Long-Term Angiographic Recurrences After Selective Endovascular Treatment of Aneurysms With Detachable Coils

Jean Raymond, MD; François Guilbert, MD; Alain Weill, MD; Stavros A. Georganos, MD; Louis Juravsky, MD; Anick Lambert, MSc; Julie Lamoureux, PhD; Miguel Chagnon, PhD; Daniel Roy, MD

Background and Purpose—Our aim in this study was to assess the incidence and determining factors of angiographic recurrences after endovascular treatment of aneurysms.

Methods—A retrospective analysis of all patients with selective endovascular coil occlusion of intracranial aneurysms prospectively collected from 1992 to 2002 was performed. There were 501 aneurysms in 466 patients (mean±SD age, 54.20±12.54 years; 74% female). Aneurysms were acutely ruptured (54.1%) or unruptured (45.9%). Mean±SD aneurysm size was 9.67±5.91 mm with a 4.31±1.97-mm neck. The most frequent sites were basilar bifurcation (27.7%) and carotid ophthalmic (18.0%) aneurysms. Recurrences were subjectively divided into minor and major (ideally necessitating re-treatment). The most significant predictors of angiographic recurrence were determined by logistic regression. These results were confirmed by χ², t tests, or ANOVAs followed, when appropriate, by Tukey’s contrasts.

Results—Short-term (≤1 year) follow-up angiograms were available in 353 aneurysms (70.5%) and long-term (>1 year) follow-up angiograms, in 277 (55%), for a total of 383 (76.5%) followed up. Recurrences were found in 33.6% of treated aneurysms that were followed up and that appeared at a mean±SD time of 12.31±11.33 months after treatment. Major recurrences presented in 20.7% and appeared at a mean of 16.49±15.93 months. Three patients (0.8%) bled during a mean clinical follow-up period of 31.32±24.96 months. Variables determined to be significant predictors (P<0.05) of a recurrence included aneurysm size ≥10 mm, treatment during the acute phase of rupture, incomplete initial occlusions, and duration of follow-up.

Conclusions—Long-term monitoring of patients treated by endovascular coiling is mandatory. (Stroke. 2003;34:1398-1403.)

Key Words: endovascular therapy ■ intracranial aneurysm ■ recurrence

Endovascular treatment has proven effective in preventing rebleeding after subarachnoid hemorrhage due to aneurysmal rupture.1-4 A randomized study comparing endovascular and surgical management of ruptured aneurysms has shown significantly improved outcomes in patients treated with coils.4 The management of unruptured aneurysms is still controversial.5-8 Endovascular treatment is less invasive, but whether this evidence translates into better long-term outcome than surgical or conservative management remains to be proven.7

The respective roles of endovascular and surgical treatment of aneurysms remain unclear, and various options are offered to patients in different countries or institutions. There is, however, no doubt that aneurysm rests and recurrences are more frequent after endovascular treatment than after surgical clipping. The magnitude and clinical significance of this important drawback of endovascular treatment are still poorly documented, because most series have followed up only a limited number of patients for relatively short periods.9-13 Emerging new embolic agents or devices might increase long-term efficacy, possibly at the cost of increased immediate complications, and there might be a need to identify a target population with lesions at higher risk of recurrence or a subpopulation of patients in whom recurrences are unlikely. We have prospectively collected all cases treated by endovascular treatments since our first patients in 1992. Because our population is sedentary and health care is provided by a universal program, we had a unique occasion to follow the evolution of treated aneurysms in a large proportion of patients for many years. We attempted to identify the risk factors that were significantly associated with angiographic recurrences after selective endovascular treatment of aneurysms.

Materials and Methods

Patients and Aneurysms
The present study included all subarachnoid aneurysms treated at our institution by endosaccular coiling with detachable coils (Guglielmi, GDC, Target Therapeutics). There were no strict inclusion criteria.

