s), size (both sac and neck), preoperative rupture (i.e., SAH), and the calcification of the aneurysmal wall (according to the Agatston score[1] or intraoperative findings) were assessed.

Various aspects of the aneurysm surgery were also recorded from the operative reports. The expertise of the surgeon was assessed in both an individual manner (analyzing the personal rates of aneurysm remnants) and nonindividual manner (years since the neurosurgical board examination). Finally, the time of surgery (7:00 AM–10:00 PM vs 10:00 PM–7:00 AM), intraoperative aneurysm rupture, as well as the use of intraoperative diagnostic tools, were also recorded for further correlations.

Statistical Analysis

In the statistical analyses, the location of the treated aneurysm was presented on a scale based on the rates of clip remnant (see Fig. 2): 1 for middle cerebral artery (MCA); 2 for posterior circulation (PC); 3 for internal carotid artery (ICA); and 4 for anterior cerebral artery (ACA). The size of the treated aneurysm was analyzed both as a continuous variable and as a categorical variable upon quadrichotomization (< 7 mm, 7–12 mm, 13–24 mm, > 24 mm) and dichotomization (1–12 mm vs > 12 mm) of aneurysm size according to cutoff values used in the ISUIA (International Study of Unruptured Intracranial Aneurysms) trial.[25]

Our primary end point was the identification of independent predictors for aneurysm retreatment after primary clipping. Furthermore, special attention was paid to the risk factors for the growth of the clip remnants on follow-up imaging.

Differences with a p value ≤ 0.05 were regarded as statistically significant. First, bivariate correlations between all assessed variables and the end points were performed. Then, significant variables were included in a multivariate logistic regression analysis. In the case of a patient's age that appeared significant in one of the multivariate correlations, the receiver operating characteristic (ROC)

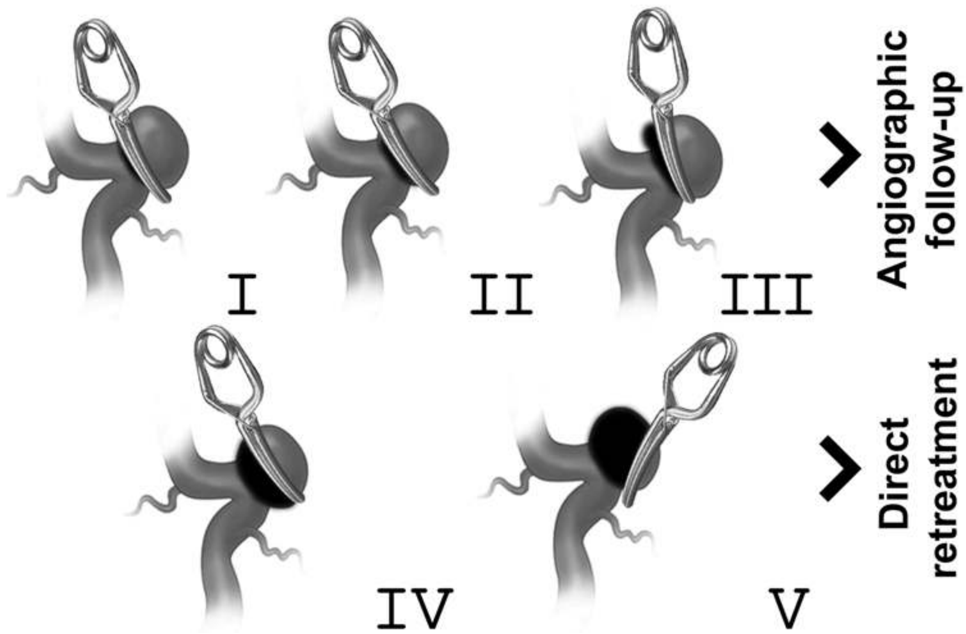

FIG. 1. Sindou classification for aneurysm remnants after surgical clipping. Grade I, less than 50% of neck size; Grade II, more than 50% of neck size; Grade III, residual lobe of a multilobulated sac; Grade IV, residual sac that is less than 75% of the aneurysmal size; and Grade V, residual sac that is more than 75% of aneurysmal size.[18]

curve analysis was applied for identification of the clinically relevant cutoff value. The diagnostic accuracy of age was judged based on the value of the area under the curve (AUC).

Data analysis was performed with use of PRISM (version 5.0, GraphPad Software Inc.) and SPSS (version 21, SPSS Inc., IBM) statistical software.

