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Long-Term Angiographic Findings in Patients Treated With Microsurgical Clipping of Intracranial Aneurysms

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Abstract

Microsurgical clipping remains a durable treatment for intracranial aneurysms. Despite the low rate of re-treatment, recurrence of subarachnoid hemorrhage is 3% within the first 10 years. This may be caused by rupture of a recurrent or residual aneurysm at the clip site or by rupture of another untreated aneurysm. We investigated the natural history of aneurysms treated with microsurgical clipping at our institution over a 10-year period. A secondary objective was to analyze our compliance rate with follow-up angiograms at three and 10 years and to investigate a role for less-invasive imaging modalities to manage microsurgical clipping patients. Ruptured and/or unruptured aneurysm patients treated with microsurgical clipping from 2000–2008 who had angiographic follow-up were included. Data were analyzed with respect to formation of de novo aneurysms, presence of residual aneurysm after clipping, and the rate of recurrence after complete clipping. There were 24 residual aneurysms (13%), two de novo aneurysms (1%) and one recurrent aneurysm (0.5%). The size of the aneurysm was significantly associated with having a residual aneurysm. Patient sex was also significantly associated with having a residual aneurysm. Compliance with angiographic follow-up occurred in 31% of patients treated with the majority only having one study at three years. Microsurgical clipping of aneurysms is durable with a low rate of recurrence and rebleeding. Residuals do not show angiographic progression and rarely require re-treatment. Compliance with angiographic follow-up is poor and this suggests that less invasive and expensive imaging modalities should be evaluated.

Categories: Neurosurgery
Keywords: aneurysm, angiogram, de novo, microsurgical clipping, rebleeding, recurrence, residual

Introduction

Microsurgical clipping remains a durable treatment modality for intracranial aneurysms. The results from the International Subarachnoid Aneurysm Trial (ISAT) showed that 3.8% of clipped aneurysms required re-treatment compared with 17.4% of those treated with endovascular coiling. The rate of re-bleeding was also higher in the coiled group [1]. Despite the low rate of re-treatment, the incidence of recurrent subarachnoid hemorrhage (SAH) after clipping is 3% within the first 10 years after treatment [2]. Recurrent SAH may be caused by rupture of a recurrent or residual aneurysm at the clip site or by rupture of an untreated additional aneurysm. Risk factors include smoking, younger age, and familial and/or multiple aneurysms, with a mean time to recurrence of 6.5 years [3]. Rates of residual aneurysms after microsurgical clipping range from 5 to 12% [4-5] and are thought to be associated with larger size, ruptured aneurysms, and technically challenging locations, such as the anterior communicating artery. Also, a postoperative suboptimal angiogram may not detect a residual aneurysm at the clip site or aneurysms in other locations. De novo aneurysms are relatively rare with an annual rate of 0.89 to 1.8% [6-7] and have been associated with a history of multiple aneurysms [8]. A major issue in the interpretation of these natural history data is the lack of compliance with angiographic follow-up. In one study, only 9% of patients treated with microsurgical clipping had an additional angiogram during the postoperative period [4]. This may be attributed in part to the fact that cerebral angiograms are costly, time-consuming, and invasive.

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The purpose of this study was to investigate the natural history of aneurysms treated with microsurgical clipping at our institution over a 10-year period. Our protocol currently recommends three and 10-year angiographic follow-up of all patients. A secondary objective was to analyze our compliance rate at three and 10 years and investigate if there may be a role for less-invasive imaging modalities in the management of patients treated with microsurgical clipping.

Materials And Methods

We used a prospectively maintained database of aneurysms treated at our institution. Data were collected prospectively since 1998 using MD Analyze (Medtech Global, Lexington, KY). A total of 460 patients with 568 aneurysms were treated with microsurgical clipping from 2000 to 2008. All patients underwent intraoperative or immediate postoperative cerebral angiograms. Patients without long-term (three year and/or 10 year) angiographic follow-up were excluded. There were 142 patients with 185 aneurysms included in the analysis of clinical results. Consent was obtained or waived for all subjects within this study. This study was conducted with the approval of Stanford University's Compliance Office of Human Subjects Research, protocol #12625.

The data obtained from these patients were analyzed with respect to formation of de novo aneurysms, presence of residual aneurysm after clipping, and the rate of recurrence after complete clipping. The authors evaluated the data retrospectively, and various demographic and clinical data points were obtained. We evaluated patient's age, sex, rupture status, and the need for additional treatment. The aneurysm characteristics, including location, size, and width of neck, were collected from the radiological images.