Received December 18, 2002; accepted January 20, 2003.
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Stroke is available at http://www.strokeaha.org DOI: 10.1161/01.STR.0000073841.88563.E9

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Patients were referred from neurosurgical centers for lesions that were judged to be difficult for surgical treatment, after failed surgical attempts, or after a consensus was reached between the attending neurosurgeon and neuroradiologist in favor of endovascular treatment over surgery or a conservative approach. Whenever possible, large and giant lesions were treated by parent-vessel occlusion, and these were excluded from analysis, unless this strategy was used after a recurrence, in which case the period of follow-up before the second treatment was included. Demographic data included age, sex, history of previous subarachnoid hemorrhage, previous surgery for aneurysms, treatment during the acute phase after subarachnoid hemorrhage, and Hunt and Hess grades at the time of treatment. Aneurysmal characteristics included the ruptured/unruptured nature of the lesion, long axis, short axis, neck size, and location.

We treated 501 aneurysms in 466 patients from August 1992 to May 2002, and 383 lesions in 356 patients were followed up at least once by angiography. The mean ± SD age was 54.20 ± 12.54 years, and 74% of patients were women. Patients had multiple aneurysms in 35.6% of cases, and 28.8% had been previously treated by surgery on the same (9%) or another lesion. Approximately half of the lesions (54.1%) were acutely ruptured at the time of treatment. The Hunt and Hess grades at the time of treatment in the ruptured group were grade I–II in 56%, grade III in 29%, and grade IV–V in 15%. Most frequent sites were basilar bifurcation (27.7%), ophthalmic carotid (18.0%), anterior (13.6%), and posterior communicating artery (11.2%) aneurysms. Only 6.8% of aneurysms were at the middle cerebral artery bifurcation. Aneurysmal dimensions were measured in all patients and found at a mean of 16.49 mm, with a median of 15.93 mm. New neurologic episodes were also noted. Rebleeding episodes due to incomplete obliteration of aneurysms, occurring within 2 weeks of the initial subarachnoid episode that prompted treatment, were not included as recurrences.

Endovascular Treatment

The technique for endovascular GDC treatment has been described previously. All procedures were performed on a monoplane C-arm angiographic system without 3-dimensional reconstruction. Most patients were treated under general anesthesia. Patients were treated once in 91.4% of cases, but 6.6% were treated twice and 2%, 3 or 4 times. Patients with a failure of coil embolization or after a major recurrence were treated with surgical clipping in 4.2% or by parent-vessel occlusion after failure or recurrences were then scheduled yearly thereafter. Multiple projections with selective injections served to define any residual lesions. Anatomic results were evaluated in a very strict fashion and classified as previously published. In brief, a class I result meant complete obliteration, including the neck. A residual neck (class 2) was defined as the persistence of any portion of the original defect of the arterial wall as seen on any single projection but without opacification of the aneurysmal sac. Any opacification of the sac was classified as residual aneurysm (class 3). When an aneurysm was considered occluded (class 1 or 2) at the end of treatment, despite minimal opacification artificially maintained by heparinization, the first angiographic follow-up result served as the “immediate result.” This definition was used to minimize the number of aneurysms showing “improved results” at follow-up. A recurrence was defined as any increase in the size of the remnant. The recurrence was qualified as major if it was saccular and its size would theoretically permit re-treatment with coils. The number of months between treatment and the first follow-up angiogram showing the recurrence was noted. When a lesion first showed a “minor recurrence” but subsequent follow-up angiograms did not show any change, the number of months of “stability” of this minor recurrence was recorded. Short-term (<1 year) follow-up angiograms were available in 353 aneurysms (70.5%) and long-term (>1 year) in 277 (55%), for a total of 383 (76.5%) followed up. Absence of angiographic follow-up was due to failure (4%), death (9.9%), patient lost to follow-up (2.6%), patient refusal (4.3%), and follow-up study planned but not yet performed (2.7%).

Clinical Follow-Up

Further clinical follow-up data were collected during hospitalization for follow-up angiography or by telephone interviews. The total number of months of clinical follow-up for each patient was recorded. The mean ± SD clinical follow-up was 31.32 ± 24.96 months. New neurologic episodes were also noted. Rebleeding episodes due to incomplete obliteration of aneurysms, occurring within 2 weeks of the initial subarachnoid episode that prompted treatment, were not included as recurrences.

