Long-term catheter angiography after aneurysm coil therapy: results of 209 patients and predictors of delayed recurrence and retreatment

Clinical article

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Object. Aneurysm recurrence after coil therapy remains a major shortcoming in the endovascular management of cerebral aneurysms. The need for long-term imaging follow-up was recently investigated. This study assessed the diagnostic yield of long-term digital subtraction angiography (DSA) follow-up and determined predictors of delayed aneurysm recurrence and retreatment.

Methods. Inclusion criteria were as follows: 1) available short-term and long-term (> 36 months) follow-up DSA images, and 2) no or only minor aneurysm recurrence (not requiring further intervention, i.e., < 20%) documented on short-term follow-up DSA images.

Results. Of 209 patients included in the study, 88 (42%) presented with subarachnoid hemorrhage. On short-term follow-up DSA images, 158 (75%) aneurysms showed no recurrence, and 51 (25%) showed minor recurrence (< 20%, not retreated). On long-term follow-up DSA images, 124 (59%) aneurysms showed no recurrence, and 85 (41%) aneurysms showed recurrence, of which 55 (26%) required retreatment. In multivariate analysis, the predictors of recurrence on long-term follow-up DSA images were as follows: 1) larger aneurysm size (p = 0.001), 2) male sex (p = 0.006), 3) conventional coil therapy (p = 0.05), 4) aneurysm location (p = 0.01), and 5) a minor recurrence on short-term follow-up DSA images (p = 0.007). Ruptured aneurysm status was not a predictive factor. The sensitivity of short-term follow-up DSA studies was only 40.0% for detecting delayed aneurysm recurrence and 45.5% for detecting delayed recurrence requiring further treatment.

Conclusions. The results of this study highlight the importance of long-term angiographic follow-up after coil therapy for ruptured and unruptured intracranial aneurysms. Predictors of delayed recurrence and retreatment include large aneurysms, recurrence on short-term follow-up DSA images (even minor), male sex, and conventional coil therapy.

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KEY WORDS • angiography • coil therapy • intracranial aneurysm • recurrence • vascular disorders • interventional neurosurgery

Endovascular coil therapy is a well-established treatment for intracranial aneurysms. The major shortcoming of coil therapy is the risk of aneurysm recurrence, which could occur in more than 30% of cases. Follow-up imaging after coil embolization is routinely performed to identify recurrent aneurysms before they rupture. Previous studies have demonstrated that most recurrences occur within the 1st year after treatment. A recent well-designed multicenter study from the Netherlands found that the vast majority of aneurysms treated with coil therapy that are adequately occluded at 6 months of follow-up remain occluded in the subsequent 5 years (on MR angiography), thus questioning the need for routine imaging follow-up beyond 6 months. In a comprehensive review of the literature on aneurysm recurrence, Crobeddu et al. concluded that imaging follow-up within the 1st year after coil therapy...
Long-term follow-up angiography

is the most important step to identify recurrence and that follow-up imaging is probably unnecessary thereafter. Any conclusion in this regard, however, was premature because long-term follow-up studies with digital subtraction angiography (DSA) were lacking.

In this study, we assess the diagnostic yield of long-term (> 36 months) follow-up DSA examinations in adequately occluded aneurysms and determine predictors of delayed aneurysm recurrence and retreatment.

Methods

Study Design and Setting

The Thomas Jefferson University institutional review board approved the study protocol. We searched our database for all patients with intracranial aneurysms who underwent coil therapy between 2003 and 2008 at Thomas Jefferson University. Inclusion criteria were as follows: 1) available short-term (≤ 36 months) and long-term (> 36 months) follow-up DSA images, and 2) no aneurysm recurrence or only minor recurrence (i.e., < 20%, not requiring further intervention) on short-term follow-up DSA images (patients who underwent retreatment were excluded). A total of 209 patients met these criteria and constituted our study population.

