Endovascular Treatment of Unruptured Aneurysms

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Background and Purpose—We sought to better define the morbidity of endovascular Guglielmi detachable coil (GDC) treatment of unruptured cerebral aneurysms and to discuss its role in the prevention of subarachnoid hemorrhage.

Methods—We conducted an observational study from August 1992 to June 1999 of 125 unruptured aneurysms treated with GDC in 116 patients: 91 women (78.4%) and 25 men (21.6%), aged 30 to 78 years (mean age, 50.6 years). Immediate and late clinical results were recorded for any neurological event or hemorrhage related to the treated unruptured aneurysm. Angiographic results are reported as immediate, early (2 to 12 months), intermediate (12 to 30 months), and late follow-up (>30 months).

Results—Immediate angiographic results showed complete obliteration (class 1) in 59 (47.2%) or residual neck (class 2) in 53 aneurysms (42.4%), leaving 6 residual aneurysms (4.8%) and 7 failures (5.6%). Early follow-up angiograms, available in 100 treated aneurysms (84%), revealed class 1 in 52% and class 2 in 41%. Intermediate angiograms, available in 53 aneurysms (44.5%), showed class 1 in 47.2% and class 2 in 43.4%, while late results, available in 37 lesions (31.1%), had class 1 and 2 in 48.6% and 37.8%, respectively. Six patients suffered a permanent neurological deficit at last follow-up (5.2%), with a good outcome in 5 patients and fair outcome in 1 patient. There was no mortality. There was no aneurysmal rupture during a mean clinical follow-up of 32.1 months.

Conclusions—Endovascular treatment with GDC for unruptured aneurysms is relatively safe. Its role in the prevention of aneurysmal rupture remains to be determined, preferably by a randomized study. (Stroke. 2001;32:1998-2004.)

Key Words: aneurysm ■ cerebral aneurysm ■ embolization, therapeutic

Clinical and autopsy studies suggest that 1% to 8% of the population harbor intracranial aneurysms.1 Because of the high morbidity and mortality (45%)2–4 associated with subarachnoid hemorrhage (SAH), a preventive treatment strategy is appealing.5–10 The annual risk of bleeding from an unruptured aneurysm is estimated to be in the range of 0.05% to 2%,11–15 but recent investigations suggest that the natural history is more benign than previously thought.16 Any preventive treatment should consequently be very safe. Unfortunately, the risks associated with surgical clipping may have been underestimated.16

During the last decade, endovascular treatment has been increasingly used, especially for ruptured lesions associated with a higher surgical morbidity or in patients in poor medical condition for surgery.17–24 It has also been considered a valuable alternative treatment for unruptured aneurysms.25 Since the morbidity related to treatment is important to know with precision in this context and because it might differ from the morbidity reported in the acute setting, our first goal was to better define the risks of endovascular treatment of intracranial aneurysms in patients treated electively. Angiographic and clinical results were also recorded in an effort to estimate the efficacy of this strategy in the prevention of aneurysmal rupture.

Subjects and Methods

All patients treated at our institution by endovascular means are prospectively evaluated. The present study included all unruptured subarachnoid aneurysms treated with Guglielmi detachable coils (GDC) between August 1992 and June 1999. There were no strict inclusion criteria. Patients were referred from neurosurgical centers for lesions that were believed 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 conservative approach. Patients with extradural or giant aneurysms or in whom the primary intention of treatment was parent vessel occlusion were excluded from this study. Very small aneurysms (<3 mm) were excluded. The endovascular team was reluctant to treat middle cerebral artery (MCA) aneurysms, which are surgically accessible and potentially prone to branch occlusion after coiling.

Patients and Aneurysms

There were 116 patients: 91 women (78.4%) and 25 men (21.6%). Age varied from 30 to 78 years (mean age, 50.6 years). Fifty-eight patients (50%) had multiple lesions, for a total of 226 aneurysms. One hundred twenty-five unruptured aneurysms in 116 patients were treated with selective GDC embolization and form the basis of this analysis. Of the other 101 aneurysms, 31 ruptured aneurysms were treated either surgically (n = 21), by GDC (n = 9), or by endovascular parent vessel occlusion (n = 1). Twenty-four unruptured aneurysms were treated by surgical clipping and 6 by endovascular parent vessel occlusion. Forty small aneurysms (all <5 mm) were observed. The locations of the 125 unruptured aneurysms treated with GDC are...
patients were given aspirin 325 mg daily for 3 months. Most patients
were treated by endovascular parent vessel occlusion (n = 5) or
surgical clipping (n = 3) or multiple aneurysms (9 patients) or
because of residual/recurrent aneurysms at follow-up (5 patients).
Four aneurysms showing unsatisfactory results (class 3) were later
treated by endovascular parent vessel occlusion (n = 3) or
surgical clipping (n = 1).