Statistics

The most significant predictors of angiographic recurrence were determined by using logistic regression, $\chi^2$ tests, ANOVAs (followed, when appropriate, by a Tukey’s contrast), or $t$ tests. When 2 aneurysms were present in the same patient, they were considered independent for the purpose of statistical studies. Aneurysmal dimensions and time were studied as continuous variables. These variables were also analyzed by groups (aneurysms ≥10 mm, aneurysmal neck ≥4 mm). Patients were also subdivided into 3 equal groups according to the duration of angiographic follow-up periods: group 1 included patients with 1 to 16 months of angiographic follow-up; group 2 were patients with 17 to 37 months; and group 3 were those with >37 months of angiographic follow-up.

Results

Angiographic Results

Angiographic follow-up studies were scheduled to be performed in all patients actually treated with coils at 6 months, and if the results were stable, for incremental periods (18 months, 3 years, etc). When a recurrence was found but the patient was considered protected from rebleeding or when, by clinical judgment, re-treatment was judged to be inappropriate, the next follow-up study was scheduled yearly thereafter. Multiple projections with selective injections served to define any residual lesions. Anatomic results were evaluated in a very strict fashion and classified as previously published. In brief, a class I result meant complete obliteration, including the neck. A residual neck (class 2) was defined as the persistence of any portion of the original defect of the arterial wall as seen on any single projection but without opacification of the aneurysmal sac. Any opacification of the sac was classified as residual aneurysm (class 3). When an aneurysm was considered occluded (class 1 or 2) at the end of treatment, despite minimal opacification artificially maintained by heparinization, the first angiographic follow-up result served as the “immediate result.” This definition was used to minimize the number of aneurysms showing “improved results” at follow-up. A recurrence was defined as any increase in the size of the remnant. The recurrence was qualified as major if it was saccular and its size would theoretically permit re-treatment with coils. The number of months between treatment and the first follow-up angiogram showing the recurrence was noted. When a lesion first showed a “minor recurrence” but subsequent follow-up angiograms did not show any change, the number of months of “stability” of this minor recurrence was recorded. Short-term (<1 year) follow-up angiograms were available in 353 aneurysms (70.5%) and long-term (>1 year) in 277 (55%), for a total of 383 (76.5%) followed up. Absence of angiographic follow-up was due to failure (4%), death (9.9%), patient lost to follow-up (2.6%), patient refusal (4.3%), and follow-up study planned but not yet performed (2.7%).

Statistics

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Recurrences

Recurrences were found in a total of 128 of 381, or 33.6%, of treated aneurysms at a mean of 12.31 ± 11.33 months. Recurrences were shown to be minor and stable at further follow-up angiography for a mean of 33.60 ± 25.60 months in 22.1% of cases. Major recurrences were found in 79 of 381, or 20.7%, of all patients and found at a mean of 16.49 ± 15.93 months. Almost half (49.4%) of major recurrences were re-treated

<table>
<thead>
<tr>
<th>TABLE 1. Angiographic Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Results</strong>, % (n=501)</td>
</tr>
<tr>
<td>Complete occlusion</td>
</tr>
<tr>
<td>Residual neck</td>
</tr>
<tr>
<td>Residual aneurysm</td>
</tr>
<tr>
<td>Failure</td>
</tr>
</tbody>
</table>
TABLE 2. Recurrences and Location of Aneurysms

<table>
<thead>
<tr>
<th>Location</th>
<th>All Recurrences</th>
<th>%</th>
<th>% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basilar bifurcation</td>
<td>43/109</td>
<td>39.4</td>
<td></td>
</tr>
<tr>
<td>Ophthalmic carotid artery</td>
<td>19/73</td>
<td>26.0</td>
<td></td>
</tr>
<tr>
<td>Anterior communicating artery</td>
<td>11/44</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>Posterior communicating artery</td>
<td>16/43</td>
<td>37.2</td>
<td></td>
</tr>
<tr>
<td>MCA bifurcation</td>
<td>9/28</td>
<td>32.1</td>
<td></td>
</tr>
</tbody>
</table>

Factors Associated With Recurrences

Age ($P=0.510$), sex ($P=0.374$), and aneurysmal location had no significant influence on recurrences ($P=0.259$ for the most frequent sites). The rates of recurrence according to the most frequent locations are summarized in Table 2. According to $\chi^2$ tests, the most significant predictors of a recurrence for the entire group were treatment during the acute phase after rupture ($P=0.013$), size of the aneurysm ($P<0.001$), width of the neck of the aneurysm ($P<0.001$), suboptimal initial angiographic result (class 2 or 3; $P<0.001$), and length of follow-up period ($P=0.003$).