Variables and Data Sources

Medical charts and imaging studies were reviewed to determine patient age, sex, size and location of aneurysm, ruptured/unruptured aneurysm status, procedural specifics, and immediate and follow-up DSA results. Short-term and long-term follow-up DSA images were compared to determine the rate of delayed aneurysm recurrence. When more than 1 short-term or long-term follow-up DSA image was available, the results of the latest DSA image were considered. Aneurysms with stable occlusion were considered nonrecurrent. Any aneurysm that displayed a decreasing percentage of occlusion on long-term follow-up DSA was considered recurrent regardless of the need for retreatment. Aneurysms with major recurrence (≥ 20%) were generally considered for retreatment.

Aneurysms were embolized with a variety of bare platinum coils at the operator’s discretion. Coiling was interrupted when the aneurysm was completely occluded or when the microcatheter pulled out of the aneurysm. The use of stent or balloon assistance was generally indicated for wide-necked aneurysms (≥ 4 mm) or those with an unfavorable fundus-to-neck ratio (< 1.5). At our institution, follow-up DSA is scheduled at 6–12 months, 2–3 years, and 5 years after treatment. Some patients, however, may opt for noninvasive imaging follow-up (MR or CT angiography).

Statistical Analysis

Data are presented as the mean and range for continuous variables and as frequency for categorical variables. Analysis was carried out using unpaired t-tests, chi-square tests, and Fisher’s exact tests as appropriate. Kaplan-Meier risk of recurrence along with retreatment was calculated based on timing of follow-up cerebral DSA examination. Univariate analysis was used to test covariates predictive of the following dependent variables assessed on long-term follow-up DSA images: 1) recurrence and 2) retreatment. Interaction and confounding were assessed through stratification and relevant expansion covariates. Factors predictive in univariate analysis (p < 0.20) were entered into a multivariate logistic regression analysis. Resulting p values of ≤ 0.05 were considered statistically significant. Sensitivity and specificity analyses assessed the value of short-term DSA in predicting long-term recurrence and/or retreatment (≥ 36 months). Statistical analysis was carried out with Stata (version 10.0; StataCorp LP).

Results

Patient Characteristics and Procedural Specifics

Patients comprised 169 (81%) women and 40 (19%) men, with a mean age of 50.7 ± 10.2 years. Of 209 patients, 88 (42%) were initially treated for subarachnoid hemorrhage. Mean aneurysm size was 7.7 ± 3.8 mm. There were 164 (78.5%) aneurysms in the anterior circulation and 45 (21.5%) aneurysms in the posterior circulation (Table 1). Among aneurysms in the anterior circulation, 130 were ≤ 10 mm in size. Coil therapy was performed with stent (n = 40) or balloon (n = 2) assistance in 42 (20%) patients. Immediate aneurysm occlusion (> 95%) was achieved in 188 (90%) patients.

Short-Term Follow-Up DSA Studies

Short-term follow-up DSA images were available at 6 months for 119 patients, at 7–12 months for 85 patients, and at 13–36 months for 67 patients. On short-term follow-up DSA images, 158 (75%) aneurysms showed no recurrence and 51 (25%) showed a minor recurrence (not retreated).

Long-Term Follow-Up DSA Studies

Long-term follow-up DSA images were available at 37–60 months for 110 patients and at > 60 months for 115 patients. On long-term follow-up DSA images, 124 (59%) aneurysms showed no recurrence, whereas 85 (41%) aneurysms showed recurrence, with 55 (26%) requiring further intervention. The rate of recurrence (or increase of known recurrence) on long-term follow-up DSA images was 67%.

<table>
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<th>TABLE 1: Location of treated aneurysms</th>
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<td>Location</td>
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<td>----------------------------------------</td>
</tr>
<tr>
<td>carotid ophthalmic artery</td>
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<tr>
<td>paracarotid artery</td>
</tr>
<tr>
<td>posterior communicating artery</td>
</tr>
<tr>
<td>vertebrobasilar artery</td>
</tr>
<tr>
<td>carotid terminus</td>
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<td>pericallosal artery</td>
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and without recurrence on short-term follow-up DSA images (49% vs 19%, p < 0.001). Mean aneurysm size was significantly larger in recurrent (8.9 mm) than in stable (6.9 mm; p = 0.001) aneurysms on long-term DSA images. The rate of delayed aneurysm recurrence was significantly higher in patients undergoing conventional coil therapy (45%, 78/167) than in those undergoing stent- or balloon-assisted coil therapy (16.7%, 7/42; p = 0.001). Higher recurrence rates were noted in male patients (62.5%, 25/40) than in female patients (35.5%, 60/169; p = 0.002). Only 1 (1.8%) clinically significant complication (a transient ischemic event) was associated with retreatment. Four patients (1.9%) suffered new hemorrhage due to aneurysm recurrence (> 36 months in all 4). Three of these patients had previously unruptured aneurysms.

