Late angiographic follow-up review of surgically treated aneurysms

CARLOS A. DAVID, M.D., A. GIANCARLO VISHITEH, M.D., ROBERT F. SPETZLER, M.D., MICHAEL LEMOLE, M.D., MICHAEL T. LAWTON, M.D., AND SHAHRAM PARTOVI, M.D.

Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, Arizona

Object. This study was undertaken to evaluate the long-term angiographic outcome of surgically treated aneurysms, which is unknown. Specifically, the incidence of recurrent aneurysms, the fate of residual necks, and the de novo formation of aneurysms were evaluated.

Methods. One hundred two patients (80 females and 22 males; mean age 49 years; range 12–78 years) harboring a total of 167 aneurysms underwent late follow-up angiography; 160 aneurysms were surgically treated. Late angiographic follow-up review was obtained at a mean of 4.4 ± 1.6 years postsurgery (range 2.6–9.7 years). Late follow-up angiography revealed two recurrent aneurysms (1.5%) of 135 clipped aneurysms without residua. Of 12 aneurysms with known residua, there were eight “dog-ear” residua, of which two (25%) enlarged. One hemorrhage was noted, yielding a hemorrhage risk of 1.9% per year. A second subgroup with broad-based residua revealed dramatic regrowth in three of four cases. Eight de novo aneurysms were found in six patients, for an annual risk of 1.8% per year. A history of multiple aneurysms was associated with de novo aneurysm formation (p = 0.049, chi-square analysis).

Conclusions. This study confirms the long-term efficacy of aneurysm clip ligation. In addition, the authors found there is a small but significant risk of de novo aneurysm formation, particularly in patients with multiple aneurysms. Most residual aneurysm rests appear to remain stable, although a subset may enlarge or rupture. These findings support the rationale for late angiographic follow-up review in patients with aneurysms.

Key Words • aneurysm • aneurysm residuum • postoperative angiography • late follow-up angiography • de novo aneurysm

POSTOPERATIVE angiography is routinely used to evaluate patients who have undergone surgical obliteration of an aneurysm. It provides information on the results of clipping, the presence of residual unclipped aneurysm, other unclipped aneurysms, and the occlusion of major vessels. Apart from this initial evaluation, however, few surgeons pursue late angiographic follow-up review in patients surgically treated for aneurysms.

Increasingly, the need for late outcome data related to various treatments has become apparent. In particular, the long-term efficacy of endovascular treatments for cerebral aneurysms has been questioned. Given this concern, establishing the long-term outcome of surgically treated aneurysms is warranted. Our study was designed to answer this question. Particular attention was given to determining the natural course of clipped aneurysms, whose angiographic appearance also makes them amenable to endovascular therapy.

At our institution, requests for late angiographic follow-up review of surgically treated aneurysms have been routine since 1985. Despite efforts to obtain late angiographic studies in all patients, only a small percentage are actually performed. In this report we review the findings from a series of consecutive late follow-up angiograms obtained in patients surgically treated for aneurysms, specifically to determine the incidence of recurrent aneurysms, the fate of residual aneurysm rests, and the incidence of de novo aneurysm formation.

Clinical Material and Methods

Late Angiography Protocol

At our institution, immediate and 3-year postoperative angiograms are obtained in patients surgically treated for aneurysms by the senior author (R.F.S.). At postoperative clinic visits, patients are advised to undergo angiography 3 years after surgery. Reminder letters are sent to the patients on their 3-year anniversary.

Complete four-vessel angiographic studies are obtained for the late follow-up review. Standard anteroposterior and lateral views are supplemented by additional views designed to delineate completely the parent vessel, clip, and any residual or recurrent aneurysm. The late angiograms are compared with preoperative and immediately postoperative angiograms by the neuroradiologist and surgeon. The data are collected prospectively and entered into a database for retrospective analysis.

The following data are collected: clinical presentation, number of aneurysms, aneurysm location and size, treatment method, and postoperative angiographic findings. The latter include the presence, size, and shape of the re-
sidual aneurysm and the finding of an unexpected aneurysm. Late postoperative angiographic findings include recurrence, change in known aneurysm residua, and the presence of new aneurysms.