Acutely Ruptured Aneurysms

Seventy-six of 191, or 39.8%, of aneurysms treated acutely after rupture and followed up recurred at least once, compared with 52 of 190, or 27.4%, of unruptured lesions ($P=0.013$). Major recurrences occurred in 48 (25.1%) and 31 (16.3%) aneurysms, respectively ($P=0.043$).

Aneurysm Size

There were strong correlations between aneurysmal dimensions. The larger the aneurysm, the wider the neck ($r=0.681$, $P<0.001$); there was also a strong correlation between short and long axes ($r=0.920$, $P<0.001$). Lesions $\geq 10$ mm in diameter had a significantly higher risk of recurrences ($P<0.001$). The relation between aneurysmal size and the incidence of recurrences is summarized in Table 3.

Neck Size

Aneurysms with necks wider than 4 mm had a significantly higher risk of developing a recurrence ($P<0.001$; Table 3). When patients were divided into groups according to the length of the follow-up period, aneurysm neck size had a strong impact on recurrences in patients who were followed up for $>17$ months ($P=0.003$) but not in patients who were followed up for 16 months or less ($P=0.122$). For all lesions, the size of the neck had a strong influence on initial angiographic results ($P<0.001$): 44.5% of aneurysms with small necks but only 20.2% of wide-necked lesions were completely obliterated ($P<0.001$).

Initial Angiographic Results

Lesions that were completely occluded with coils, without a residual neck, had a significantly lower risk of developing a recurrence ($P<0.001$). When patients were divided into 3 groups according to the length of the follow-up period, complete occlusions were at a lower risk of developing a recurrence in the first 2 groups ($<17$ months and 18 to 37 months; $P=0.007$), but initial angiographic results did not have a statistically significant impact on patients with the longest follow-up period ($>37$ months; $P=0.200$). The relation between initial angiographic results and recurrences is summarized in Table 4.

Length of Follow-Up Period

When patients were divided into 3 groups according to the length of angiographic follow-up, the group followed up for $<17$ months was at lesser risk of showing a recurrence ($P=0.003$) than the 2 groups followed up for 17 months or more. Results are summarized in Table 5.

The only significant predictor of a recurrence in the group followed up for 1 to 16 months was the initial angiographic result. When the lesion was completely obliterated, recurrences were less likely ($P=0.002$). For patients in the group followed up for 17 to 37 months, predictors of a recurrence included aneurysm size ($P<0.001$), neck size ($P<0.001$), and initial angiographic result ($P<0.001$). For patients followed up for $>37$ months, predictors included aneurysm size ($P=0.003$), neck size ($P=0.003$), and ruptured lesions ($P=0.02$). When we compared the characteristics of the first and the last 100 patients treated, there was no difference between the 2 groups, except that more recent patients tended to be older (mean $\pm$ SD age, $55.87 \pm 13.17$ vs $51.87 \pm 11.60$ years; $P=0.034$). When the number of recurrences detected by 6 months was compared, there was no significant difference between the 3 groups of patients subdivided according to length of follow-up period. Another way of looking at the influence of the duration of the follow-up period on the incidence of recurrences is illustrated in Figure 1. Only 46.9% of all recurrences had been detected by 6 months. By 36 months, 96.9% of all recurrences detected in our population were diagnosed.

Logistic Regression Analysis

Significant factors predicting the risk of developing any type of recurrence and studied by logistic regression are summarized in Table 6. The effects of the width of the neck of...
TABLE 4. Initial Angiographic Results and Recurrences

<table>
<thead>
<tr>
<th>Residual aneurysm</th>
<th>All Patients</th>
<th>1 to 16 Mo</th>
<th>17 to 37 Mo</th>
<th>&gt;37 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete occlusion</td>
<td>20.0 (29/145)</td>
<td>9.0 (13/145)</td>
<td>6.7 (3/45)</td>
<td>4.4 (2/45)</td>
</tr>
<tr>
<td>Residual neck</td>
<td>40.1 (75/187)</td>
<td>23.5 (44/187)</td>
<td>28.8 (19/66)</td>
<td>16.7 (11/66)</td>
</tr>
<tr>
<td>Residual aneurysm</td>
<td>51.1 (24/47)</td>
<td>46.8 (22/47)</td>
<td>35.0 (7/20)</td>
<td>30.0 (6/20)</td>
</tr>
</tbody>
</table>

Discussion

Angiographic recurrences after endovascular treatment of aneurysms are more common in large, ruptured lesions with suboptimal initial results and will be detected more frequently with long-term follow-up studies. Clearly, the 6-month follow-up angiographic study that is commonly recommended is insufficient to detect all recurrences.