The following factors were tested for as predictors of recurrence and retreatment in univariate analysis: age, sex, aneurysm size, aneurysm location, ruptured/unruptured status, type of procedure, and follow-up time. Recurrence was predicted by larger aneurysm size (p = 0.001), male sex (p = 0.002), conventional coil therapy (p = 0.001), a minor recurrence on short-term follow-up DSA image (p < 0.001), and aneurysm located in anterior or posterior communicating artery, carotid terminus, paracclinoid artery, or middle cerebral artery (p = 0.07). In multivariate analysis, the predictors of recurrence on long-term follow-up DSA images were: 1) larger aneurysm size (OR 1.2, 95% CI 1.1–1.4; p = 0.001), 2) male sex (OR 3.8, 95% CI 1.5–10; p = 0.006), 3) conventional coil therapy (OR 3.3, 95% CI 1.1–10; p = 0.05), 4) a minor recurrence on short-term follow-up DSA image (OR 3.1, 95% CI 1.3–7; p = 0.007), and 5) aneurysm located in anterior or posterior communicating artery, carotid terminus, paracclinoid artery, or middle cerebral artery (OR 3.1, 95% CI 1.3–8; p = 0.01). Ruptured aneurysm status was not a predictive factor.

In univariate analysis, retreatment was predicted by larger aneurysm size (p = 0.001), male sex (p = 0.004), conventional coil therapy (p = 0.02), a minor recurrence on short-term follow-up DSA image (p = 0.001), and aneurysm located in anterior or posterior communicating artery, carotid terminus, paracclinoid artery, or middle cerebral artery (p = 0.01). The predictors of retreatment at long-term follow-up DSA examination were: 1) larger aneurysm size (OR 1.2, 95% CI 1.1–1.4; p = 0.001), 2) male sex (OR 3.5, 95% CI 1.4–10; p = 0.01), 3) a minor recurrence on short-term follow-up DSA image (OR 3.4, 95% CI 2.0–55; p = 0.005), and 4) aneurysm located in anterior or posterior communicating, paracclinoid, or vertebrobasilar artery (OR 10.5, 95% CI 1.3–80; p = 0.005).

For short-term follow-up DSA studies, the sensitivity, specificity, negative predictive value, and positive predictive value for detecting delayed aneurysm recurrence were 40.0%, 86.3%, 67.7%, and 66.7%, respectively, and for detecting those requiring further treatment, they were 45.5%, 83.1%, 81.0%, and 49.0%.

At 3, 5, and 7 years, Kaplan-Meier actuarial recurrence-free rates were 98.6%, 82.5%, and 54.6%, respectively (Fig. 1); retreatment-free rates were 98.6%, 88.0%, and 58.8% (Fig. 2).

Discussion
This is the first study to assess the diagnostic yield of long-term DSA studies in adequately occluded aneurysms and determine the predictors of delayed recurrence and retreatment. The results clearly demonstrate that long-term follow-up DSA examination is indicated after coil of intracranial aneurysms. In over 40% of patients who had adequate aneurysm occlusion within the first 36 months of coil therapy, a recurrence was shown on long-term follow-up DSA images, with 26% requiring further intervention. In other words, more than 1 in every 4 patients undergoing coil therapy required additional treatment based on the findings of long-term follow-up DSA. Also, results of short-term follow-up DSA did not predict delayed aneurysm recurrence and retreatment (test sensitivity 40% and 45.5%, respectively). These results challenge previous studies reporting that aneurysm recurrence occurs mostly within 6–12 months after coil therapy and that follow-up imaging beyond that period is unnecessary. Using 3-T MR angiography, Ferns et al. assessed the occurrence of late (> 4.5 years) aneurysm recanalization after coil therapy in a series of 400 patients with 440 aneurysms. The authors reported delayed aneurysm recurrence in 11 patients (2.8%), with only 3 lesions (0.7%) requiring further treatment. They also identified aneurysm size larger than 10 mm and location on the basilar tip as predictors of late aneurysm reopening. Based on these data, Ferns et al. concluded that, for the vast majority of intracranial aneurysms adequately occluded at 6 months, longer imaging follow-up within the first 5–10 years after coil therapy was not beneficial.