Results

Between January 2003 and December 2013, a total of 517 patients (with 659 cerebral aneurysms) were surgically treated at our institution. However, 43 aneurysms had to be excluded for the following reasons: 4 aneurysms were operated on without use of a clip (3 aneurysms were wrapped and 1 aneurysm was closed by bipolar coagulation), and 39 clipped aneurysms were not postoperatively controlled using DSA. Therefore, 480 patients with 616 cerebral aneurysms fulfilled all inclusion criteria and were included to the final analysis. The mean age of patients was 52.4 years (range 14–82.4 years), the female-to-male ratio was 2:1, and 235 aneurysms (38.2%) had previously ruptured. In 112 clipped aneurysms (18.2%), postoperative DSA revealed a residual aneurysm. Detailed information on the population characteristics is given in Table 1.

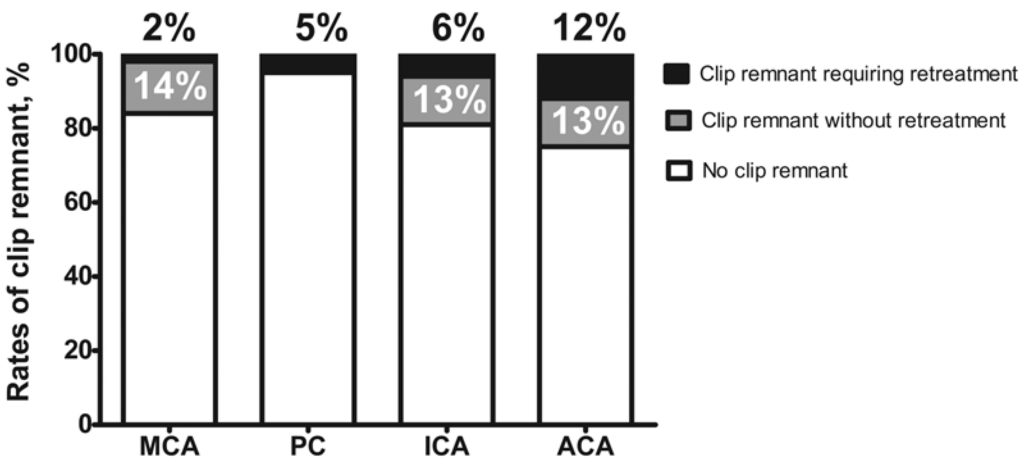

FIG. 2. The rates of aneurysm residuals after clipping depend on the location of the treated aneurysm. The rates of the remnants requiring retreatment are shown above the columns, and the rates of the remnants without retreatment are shown within the columns.

TABLE 1. Population characteristics*

Parameter	Value*
Mean age, yrs	52.4 ± 11.5
Female	435 (70.6%)
Aneurysm location	
MCA	379 (61.5)
ACA	124 (20.1)
ICA	93 (15.1)
PC	20 (3.3)
Mean aneurysm size, mm	6.4 ± 4.2
Mean aneurysm neck size, mm	4.1 ± 1.8
Aneurysm calcification	102 (16.6%)
Ruptured aneurysm	235 (38.2%)
Surgery w/in 3 wks after SAH	281 (45.6%)
Mean surgeon's individual remnant rate, %	17.4 ± 8.1
Mean surgeon's experience, yrs	9.3 ± 7.1
Time of surgery (btwn 10:00 PM & 7:00 AM)	43 (7%)
Intraop aneurysm rupture	102 (16.6%)

* Values are shown as the mean ± SD or number of patients (%).