Complications
Complications are summarized in Table 2.

Nonneurological Complications
Two patients presented symptomatic hypotension from large
femoral hematomas that responded to volume expansion and
local compression and did not require blood transfusion or
surgical repair.

Thromboembolic Complications
Thromboembolic incidents occurred in 9 patients (7.8%). Three
patients had occlusive symptomatic clots that were
treated by local injection of urokinase (Abbott Laboratories)
with complete clinical recovery in <24 hours. One patient
with fibromuscular dysplasia presented a carotid dissection
by the guiding catheter, leading to transient carotid occlusion.

Figure 1. Distribution of treated aneurysms according to size.

Figure 2. Classification of angiographic results: class 1, complete
obliteration; class 2, residual neck; and class 3, residual
aneurysm. See Subjects and Methods for details.

Angiographic Results
Angiographic findings were recorded immediately, at 6 months,
and yearly thereafter. Multiple projections with selective contrast injec-
tions served to define any residual lesions. Anatomic results were
evaluated in a very strict fashion and classified as illustrated in
Figure 2. A class 1 result meant complete obliteration. 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) and considered
a failure of treatment. Because of difficulties in comparing angio-
graphic projections from one study to the other, recurrence was
defined as a change of classification of the anatomic result. When
the aneurysm was considered occluded (class 1 or 2) despite minimal
residual flow within the aneurysmal sac artificially maintained by
systemic 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. Patients treated by surgery or parent vessel occlusion after
failure of endovascular treatment or after recurrence were excluded
from the tables reporting long-term angiographic outcome.

TABLE 1. Location of Unruptured Aneurysms Treated by GDC

<table>
<thead>
<tr>
<th>Location</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmic</td>
<td>50</td>
<td>40.0</td>
</tr>
<tr>
<td>Basilar bifurcation</td>
<td>18</td>
<td>14.4</td>
</tr>
<tr>
<td>MCA</td>
<td>14</td>
<td>11.2</td>
</tr>
<tr>
<td>Posterior communicating</td>
<td>12</td>
<td>9.6</td>
</tr>
<tr>
<td>Anterior communicating</td>
<td>10</td>
<td>8.0</td>
</tr>
<tr>
<td>Internal carotid (others)</td>
<td>10</td>
<td>8.0</td>
</tr>
<tr>
<td>Posterior circulation (others)</td>
<td>9</td>
<td>7.2</td>
</tr>
<tr>
<td>Anterior cerebral artery (others)</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Total</td>
<td>125</td>
<td>100</td>
</tr>
</tbody>
</table>

Endovascular Treatment
The technique for endovascular GDC treatment has been described
previously.17,18 All procedures were performed on a monoplane
C-arm angiographic system without 3-dimensional reconstruction.
The procedure was performed with systemic heparinization in all
cases. In some instances, heparin was continued for 24 hours, and
patients were given aspirin 325 mg daily for 3 months. Most patients
were treated under general anesthesia.

Complications
Neurological procedure-related complications were divided into
thromboembolic or hemorrhagic events. Nonneurological complica-
tions such as puncture site hematomas or cardiopulmonary compli-
cations were also recorded. Significant thromboembolic events
were defined as complications leading to persistent symptoms or those
handled by thrombolytic agents or prolonged anticoagulation. All
clinical complications were recorded before discharge and 1 month
text after treatment. All patients had a CT scan 24 hours after the
procedure to detect asymptomatic lesions. Complications were
defined as temporary when the deficit resolved within 1 month or
permanent when present after 1 month. Morbidity was defined as the
number of patients who sustained a permanent deficit.

Outcome
Further clinical follow-up data were collected during hospitalization
for follow-up angiography or by telephone interviews. Patient’s
outcome was graded according to the Modified Rankin Scale.27

Statistical Analysis
Proportions were compared with the χ² test for categorical variables.
ANOVA and Student’s t tests were used to compare continuous
variables. All tests were performed with the use of a 5% confidence
level. The incidence of thromboembolic events and initial morpho-
logical results were studied against age, aneurysm size, neck size,
and aneurysm site. Recurrences were studied according to initial
results, aneurysm size, neck size, and aneurysm site.