**Patient Population**

Between July 3, 1988 and December 1, 1997, 102 patients surgically treated for aneurysms underwent late follow-up angiography. The consecutive series of angiograms were obtained in a population of patients harboring 1100 aneurysms treated by the senior author during this same time period. There were 80 females and 22 males (mean age 49 years; range 12–78 years). Sixty-two patients presented with subarachnoid hemorrhage (SAH); in 33 patients the aneurysms were found incidentally (during diagnostic work up for headache, dizziness, and other symptoms); in two, they were found after an investigation was made because there was a family history of aneurysms; two presented with visual symptoms; and two presented with oculomotor dysfunction. In one patient the aneurysm was found associated with an arteriovenous malformation. Of 167 aneurysms, 160 were surgically treated. Treatment methods included clip ligation in 147 instances (91.8%), wrapping in eight (5%), bypass with trapping in three (1.9%), and parent-vessel occlusion in two instances (1.3%). The seven untreated aneurysms consisted of five intracavernous internal carotid artery (ICA) aneurysms, one fusiform basilar artery (BA) dilation, and one anterior choroidal artery (AChA) aneurysm that measured 1 mm. The mean late angiographic follow-up period was 4.4 ± 1.6 years (range 2.6–9.7 years). There was a total of 443 patient follow-up years.

**Calculation of Annual Rates of Aneurysm Recurrence or Hemorrhage**

Annual rates of aneurysm recurrence or hemorrhage were determined by dividing the number of clinical events (aneurysm formation or hemorrhage) by the number of patient years of observation for the population or particular subgroup.

**Statistical Analysis**

The data were analyzed using commercially available statistical software (Statview version 4.02; Abacus Concepts, Inc., Berkeley, CA). Chi square analysis was used when appropriate. Data are presented as means ± standard deviations. Statistical significance was set at a probability value less than 0.05.

**Results**

The data were subdivided by treatment groups: clipped aneurysms, wrapped aneurysms, other treatments (bypass with trapping and parent-vessel occlusion), and no treatment. Clipped aneurysms were further subdivided into those with and without residuum.

**Clipped Aneurysms**

**Aneurysms Without Residual Neck.** Of the 147 clipped aneurysms, 135 (91.8%) were clipped without evidence of residua on postoperative angiography. Late follow-up angiography revealed two recurrent aneurysms (1.5%)—a small anterior communicating artery (ACoA) aneurysm and a small posterior communicating artery (PCoA) aneurysm. The latter occurred in a patient with a history of fibromuscular dysplasia. Focusing only on completely clipped aneurysms, the corresponding observation time is 386 years. Hence, the annual recurrence rate for a completely clipped aneurysm was approximately 0.52%. There were no recurrent SAHs in this subgroup.

**Aneurysms With Residual Neck.** Of the 147 clipped aneurysms, 12 (8.2%) displayed a residual neck on immediate postoperative angiography. These residua consisted of two different morphological varieties. The first subgroup consisted of classic “dog-ear” residua (Fig. 1), in which a small remnant of aneurysm is observed between the parent vessel and the base of the clip. The second subgroup, consisting of what are termed “broad-based” residua, occurred with aneurysms that encompassed such a large percentage of the parent-vessel circumference that clipping could only be achieved by incorporating the aneurysm wall into the reconstructed vessel (Fig. 2). We refer to these aneurysms as “expansive” aneurysms.

There were eight dog-ear residua, two of which were recognized at surgery and reinforced with cotton. Of the eight dog-ear residua, six (75%), including the two reinforced with cotton, remained stable throughout the follow-up period. The other two (25%) enlarged slightly, one (12.5%) of which came to attention after the patient suffered an SAH. There were 52.9 years of observation for the dog-ear subgroup, suggesting an annual hemorrhage risk of approximately 1.9%.

There were four broad-based residua: one with a small ACoA aneurysm, one with a large PCoA aneurysm, and two with giant BA aneurysms. Three (75%) of these broad-based residua were associated with aneurysm regrowth (Fig. 3). No SAHs occurred. The 15.8 years of observation for this subgroup suggest an annual recurrence
rate of 19% for broad-based residua. Although data are insufficient for meaningful statistical analysis, the residua- 
necks that regrew into aneurysms tended to be of the 
broad-based variety.