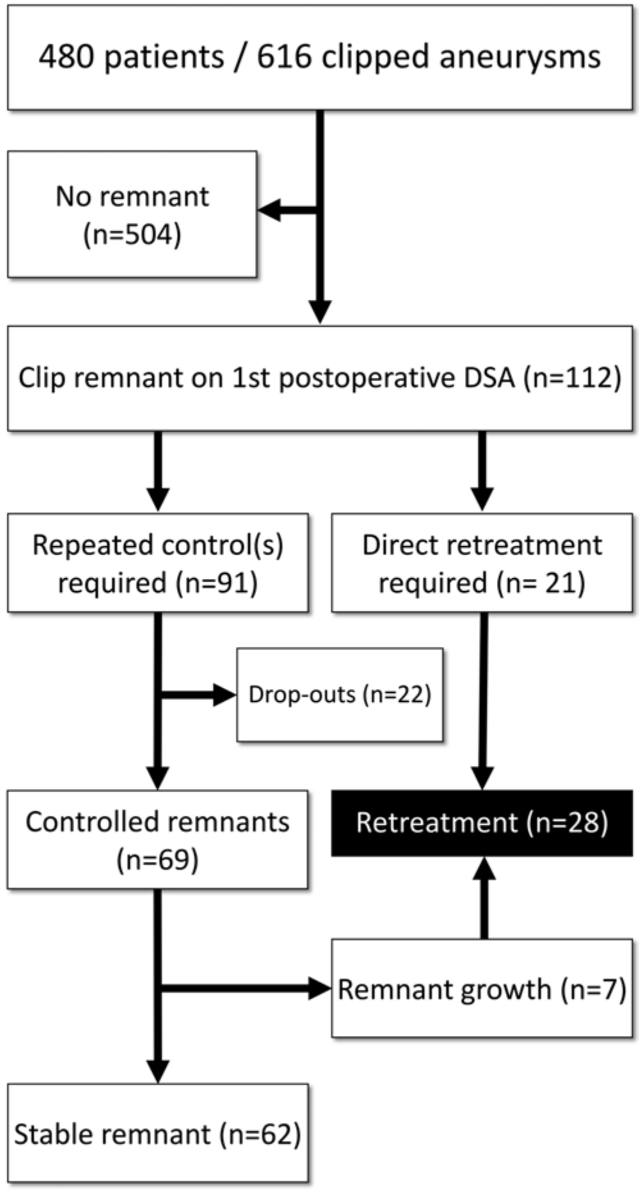

FIG. 3. Flowchart of the decision algorithm regarding postoperative aneurysm residuals.

Clinical Management of Clip Remnants

Twenty-one aneurysms showed sac residuals on the first postoperative DSA that were Sindou Grade IV or V. Consequently, these patients were directly retreated by reclipping or coiling. The remaining 91 aneurysms did not require direct retreatment and were supposed to be controlled. However, due to poor postoperative outcome or incompliance, 22 patients did not receive the recommended vascular follow-up (the "drop-out" group).

Therefore, only 69 aneurysm remnants were repeatedly controlled with a mean follow-up of 29.1 ± 25.9 months. During this period, 5 residual aneurysms showed growth on the routine follow-ups and were accordingly considered for retreatment. In addition, 2 patients were readmitted to our institution because of SAH from the remnants of MCA and anterior communicating artery aneurysms at 2 and 67 months after initial clipping, respectively. In both cases, DSA showed remnant growth. The detailed flowchart with the description of the treatment decisions with regard to the clip remnants is presented in the Fig. 3.

Independent Predictors for Clip Remnant

Over 20 variables were evaluated stepwise in the bivariate (Table e1 in the supplementary materials) and multivariate analyses (Table 2).

Accordingly, the need for retreatment (direct or delayed) of the identified clip remnants was independently associated with the location (assessed in a scale manner according to the remnant rates; p = 0.003; OR 1.85; see Fig. 2) and size (> 12 mm; p = 0.035; OR 3.22) of the treated aneurysms. Hence, the rate of remnant retreatment for large (> 12 mm) non-MCA aneurysms in our cohort was 18.2%, whereas only 1.2% of smaller (≤ 12 mm) MCA aneurysms had to be retreated after primary clipping (p = 0.001; OR 28.33; 95% CI 5.5–145.6).

Moreover, age (as continuous variable) was an independent risk factor (p = 0.022) in the multivariate analysis as a predictor for remnant growth. The appropriate ROC curve (Fig. 4) also revealed the high diagnostic value of age for predicting remnant growth (AUC 0.807). Thereafter, the cutoff for age was defined on the ROC curve as 45 years. Accordingly, younger age (< 45 years old; p = 0.004; OR 33.31) was the only independent risk factor for remnant growth. Of note, the duration of the postoperative angiographic follow-up was also included with the multivariate analysis predictors of remnant growth.

Finally, we have also identified the risk factors for angiographic evidence of all clip remnants (both retreated and not retreated) on the first postoperative DSA. Therefore, only aneurysm size > 12 mm (p = 0.013; OR 2.21)

TABLE 2. Multivariate logistic regression analyses

Parameter	OR (95% CI)	p Value*
Predictors for clip remnants requiring retreatment		
Aneurysm location†	1.85 (1.24–2.76)	**0.003**
Aneurysm size >12 mm	3.22 (1.08–9.57)	**0.035**
Ruptured aneurysm	1.55 (0.32–7.55)	0.588
Surgery w/in 3 wks after SAH	1.16 (0.24–5.64)	0.852
Multiple aneurysms	0.63 (0.27–1.46)	0.277
Intraop aneurysm rupture	1.72 (0.68–4.30)	0.251
Predictors for growth of clip remnant		
Age <45 yrs	33.31 (2.98–372.67)	**0.004**
Aneurysm location†	2.28 (0.67–7.73)	0.187
Surgery w/in 3 wks after SAH	0.39 (0.05–3.00)	0.368
Duration of postop follow-up	1.01 (0.98–1.04)	0.620

* Boldface type indicates statistical significance.