Results
A total of 130 GDC procedures were performed in 116
patients. Multiple procedures were necessary because of
multiple aneurysms (9 patients) or because of residual/
recurrent aneurysms at follow-up (5 patients). Four aneu-
ysms showing unsatisfactory results (class 3) were later
treated by endovascular parent vessel occlusion (n = 3) or
surgical clipping (n = 1).
She secondarily developed a small subcortical infarct in the left sylvian territory and was left with very mild dysphasia (Rankin score I) at 20 months. Another patient, treated for a small carotid-ophthalmic aneurysm, presented ipsilateral blindness 4 hours after embolization. The ophthalmic artery was catheterized and infused with 750,000 U of urokinase, but the occlusion recurred and the patient did not recover useful vision of her eye. A third patient treated for a wide neck ophthalmic aneurysm presented acute right hemiplegia and aphasia from late coil displacement with protrusion and clot emboli 24 hours after treatment. Local injection of urokinase resulted in complete recanalization of the artery. She suffered a small parietal infarct with a right parietal hand (Rankin score I) at 43-month follow-up. One patient treated for a right MCA aneurysm developed transient ischemic attacks 1 week after embolization. Despite systemic heparinization, he developed a right frontal infarct with persisting constructive apraxia at 9 months (Rankin score II). Another patient showed transient right hemi-paresis and right hemianopia the day after embolization of a wide neck basilar bifurcation aneurysm. Angiogram showed a nonocclusive clot in the P1 segment of the left posterior cerebral artery. Being asymptomatic at the time of angiography, she was put on anticoagulation therapy without recurrence of symptoms.

A significant neurological complication also occurred during follow-up angiography in a patient with a proximal basilar fenestration aneurysm. Vertebralbasilar emboli resulted in cerebellar and occipital infarction with a fair outcome score (Rankin III).

**TABLE 2. Complications of Endovascular Treatment of Unruptured Aneurysms***

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic</th>
<th>Temporary</th>
<th>Permanent (Rankin Score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic (n=9)</td>
<td>2</td>
<td>3</td>
<td>4 (3 Rankin I, 1 Rankin II)</td>
</tr>
<tr>
<td></td>
<td>1.7%</td>
<td>2.6%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Aneurysmal rupture (n=3)</td>
<td>1</td>
<td>1</td>
<td>1 (Rankin II)</td>
</tr>
<tr>
<td></td>
<td>0.86%</td>
<td>0.86%</td>
<td>0.86%</td>
</tr>
<tr>
<td>Total (n=12) (10.3%)</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>2.6%</td>
<td>3.5%</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

*Complications of follow-up angiograms are excluded from this table.

**Hemorrhagic Complications**

There were 3 perioperative aneurysm perforations (2.4%). Two occurred during initial catheterization of small aneurysms (<5 mm): 1 anterior communicating and the other pericallosal. The third occurred during attempts to recatheterize a large ophthalmic aneurysm that had already been partially filled with coils. Two were due to perforation by the guidewire and 1 by the microcatheter. In all 3 patients, extravasation was minimal and subsided rapidly after protamine injection and further coil embolization. One patient was asymptomatic. Another patient had monoparesis of her left leg due to secondary vasospasm but was asymptomatic at 1 month and at the 72-month follow-up. The third patient had complications not clearly related to the perforation itself. The lesion, a small anterior communicating aneurysm, was occluded, and the hemorrhage was rapidly controlled. The patient woke up with dense hemiplegia and aphasia. Angiography repeated immediately did not show any arterial occlusion or vasospasm. No clots were retrospectively found on multiple angiographic runs performed during treatment. MRI later showed ischemic lesions in the left anterior, middle cerebral, and anterior choroidal artery territories. The patient recovered in the following months but still suffers a minor motor deficit as well as mild neuropsychological impairment (Rankin score II) 1 year later. There was no statistical relationship between age and complication rate ($P=0.4237$). There was no significant association between adverse events and either site ($P=0.483$) or size ($P=0.2899$) of aneurysm.

Thus, the overall morbidity lasting >1 month related to endovascular management, including follow-up angiograms of unruptured aneurysms, was 5.2%, with 5 patients presenting a good outcome (3 Rankin score I and 2 Rankin score II) and 1 presenting a fair outcome (Rankin III). The morbidity strictly related to treatment was 4.3%, without any poor outcome. There was no mortality related to treatment.

**Morphological Results**

The morphological data are summarized in Table 3. Each patient had an average of 1.49 follow-up angiograms. Initially, 59 aneurysms (47.2%) were completely obliterated (class 1), and 53 (42.4%) showed a residual neck (class 2). There were 6 residual aneurysms (4.8%) (class 3) and 7 failures (5.6%). All failures occurred in aneurysms harboring an unfavorable neck-to-dome ratio. Of the 6 patients showing residual aneurysms, 3 were observed, 1 was treated by parent vessel occlusion, and 1 was retreated with GDC, but his large basilar bifurcation aneurysm with a wide neck keeps recurring. The sixth patient is planned for retreatment by parent vessel occlusion. When we analyzed variables associated with immediate angiographic outcome, small size of the aneurysm and small neck were associated with a higher percentage of 100% obliteration ($P=0.002$ and $P=0.001$, respectively). There was no other significant prediction of outcome.