Univariate analyses were conducted using chi-square and Fisher exact tests. Multivariate analyses of rates of residual, de novo, and recurrent aneurysm formation were conducted using standard logistic regression techniques. We used the LOGISTIC procedure (SAS Institute, Cary, NC), which performs conditional logistic regression for binary response data. The maximum likelihood estimation was carried out with a Fisher scoring algorithm. Odds ratio estimates were displayed with parameter estimates. Step-wise selection model-building strategies were used to test variables in the model. Any observations with missing values were excluded from the analysis. The level of significance was set at 0.05. All analyses were performed using SAS software 9.3.

Results

Patient population

Between 2000 and 2008, 460 patients with 568 aneurysms were treated with microsurgical clipping at our institution. Of these, 142 patients (31%) had angiographic follow-up at least once between 3 and 10 years post-clipping. The majority of these patients (94%) had an angiographic follow-up only at year three. These 142 patients with 185 aneurysms were included in our analysis and the baseline characteristics are described in Table *1*.

Variable	Frequency (of 185 aneurysms)	Percent (%)
Anterior Circulation	141	76
Size < 13 mm	157	85
Wide Neck	110	59
Ruptured	72	39
Age ≥ 50	117	63
Female	134	72
Age	52.6 years (mean) 14–71 year (range)	–

TABLE 1: Baseline Characteristics of Patients with Angiographic Follow-up

Mean patient age was 52.6 years and 72% were female. Seventy-six percent of the aneurysms were in the anterior circulation and 85% were < 13 mm. Thirty-nine percent were ruptured aneurysms, and 59% had a wide neck (⩾ 4 mm) as measured on the preoperative angiogram. Angiographic review was completed by the first author and confirmed by radiology reports that demonstrated 24 residual aneurysms (13%), two de novo aneurysms (1%), and one recurrent aneurysm (0.5%) (Table *2*).

	Age	Sex	Location	Size	Neck	SAH	Details
Residual	50	m	R-ICA	6 mm	Narrow	No	4 mm R-ICA
Residual	54	f	Acomm	16 mm	Wide	Yes	3 mm Acomm
Residual	68	m	L-MCA	14 mm	Wide	No	11 mm L-MCA
Residual	51	m	Acomm	5 mm	Wide	Yes	3 mm L-ACA
Residual	61	f	L-ophthalmic	5 mm	Narrow	No	3 mm L-Ophthalmic
Residual	38	m	Acomm	5 mm	Narrow	Yes	3 mm Acomm
Residual	61	f	R-MCA	15 mm	Wide	No	3 mm R-MCA
Residual	69	f	R-MCA	20 mm	Narrow	No	3 mm R-MCA
Residual	68	m	R-MCA	8 mm	Wide	No	3 mm R-MCA
Residual	66	f	R-Pcomm	4 mm	Wide	Yes	2 mm R-Pcomm
Residual	66	f	R-Pcomm	8 mm	Narrow	Yes	2 mm R-Pcomm
Residual	54	m	L-SCA	4 mm	Wide	No	2 mm L-SCA
Residual	39	m	L-PCA	20 mm	Wide	No	2 mm L-PCA
Residual	41	m	L-PCA	15 mm	Wide	No	3 mm L-PCA
Residual	36	f	R-Pcomm	7 mm	Wide	No	3 mm R-Pcomm
Residual	57	m	L-Pcomm	4 mm	Wide	No	3 mm L-Pcomm
Residual	49	m	R-Ophthalmic	18 mm	Narrow	Yes	4 mm R-Ophthalmic
Residual	56	m	Acomm	15 mm	Wide	No	2 mm Acomm
Residual	66	f	R-ICA	7 mm	Wide	No	3 mm R-ICA
Residual	16	m	L-MCA	10 mm	Wide	No	3 mm L-MCA
Residual	44	f	R-Ophthalmic	4 mm	Narrow	No	2 mm r-Ophthalmic
Residual	55	f	R-Ant.chor	3 mm	Narrow	No	3 mm R-Ant-Chor
Residual	55	f	L-CavICA	20 mm	Wide	No	2 mm L-Cav ICA
Residual	34	f	L-Ophthalmic	12 mm	Wide	No	2 mm L-Ophthalmic
DeNovo	36	f	R-Pcomm	7 mm	Wide	No	3 mm R-PCA
DeNovo	44	f	Acomm	5 mm	Narrow	Yes	5 mm L-ICA
Regrowth	47	f	L-Pcomm	8 mm	Narrow	Yes	2 mm L-Pcomm

TABLE 2: Baseline Characteristics of Patients with Residual, Recurrent, or De Novo Aneurysm Formation

L = Left; R = Right; Acomm = anterior communicating artery; Pcomm = posterior communicating artery; Ant.chor = anterior choroidal artery; ICA = internal carotid artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; SCA = superior cerebellar artery

Univariate analyses were performed on the residual aneurysms. The size was significantly predictive of the presence of a residual aneurysm, where clipping smaller aneurysms (< 13 mm) was statistically less likely to result in residuals (P = .003). Sex was also a significant variable as statistically more males had a residual aneurysm after clipping (P = .01). There was no significant difference in residual aneurysms by location, age, width of neck, or rupture. None of the residual aneurysms increased in size or resulted in a hemorrhage (Figure *1*).