Another study that questioned the diagnostic yield of long-term follow-up angiography, by Tailor et al., included 59 patients with 65 aneurysms treated with coil therapy. The authors found that 96% of Raymond Class I and 100% of Class II and III aneurysms remained unchanged at 2 years compared with 6 months. They concluded that, in the absence of a residual lesion in the early angiographic study, a long-term catheter angiogram is not warranted. The most
The risk of aneurysm rupture after coil therapy has been shown to be very low in several studies, especially for previously unruptured aneurysms. A meta-analysis by Naggara et al. reported an annual risk of bleeding after endovascular therapy of unruptured aneurysms as low as 0.2%. Some authors have even published case reports on the rupture of previously unruptured aneurysms treated with coil therapy. In our study, however, 4 patients suffered a new hemorrhage due to delayed aneurysm recurrence, and 3 of these patients had previously unruptured aneurysms. Although our study was not specifically designed to address this question, it appears that the risk of delayed rupture of previously unruptured aneurysms is not insignificant (2.5%), as previously suspected. Thus, careful long-term angiographic follow-up should be recommended not only for ruptured but also for unruptured cerebral aneurysms. This is further corroborated by the fact that ruptured/unruptured aneurysm status did not predict delayed aneurysm recurrence or retreatment.

It should be stated that there are alternative approaches to treat cerebral aneurysms with more durable results than coil therapy, such as surgical clipping and flow diversion. The latter approach has been increasingly used to treat large and giant aneurysms of the internal carotid artery, and recent studies have shown flow diverters to have a safety profile comparable to that of traditional endovascular techniques.

Limitations

This study is limited by its retrospective design. Many aneurysms treated with coil therapy during the study period were not included in the analysis because the patients did not have available short-term and long-term follow-up DSA images. However, we are not aware of any selection bias in our study. There may be some interobserver variability when determining recurrence or no recurrence after treating an aneurysm with coil therapy. Also, the decision to retreat an aneurysm is subject to a large interobserver variability, but this is an inherent limitation of all studies reporting on the angiographic outcomes of intracranial aneurysms.

Conclusions

The results of this study support that the diagnostic yield of long-term follow-up DSA studies is high for the detection of delayed aneurysm recurrence compared with short-term DSA examination. Long-term imaging follow-up is therefore recommended after coil therapy for ruptured and unruptured intracranial aneurysms. Predictors of delayed recurrence and retreatment include large aneurysms, recurrence on short-term follow-up DSA image (even minor), male sex, and conventional coil therapy.

Disclosure

Dr. Tjoumakaris reports being a consultant for Stryker. Dr. Dumont reports being a consultant for ev3.

Author contributions to the study and manuscript preparation include the following. Conception and design: Tjoumakaris, Chalouhi, Jabbour, Starke, Gonzalez. Acquisition of data: Bovenzi, Thakkar, Dressler. Analysis and interpretation of data: Tjoumakaris.
Chalouhi, Bovenzi, Thakkar, Dressler, Jabbour, Starke, Teufack, Dalayai. Drafting the article: Chalouhi, Dalayai. 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: Tjoumakaris. Statistical analysis: Starke. Administrative/technical/material support: Tjoumakaris, Chalouhi, Bovenzi, Thakkar, Dressler, Jabbour, Teufack, Gonzalez, Dalayai. Study supervision: Tjoumakaris, Chalouhi, Jabbour, Dumont, Rosenwasser.

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