Grouping the incompletely clipped aneurysms together, 
the corresponding observation time is 68.7 years. Thus, 
the risk of recurrence from an aneurysm residuum is 2.9% 
per year, with a risk of hemorrhage at 1.5% per year. Com-
bining all clipped aneurysms, regardless of the presence or 
lack of residuum, yields an overall risk of hemorrhage 
from a clipped aneurysm at 0.26% per year.

Wrapped Aneurysms

Eight aneurysms were treated by wrapping with cotton. 
Late follow-up angiography revealed no change in seven 
(87.5%) and an enlargement of one (12.5%) aneurysm. 
The latter was a large middle cerebral artery (MCA) aneu-
rysmb that had been deemed unclippable because multiple 
perforating vessels were involved at the aneurysm dome. 
One hemorrhage was observed from a wrapped aneurysm 
that was unchanged at follow-up angiography. With 31 
years of observation for this subgroup, we infer from the 
data a 3.2% annual hemorrhage rate.

Other Treatment Modalities

Three aneurysms were treated by bypassing the parent 
vessel and trapping the aneurysm. On late angiographic 
follow-up review, all bypasses were patent and there was 
no evidence of recurrent or residual aneurysm. The two 
cavernous ICA aneurysms were treated with parent-vessel 
occlusion and balloon occlusion, respectively. Follow-up 
angiography revealed no recurrent or residual aneurysm 
filling in either case.

![Images of aneurysms and treatment modalities]
Untreated Aneurysms

Of the seven untreated aneurysms, follow-up angiography revealed slight enlargement in one of the five cavernous ICA aneurysms, the disappearance of the 1-mm AChA aneurysm, and continued enlargement and brainstem compression from a fusiform BA aneurysm in an elderly patient who eventually died.

De Novo Aneurysm Formation

Overall, eight new aneurysms formed in six patients (five women and one man). To be considered a de novo aneurysm, the aneurysm had to be located at a site remote from the original aneurysm and not seen on the patient’s original pre- and postoperative angiograms (Fig. 4). The new aneurysms were located on the pericallosal artery, AChA, PCoA, and ACoA in two patients, and the MCA in three patients. Of the six patients, five had a history of multiple aneurysms.

Based on 443 patient years of observation, we determined that the annual risk of de novo aneurysm formation was 1.8% per year. A search for predisposing factors suggested that a history of multiple aneurysms is associated with de novo aneurysm formation (p = 0.049, chi-square analysis). Hypertension was not found to be a risk factor (p = 0.82).

Discussion

Few data exist on the long-term (> 2 years) angiographic follow-up review of surgically treated aneurysms. A wealth of previous observations suggests that aneurysms can recur from residual rests and even from apparently perfectly clipped aneurysms.\textsuperscript{3,4,9,13,14} The rationale for obtaining postoperative angiograms of clipped aneurysms has been presented.\textsuperscript{1} Even though postoperative angiograms confirm aneurysm obliteration, clips can slip or break and aneurysms can regrow and hemorrhage several months to years after treatment.\textsuperscript{4} These occurrences in conjunction with the need for late outcome data underline the importance of long-term angiographic follow-up review.

Recurrent Aneurysms

Recurrent aneurysms have been encountered since McKissock\textsuperscript{11} reported a recurrent MCA aneurysm 11 years after its initial excision. Despite such reports, it cannot be ruled out that many of these aneurysms may have been incompletely clipped. It is therefore difficult, based on the literature, to determine the exact risk of recurrence once an aneurysm is believed to be completely clipped.

Although the frequency of aneurysm recurrence after complete clipping is difficult to determine, we infer from our data an incidence of approximately 0.5% per year. This finding, however, must be viewed with caution. Only two patients experienced a recurrence, one of whom suffered from fibromuscular dysplasia. To what degree this disorder predisposed the patient to a recurrence is unknown. Furthermore, even though postoperative angiography revealed no residual aneurysm and perfect clipping, a small aneurysm rest cannot be ruled out completely. As Feuerberg, et al.,\textsuperscript{7} noted, angiographic identification of aneurysm rests can be difficult.