Factors previously identified as significant predictors of a recurrence include suboptimal initial angiographic results, treatment after rupture, and aneurysm size. These risk factors have been confirmed in our study. We, as well as others, have not found a significant impact of location on recurrence, although this might be due to insufficient statistical power. The difference in the incidence of recurrences after treatment of unruptured and ruptured lesions cannot be explained by a difference in other factors, such as aneurysm size, neck width, or quality of initial angiographic result. There is a significant difference in the frequency of certain anatomic sites (overrepresentation of ophthalmic aneurysms in the unruptured group, for example) between the 2 groups, but we could not explain the dramatic increase in recurrences after treatment during the acute phase after rupture with this factor alone. One has to hypothesize that some biologic difference exists between the 2 groups.

The magnitude of the recurrence problem will vary according to selection bias, as well as to the length of the follow-up period. Because endovascular treatment is increasingly being used, most series include a larger number of patients being followed up for short periods, compared with a smaller number of patients followed up for longer periods. Therefore, recurrence rates expressed as the ratio of cases showing a recurrence over total cases treated are artificially minimizing the magnitude of the problem. If we limit our evaluation to patients with long follow-up periods, the percentage of patients showing any recurrence is 40% (major in 24%). Because these patients were treated early in our experience, 1 hypothesis is that techniques have improved with time. This hypothesis might be supported by the finding that aneurysmal characteristics had no significant impact on recurrences in patients followed up for <17 months, a group in whom the initial angiographic result was the single, significant predictor of a recurrence. The more frequent use of advanced techniques, such as the balloon-assisted technique and the aneurysmal neck-bridge device, might have permitted us to achieve complete obliterations in large, wide-necked lesions previously associated with suboptimal results. Another hypothesis is that recurrences occur in a delayed fashion, according to characteristics that are intrinsic to the lesion. This second hypothesis is supported by the lesser impact of initial results on recurrences in groups followed up for >37 months, a group in whom the ruptured nature of the lesion, size of the neck, and lesion size had the strongest impact on recurrences. One interpretation is that complete obliteration of the lesion is important to decrease early recurrences, and this can be achieved more frequently with technical advances, but recurrences might still occur in a delayed fashion.

The characteristics of our population follow the common North American bias in the selection of patients referred for endovascular treatment, with a high proportion of lesions considered at higher risk for surgical clipping, such as basilar bifurcation or ophthalmic aneurysms. Another weakness of this study is that it was retrospective, and although patients

TABLE 5. Length of Follow-Up Period and Recurrences

<table>
<thead>
<tr>
<th>Angiographic Follow-Up</th>
<th>All Patients</th>
<th>Major</th>
<th>All Patients</th>
<th>Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 16 mo (n=131)</td>
<td>22.1 (29)</td>
<td>14.5 (19)</td>
<td>22.1 (29)</td>
<td>14.5 (19)</td>
</tr>
<tr>
<td>17 to 37 mo (n=122)</td>
<td>39.3 (48)</td>
<td>23.8 (29)</td>
<td>39.3 (48)</td>
<td>23.8 (29)</td>
</tr>
<tr>
<td>&gt;37 mo (n=128)</td>
<td>39.8 (51)</td>
<td>24.2 (31)</td>
<td>39.8 (51)</td>
<td>24.2 (31)</td>
</tr>
</tbody>
</table>

Recurrences and follow-up angiography. Bar graph shows the percentage of all (black) and major (gray) recurrences detected by follow-up angiography according to the time it was performed after selective endosaccular coil occlusion.
were prospectively entered into the database, the frequency and intervals for angiographic follow-up studies, though somewhat standardized, were not systematic. The classification of angiographic results and the diagnosis of a recurrence are subjective evaluations that might differ from 1 center to another.9 We have chosen to distinguish “minor” from “major” recurrences. Minor changes from the initial or first follow-up angiogram can be detected objectively by a rigorous evaluation, but there might be concerns of increasing sensitivity of detection of recurrences at the expense of specificity by overcalling lesions that might show stability later on. The clinical significance of a nonprogressing residual neck, found in 22% of all recurrences, has not been determined with certainty, although it is probably not without hemorrhagic risks.20 Major recurrences are more definitely of concern. Patients who bled during follow-up were shown to have unstable results, with residual aneurysms that had progressed since the previous angiographic study.