† Assessed using a scale based on the remnant rates: MCA < PC < ICA < ACA.

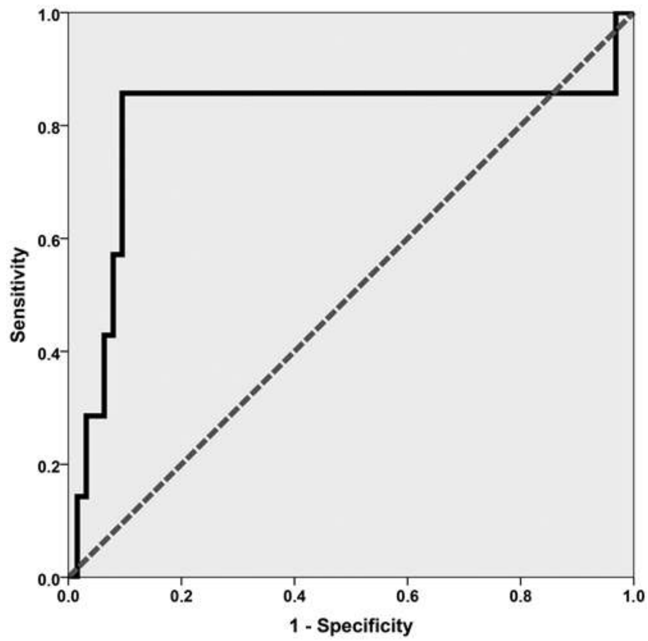

FIG. 4. The ROC curve of the correlation between age and remnant growth on repeated postoperative angiographic controls. The AUC of 0.807 points to the high diagnostic value of age as the predictor of remnant growth. In addition, the presented curve points to the age cutoff at 45 years (according to the "1 − specificity" of 0.143 and "sensitivity" of 0.857; see also Table e2 in the supplementary materials).

and intraoperative aneurysm rerupture (p = 0.03; OR 1.8) showed independent correlations here (Table e3 in the supplementary materials).

Discussion

In the current study, we performed a multifactorial analysis of the predictors for postclipping aneurysm remnant in a large monocentric series. In the bivariate and multivariate analyses, we evaluated the demographic and clinical data of the patients as well as the radiographic characteristics of the clipped aneurysms. We also analyzed different surgical aspects of aneurysm treatment that could have an impact on the success of aneurysm clipping.

Aneurysm Remnant After Clipping: Is It Worth Mentioning?

The occlusion rates and the rebleeding risk after microsurgical clipping of cerebral aneurysms are better than those after endovascular coiling.[12] However, the complete closure of an aneurysm by a clip is not always possible, thereby requiring postoperative angiographic proof of the clipping success.[7]

The reported rates of clip remnants are very inhomogeneous and range between 1.6% and 42%.[2,7,10,16,18,21] Higher remnant rates have been reported in more recent publications,[2,7,10] including this one (18.2%). This fact is basically attributed to a higher detection rate of rotational DSA, which has been increasingly used in the last decade.[2,7,20] Another possible reason for the higher remnant rate in our cohort might be due to the inconsistent use of intraoperative visualization of the intracranial vasculature, albeit the use of ICG videoangiography was not associated with a lower risk for clip remnant in our cohort. Intraoperative catheter angiography is an acknowledged tool used to increase the safety of aneurysm clipping.[24] However, intraoperative catheter angiography was not applied in our cohort, which could also have a certain impact on the remnant rate.

It is generally accepted that the degree of aneurysm occlusion after treatment is strongly associated with the risk of rerupture.[8] The annual risk for rebleeding from an aneurysm residual has been reported as 1.9%.[6] That number is higher than the bleeding risk from unruptured untreated aneurysms.[23] Therefore, the majority of authors recommend late angiographic follow-up review for incompletely obliterated aneurysms, while for completely clipped aneurysms such follow-up studies are not performed so far.[6,22]

There is still no consensus about the required duration of angiographic follow-up after aneurysm clipping. Tsutsumi et al. reported cases of re-SAH from previously clipped aneurysms after 9 years.[22] In our cohort, we saw 2 cases with delayed SAH from aneurysm remnants. One patient suffered aneurysmal bleeding longer than 5.5 years after initial clipping. Therefore, a remnant aneurysm after clipping unambiguously carries a life-threatening risk that justifies long-term follow-up in these patients.