If the aneurysm is perfectly clipped, however, some factor must underlie its regrowth. Although we found no reason in our series besides that described earlier, other workers have suggested several possibilities. Drake and Allcock\textsuperscript{1} attributed the appearance of remaining aneurysm on postoperative angiograms to slipped clips. Ebina, et al.,\textsuperscript{4} questioned whether the clips, combined with the fragility of the parent vascular wall and hemodynamic stress could be responsible. The silver aneurysm clip used in the past is known to incite a granulomatous tissue reaction.

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Residual Aneurysm Rests

The significance of postoperative aneurysm rests and their management has been the subject of several re-
Macdonald, et al.,\textsuperscript{10} pointed out that postoperative angiography may reveal a significant number of aneurysms with residua. Based on the results of postoperative angiography in 715 patients, Feuerberg, et al.,\textsuperscript{5} reported a 4% incidence of aneurysm rests. The incidence of residua is estimated to range between 4% and 18%.\textsuperscript{10}

The prognostic significance of these rests, however, remains controversial. Many residua are believed to undergo spontaneous thrombosis, although a small number have been noted to enlarge and even hemorrhage. The risk of hemorrhage from an aneurysm rest may be approximately 0.5% per year;\textsuperscript{3} but scant long-term information is available. In our series, the overall incidence of residua was 8.2%, whereas that of the dog-ear residuum was 5%, well within the reported range. None of these residua thrombosed and only 25% enlarged slightly. Only one (12.5%) hemorrhaged, yielding a 1.9% risk of hemorrhage per year. Although this number is slightly larger than that previously reported, it furthers the argument that the cumulative risk is significant, particularly in younger patients.

**Broad-Based Aneurysms**

The expansive types of aneurysm were not quite fusiform but encompassed so much of the parent vessel wall as to suggest that they had expanded from it. Although difficult to treat, these aneurysms were clipped by reconstructing the vessel lumen and eliminating most of the expansion (Fig. 2). To achieve this goal, however, obvious aneurysm wall is incorporated into the reconstructed lumen. Hence, although they appear completely clipped on postoperative angiography, they constitute a broad-based residuum.

The fate of these residua was dramatic. Although only four such aneurysms occurred, three (75%) had completely regrown on late angiographic studies, suggesting an annual recurrence rate of 19%. We identified no underlying connective tissue disorders or predisposing factors in these patients. It appears that these aneurysms constitute a completely separate subtype of aneurysm with a high risk for recurrence.

**Wrapped Aneurysms**

For many years, gauze or muscle was used to wrap the aneurysm when it was believed that the neck was not amenable to clipping. There were only eight such cases in our series. This small number reflects the contemporary neurosurgical technique of using temporary vessel occlusion and, when necessary, hypothermic cardiac arrest, which make most aneurysms amenable to treatment.

Of these eight cases, one enlarged over the follow-up period. A second appeared stable and was associated with an SAH. Consequently, the annual risk of hemorrhage for a wrapped aneurysm was 3.2%. On initial observation, this outcome is similar to the natural history of an untreated ruptured aneurysm.\textsuperscript{7} It would lead one to conclude that wrapping offers no protection. However, three of the eight wrapped aneurysms in this series were unruptured, making comparisons difficult. Nonetheless, we agree with Drake and Vanderlinden\textsuperscript{1} and Yaşargil\textsuperscript{11} that wrapping does not confer long-term protection.

**Formation of De Novo Aneurysms**

Since the first description by Graf and Hamby\textsuperscript{6} in 1964, other authors\textsuperscript{8,12,15} have substantiated the occurrence of de novo aneurysms with many well-documented cases. In fact, Miller and colleagues\textsuperscript{12} suggested an annual incidence of 100 per 100,000 cases of known aneurysm patients. Although many have criticized this estimate as too large, it does raise questions concerning the risk of de novo formation of aneurysms and which patients should undergo late angiographic studies.

In our study, the risk of de novo formation of aneurysms was approximately 1.8% per year. Although this frequency is higher than previously estimated, Miller and colleagues\textsuperscript{12} speculated that the true incidence of de novo formation of aneurysms would be higher than reported, primarily because some patients may die before diagnosis and others may harbor new unruptured aneurysms.