One of the important objectives of this work was to identify patients who might benefit from an improved endovascular intervention, which might carry added risks,21,22 or patients in whom standard coil embolization might be sufficient. In our opinion, we have not identified a category of patient who would not benefit from the use of “improved” treatment, because the best aneurysmal characteristics, such as small size and a small neck, were still associated with a recurrence rate >20% (11% of major recurrences).

One important factor in the detection of recurrences was the length of the angiographic follow-up period. Clearly, the 6-month angiogram is insufficient to detect a majority of cases (only 48% of recurrences were detected). Although repeated angiographic studies carry their own risk, we believe that all patients should at least be followed up by noninvasive imaging studies, if not by angiography, for 36 months or more. The complications related to multiple angiograms were 0.3% in this study, a figure that is compatible with other published rates.23,24 Although patients who have already experienced recurrences have a high incidence of second recurrences (almost 50% so far), we often chose to treat recurrences by coiling, because surgical risks might be compounded by the presence of coils at the neck.25

Regarding current treatment options, as well as future modifications that might be proposed to improve long-term results of coil embolization, a question remains: how much risk is worth taking immediately to prevent a potential angiographic recurrence in the future? We have found a risk of bleeding in 0.8% of patients, for a mean period of observation of 31.3 months. Others have shown a hemorrhagic risk of the same magnitude.2,9–11 In the context of acutely ruptured lesions, for which endovascular treatment has proven effective in preventing rebleeding in the first 6 months, these risks of future hemorrhages are small compared with the immediate morbidity of the disease and of treatment.4 Endovascular treatment has proven to improve clinical outcome 1 year after treatment compared with surgical clipping.4 This benefit of the endovascular approach should not be negated by a more efficient though riskier treatment. Conversely, in unruptured aneurysms where there is no obvious immediate benefit, long-term efficacy might be essential to justify any intervention. Operative risks should nevertheless be very low, because the annual risk of rupture might be lower than we had previously hypothesized.5,26

Conclusions
Endovascular treatment with detachable coils is followed by angiographic recurrences in 33.6% of cases. These recurrences are sizable in 20.7%. The most important factors associated with recurrences are treatment after rupture, size >10 mm, and incomplete occlusions. The 6-month follow-up angiogram is insufficient to detect most recurrences.

Acknowledgments
This work was supported in part by the Canadian Institutes of Health Research. We thank Rosemary Roy and Guylaine Gevry for assistance with the preparation of the manuscript.

References

**TABLE 6. Risk Factors for Recurrences**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Significance</th>
<th>Relative Risk</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneurysm ≥ 10 mm</td>
<td>0.002</td>
<td>2.49</td>
<td>1.40–4.43</td>
</tr>
<tr>
<td>Neck ≥ 4 mm</td>
<td>0.086</td>
<td>1.69</td>
<td>0.93–3.09</td>
</tr>
<tr>
<td>Ruptured aneurysm</td>
<td>0.007</td>
<td>1.96</td>
<td>1.21–3.17</td>
</tr>
<tr>
<td>Residual neck</td>
<td>0.002</td>
<td>2.44</td>
<td>1.40–4.23</td>
</tr>
<tr>
<td>Residual aneurysm</td>
<td>0.002</td>
<td>3.60</td>
<td>1.60–8.09</td>
</tr>
<tr>
<td>Follow-up (per month)</td>
<td>0.000</td>
<td>1.02</td>
<td>1.01–1.03</td>
</tr>
</tbody>
</table>
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Stroke. 2003;34:1398-1403; originally published online May 29, 2003; doi: 10.1161/01.STR.0000073841.88563.E9

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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