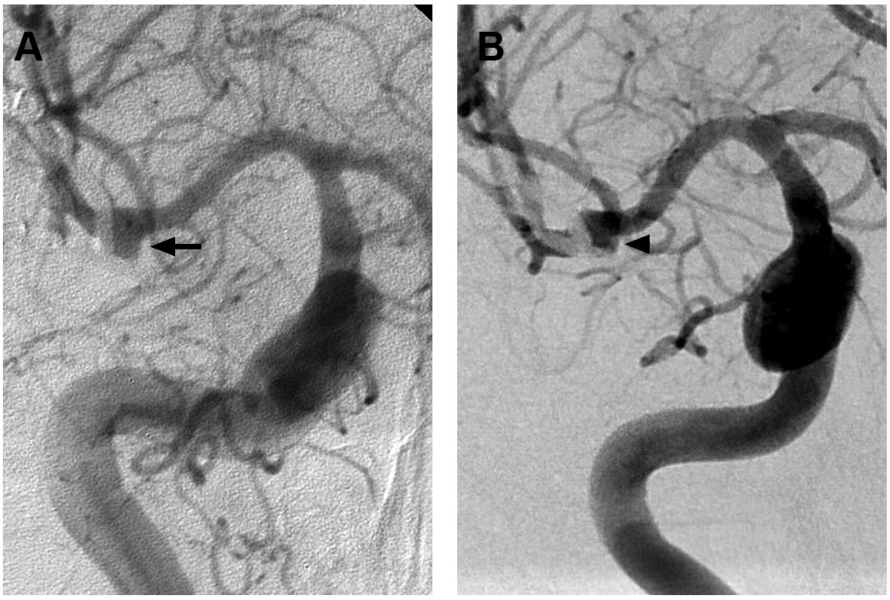

FIGURE 1: Cerebral angiogram (AP) of a 68-year-old male.

Cerebral angiogram (AP) of a 68-year-old male who presented with a generalized tonic-clonic seizure, which led to a magnetic resonance image demonstrating an 8 mm broad-based right middle cerebral artery aneurysm which was clipped in 2004. A 3 mm residual (arrow) was detected on the immediate postoperative angiogram and this remained stable (arrowhead) on his three-year follow-up angiogram in 2007.

One patient did subsequently receive Pipeline embolization of a left middle cerebral artery residual aneurysm, and another underwent microsurgical clipping for a small anterior communicating artery residual aneurysm. Only two de novo aneurysms were identified. Both were in female patients who were < 50 years old and who had small aneurysms (< 13 mm). One recurrence was identified in a 47-year-old female patient who had a ruptured posterior communicating artery aneurysm with a wide neck (Figure *2*).

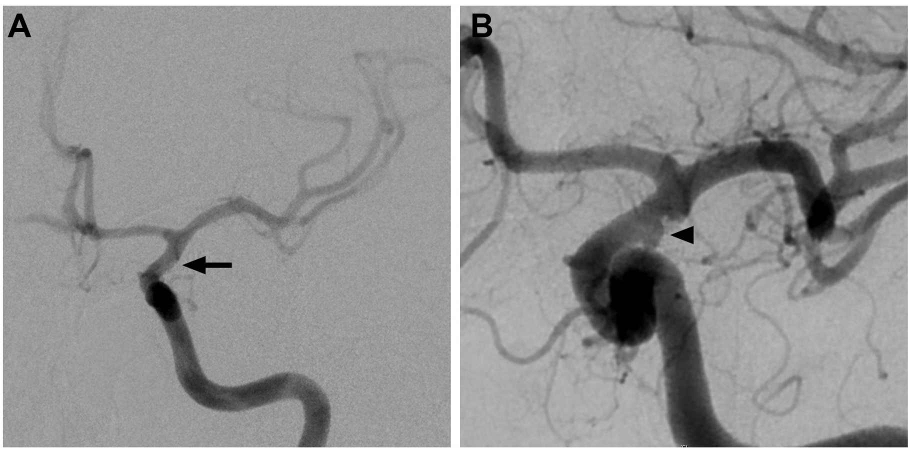

FIGURE 2: Cerebral angiogram (AP) of a 47-year-old female.