The pathogenesis of de novo aneurysms raises many interesting possibilities regarding the genesis of cerebral aneurysms. Van Alphen and Yong-Zhong\textsuperscript{15} described the existence of “aneurysms in statu nascendi” referring to early aneurysm “blebs” identified on angiography and at surgery. They believe these blebs represent an early stage of the de novo aneurysm. We identified only one bleb on an original angiogram. Van Alphen and Yong-Zhong\textsuperscript{15} believe that these blebs occur at weak points in the parent vessel, “locus minoris resistentiae.” The hemodynamic forces associated with aneurysm formation would affect these locations and lead to the formation of new aneurysms.

An interesting issue raised by van Alphen and Yong-Zhong\textsuperscript{15} is the significant preponderance of females with de novo aneurysms. Of 25 cases reported at the time of their publication, 15 occurred in females. The reasons for this gender skew are unclear. It has been suggested that female hormones and oral contraceptives may be involved. In our study, the female/male ratio of de novo aneurysms was 5:1. Although this finding agrees with previous reports, it was not statistically significant (p = 0.83).

With the exception of aneurysm multiplicity, a search for other predisposing factors was unfruitful. In our study, the association between a history of multiple aneurysms and the de novo formation of aneurysms was statistically significant, a possibility first alluded to by Koeleveeld, et al.,\textsuperscript{8} who recommended late angiographic follow-up review in very young patients with multiple aneurysms. In fact, de novo aneurysms may be considered a special case of multiple aneurysms appearing in series rather than in parallel.\textsuperscript{8}

**Potential Biases and Deficiencies**

Because of obvious weaknesses and biases inherent in our study, the clinical relevance of the results must be interpreted with caution. The study suffers from follow-up bias in that not all requested late angiograms were obtained. This bias is not surprising, given the reluctance of a patient who is doing well and who feels cured to submit to a stressful and uncomfortable examination attended by a small but significant risk. In addition, the aneurysms in our patients represent a very small percentage of the approximately 1100 total aneurysms treated by the senior...
Late angiographic study of surgically treated aneurysms

author during the study period. The impact of this situation on the results is minimal, if one considers that the study population consisted of a consecutive series of follow-up angiograms rather than surgically treated patients. Furthermore, the patients were not selected for the study; or rather, the study population consisted of random patients who elected to undergo the requested angiography. Although we cannot provide evidence, based on the reasoning given earlier, we believe that this 10% of patients does not differ significantly from the other 90% who declined follow-up angiography.

Last, although we believe that all SAHs that occurred during the follow-up period are included, we cannot exclude with certainty the possibility that some were lost to follow up. Any such loss would affect some of the calculated hemorrhage rates.

Notwithstanding, we believe that this study represents a reasonably unbiased follow-up review of angiographic outcome for surgically treated aneurysms. No similar data are yet available for other surgical or endovascular treatment series. Whether the results of this study will be confirmed in a prospective series of surgically treated patients remains to be seen. More important, a similar study of endovascular occlusion of aneurysms is needed.

Conclusions

We have presented data regarding the late angiographic outcome of surgically treated aneurysms. The data confirm the long-term efficacy of aneurysm clip ligation with a 98.5% permanent obliteration rate. Furthermore, it appears that residual aneurysm necks continue to pose a small but significant risk for hemorrhage despite change or stability in their size. Broad-based, expansive aneurysms emerged as an alarming subset with a high propensity for regrowth. Finally, there appears to be a small but significant risk of de novo aneurysm formation, particularly in patients with multiple aneurysms.

Based on these findings, we believe that late angiographic follow-up review is probably not required for routine, completely clipped aneurysms. Continued surveillance, however, of patients with aneurysms with known residual necks; broad-based, expansive aneurysms; and multiple aneurysms is warranted.

References

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Address for Dr. David: University of Missouri School of Medicine, Columbia, Missouri.
Address for Dr. Lawton: University of California San Francisco, San Francisco, California.
Address correspondence to: Robert F. Spetzler, M.D., c/o Neuroscience Publications, Barrow Neurological Institute, 350 West Thomas Road, Phoenix, Arizona 85013–4496. email: neuropub@chw.edu.