Independent Predictors of Clip Remnant

The location of an aneurysm has been recognized as a predictor of incomplete aneurysm occlusion after clipping.[7,11,15,16] In particular, aneurysms located in the ophthalmic,[16] anterior communicating,[7] and posterior communicating arteries,[15] and the PC[11] have been reported to be associated with higher rates of postclipping residuals than MCA aneurysms. Furthermore, large to giant aneurysms with complex morphology were also shown to be prone to clip remnants.[11] However, all of these reports were based on univariate correlations, and hence no judgment about the independent predictive value of prior risk factors was possible.

In our multivariate analyses, the location (ACA > ICA > PC > MCA) and size (> 12 mm) of the aneurysm appeared as significant risk factors for remnants that required retreatment. So, the individuals with both risk factors (non-MCA aneurysm with a large sac > 12 mm) were at a 28.33-fold higher risk for remnant retreatment than patients with small MCA aneurysms. The occurrence of intraoperative aneurysm rupture influenced only the perfectness of the clip placement, but not the risk for retreatment or growth. Of note, the presence of acute SAH, as well as different surgery-related aspects (such as surgeon's experience, time of surgery, and intraoperative aneurysm rupture) had no effect on the retreatment rates for the clipped aneurysms.

Our data are in line with previous reports.[7,11,15,16] Here, we present various independent risk factors for unsatisfactory aneurysm clipping. We believe that the risk for clip remnants from non-MCA aneurysms, especially those with a larger aneurysm sac, should be considered when patients are evaluated for a microsurgical or endovascular treatment.

Remnant Growth: Age Matters

Knowing the risk factors that influence the progression of postclipping remnants is of high clinical importance, as 3.5% to 15% of all clip remnants exhibit growth and lead to re-SAH in up to 28% of cases.[7] In a small series of 11 patients, younger age has already been disputed to be a risk factor for the recurrence of aneurysms after clipping.[15]

In the present study, we showed that patient age is the only predictor of remnant growth. We also identified the clinically relevant cutoff for age on the ROC curve (see Fig. 4 and Table e2). Accordingly, younger individuals (< 45 years old) showed significantly higher rates of remnant regrowth (OR > 33). The association between age and the risk for remnant growth was independent of the duration of the follow-up controls.

In summary, the presented data show the importance of long-term angiographic follow-up in younger individuals with incomplete aneurysm clipping.

Study Limitations

The main limitation of this study is its retrospective nature. The analyzed data were collected from radiological and operative reports and documented electronic records of the patients. Therefore, a prospective correlation between medical history (especially cigarette smoking, which is known to impact the growth of untreated cerebral aneurysms[4,9]) and aneurysm remnants could not be performed. Furthermore, the frequency, duration, and chosen modality (DSA or CTA) of the repeated postoperative follow-ups was inhomogeneous. In addition, in our series, 22 patients with aneurysm remnants had to be excluded from the study for various reasons. Finally, intraoperative diagnostic tools, particularly ICG videoangiography, were inconsistently used in our series. However, these parameters were also statistically analyzed with regard to aneurysm remnant, and no significant impact could be found. Moreover, intraoperative catheter angiography, which is the gold standard for the evaluation of clip remnants,[24] was not used in our series at all. Nevertheless, our analysis is based on one of the largest series of primarily clipped aneurysms and includes a multivariate assessment that shows the independent predictive values of various variables.

Conclusions

The location (ACA > ICA > PC > MCA) and larger size (> 12 mm) of a cerebral aneurysm are the most important risk factors for aneurysm remnants after microsurgical clipping. Even after many years, residual aneurysms carry a rebleeding risk that justifies their repeated follow-up with CTA. Because of the significant risk for remnant growth, younger individuals (< 45 years) with incomplete clipping should undergo long-term (> 5 years) vascular follow-up.

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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: Jabbarli, Pierscianek, Wrede, Schlamann, Sure. Acquisition of data: Jabbarli, Schlamann. Analysis and interpretation of data: Jabbarli, Dammann, Forsting, Mueller, Sure. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Jabbarli. Statistical analysis: Jabbarli. Administrative/technical/material support: Jabbarli. Study supervision: Jabbarli, Sure.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Tables e1–3. http://thejns.org/doi/suppl/10.3171/2015.10.JNS151536.

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