Cerebral angiogram (AP) of a 47-year-old female who presented with a ruptured posterior communicating artery aneurysm and had complete clipping, as seen on the postoperative angiogram in 2007 (arrow). Her three-year follow-up angiogram in 2010 demonstrates a recurrence (arrowhead).

Logistic regression analysis was performed to predict residual aneurysm formation from selected variables. Six predictor variables included in the model were age, sex, location, size, width of neck, and rupture status. Results of the logistic regression analysis showed that the full model, which considered all six independent variables together, was statistically significant (P = .004). Aneurysm size was significantly associated with having a residual aneurysm (PE = 1.45 P = .004 OR: 4.3, 95% CI: 1.6-11.4). This suggests that a patient is 4.2 times more likely to have a residual aneurysm if the aneurysm is large (⩾ 13 mm), independent of all other variables. Patient sex was also significantly associated with residual aneurysms (PE = -1.09 P = .018 OR: 0.34, (95% CI: 0.136-0.831). This suggests that a male patient is three times more likely to have a residual aneurysm than a female patient, independent of all other variables. At the time of submission, there were no patients with residual, de novo, or recurrent aneurysms from microsurgical clipping who required re-treatment or who developed a delayed hemorrhage.

Discussion

Aneurysms treated with microsurgical clipping rarely require further treatment, and the rate of recurrent SAH from the treated aneurysm is extremely low. These patients, however, do have a higher risk of future bleeding than the general population, thought to be the result of aneurysm formation in other locations or re-growth at the clip site [3, 6]. Natural history data suggests that the rate of recurrence or de novo aneurysm formation is 0.26 to 0.52%/year [6, 8]. Our study found that the incidence is even lower with an absolute rate of 1% for new aneurysms and 0.5% for recurrence over a 10-year period. Some residual aneurysms were detected on the immediate postoperative angiogram (13%), which is consistent with the rates from ISAT [5]. In our subgroup analyses of residual aneurysms, we found that larger aneurysms and male sex were predictive variables, but unlike in prior studies, location and rupture status were not [9]. In a series reported by David, et al. [8], 25% of residuals enlarged and 2% had re-hemorrhaged. On angiographic follow-up, we did not see any change in residual size nor were there any hemorrhages.

Studies have shown that compliance with angiographic follow-up is low, with less than 5% of patients having an additional angiogram after the postoperative period [2, 10]. This presents a limitation to interpretation of the natural history. All our patients underwent an intraoperative or immediate postoperative angiogram. We achieved a 31% compliance rate for three-year angiographic follow-up, but had only 6% compliance for 10-year follow-up. Although this rate is significantly higher than in previously published studies, we still do not know the long-term outcome of the majority of the aneurysms treated. Possible explanations for poor compliance include distance and cost of travel to a tertiary care center, as well as a patient's unwillingness to undergo a cerebral angiogram due to its risks and cost. As such, the major limitation to our data is that the rates of SAH recurrence, aneurysm recurrence, and de novo aneurysm formation may be underestimated.

Technological developments have led to increasing use of three-dimensional computed tomographic angiography (CTA) for pre- and postoperative surveillance of aneurysms. In a meta-analysis of 10 studies, the pooled sensitivity and specificity for detecting residual or recurrent aneurysms after clipping were 71% and 94%, respectively. CTA appears to be limited in detecting aneurysms less than 3 mm or when multiple clips were used [11]. Accuracy is also improved with the use of titanium clips and a multi-slice detector CTA [11-12].

Conclusions

The rates of recurrence and de novo aneurysm formation in our study were much lower than in other published series, and this may be attributable to the fact that postoperative suboptimal diagnostic angiograms in the past did not identify other existing or residual aneurysms, leading them to be classified as de novo or recurrent. Our data suggest that a high-quality postoperative angiogram can define any residual or additional aneurysms and may obviate the need for further invasive testing in most cases. Only patients who have residual aneurysms that are small (< 3 mm) or were treated with multiple clips may need intra-arterial digital subtraction angiography (DSA), as CTA may not have the sensitivity to detect progression. In most cases, however, multi-slice CTA with 16 or more detector rows has a high diagnostic value and may be used routinely after microsurgical clipping. With the use of titanium clips, artifact on CTA is now usually minimal, allowing for adequate evaluation of de novo aneurysms, recurrent aneurysms, and enlargement of residual aneurysms. Because of this study, we are revising our current protocol that submitted patients to three-year and 10-year angiograms and will analyze if compliance with radiographic follow-up improves with the use of CTA. Future studies also need to investigate the cost-effectiveness of CTA versus DSA and how to better define which patients are at risk for recurrent SAH after microsurgical clipping.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. Stanford University Panel on Human Subjects in Medical Research issued approval Protocol ID 12625. This study was conducted with the approval of our institution's Compliance Office of Human Subjects Research. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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