Early angiographic follow-up (2 to 12 months) was available for 100 of the 118 treated aneurysms (84.7%). The results showed class 1 (n=52) or class 2 (n=41) results in 93% (95% CI, 85.6 to 96.9) of treated lesions. Intermediate angiographic follow-up (12 to 30 months), available in 53 aneurysms (44.9%), showed class 1 (n=25) or class 2 (n=23) results in 90.6% (95% CI, 78.6 to 96.5). Late angiographic follow-up (>30 months), available for 37 aneurysms...
(31.4%), revealed class 1 (n = 18) or class 2 (n = 14) results in 86.5% (95% CI, 69.7 to 94.8).

Recurrences
Four of the 50 completely obliterated lesions (8%) that had at least 1 follow-up angiogram showed a small recurrent neck on early (3 aneurysms) or intermediate (1 aneurysm) studies. In 2 of these patients, the residuum remained stable on subsequent follow-up angiogram, so that all aneurysms were in class 1 or 2 during the entire follow-up period. Of the 50 aneurysms with residual necks that had at least 1 follow-up angiogram, 6 (12%) evolved to the residual aneurysm category on either early (n = 3) or late (n = 3) follow-up studies. Of these, 3 were retreated by GDC and 1 by parent vessel occlusion. One is planned for retreatment with GDC, and 1 is being observed because of the patient’s age (70 years) and neurological deficits. The evolution of angiographic results of aneurysms with initial complete obliteration differed significantly from aneurysms with initial residual neck (P = 0.011). None of the lesions that were initially 100% obliterated recurred to a class 3, while 12% of aneurysms left with residual necks became recurrent aneurysms. There was a clear trend of a higher incidence of recurrence to a class 3 result for wide-necked aneurysms, although this did not reach statistical significance (P = 0.093). With the use of ANOVA, a statistically significant link was found between the risk of recurrence to a class 3 morphological outcome and the size of the aneurysm (P = 0.0356). The aneurysmal site was not related to the risk of recurrence (P = 0.585).

Clinical Follow-Up
Five patients died from unrelated causes during follow-up: 2 from lung cancer, 2 from myocardial infarction, and 1 from an intracerebral hematoma secondary to the rupture of an associated brain arteriovenous malformation. There was no SAH during a follow-up period varying from 1 to 81 months (mean, 32.1 months).

Discussion
Recent advances in surgical, endovascular, and medical management have not yet succeeded in improving the overall outcome of patients suffering from SAH. Since cerebral damage is more commonly due to the initial hemorrhage, it may be impossible to significantly change these statistics without a preventive strategy. Surgical management of un-ruptured aneurysms was until recently widely accepted on the basis of assumptions that the annual bleeding risk was as high as 1% to 4% and that the surgical mortality and morbidity rates were as low as 1% and 4.1%, respectively. The International Study of Unruptured Intracranial Aneurysms (ISUIA) reported a much lower annual hemorrhagic risk and a much higher complication rate of surgery. Although this study harbors bias and imperfections, it raised the probability that overall surgical risks outweigh the benefits. Since most neurosurgical centers cannot show safety levels as low as the best published series, the impact of the ISUIA report is likely to be strong, and a shift toward a more conservative attitude is expected. To support this attitude, another recent article suggests that current surgical morbidity is not cost-effective for patients with small unruptured aneurysms. While this debate has traditionally involved surgical and conservative treatment, a third option, endovascular treatment, has grown in importance during the last decade and must now be considered in this context. In acutely ruptured aneurysms, endovascular treatment has proven to be effective in preventing subsequent bleeding in 98% of patients provided that the aneurysm sac was excluded. Because some patients present with multiple lesions or with lesions believed to be at increased risk for surgery, unruptured lesions have been treated with GDC on the basis of the assumption that prevention against hemorrhage could be inferred from the experience with acutely ruptured aneurysms. However, this hypothesis remains to be confirmed by long-term follow-up studies.

The first goal of our study was to evaluate the morbidity associated with endovascular treatment of unruptured aneurysms. It may differ from morbidity associated with coiling during the acute phase after SAH. Since the bias introduced by case selection is likely to influence the results, we will discuss the characteristics of our study population and the potential implications on outcome. Complications will be reviewed and compared with other studies to identify the potential benefits of the endovascular approach in unruptured aneurysms. If endovascular treatment is shown to be safe, this advantage may be obtained at the cost of insufficient efficacy. We will finally discuss the problem of residual necks and recurrences: are they frequent enough to undermine any preventive endovascular strategy?

### Table 3. Morphological Results†

<table>
<thead>
<tr>
<th></th>
<th>Immediate</th>
<th>2–12 mo</th>
<th>12–30 mo</th>
<th>&gt;30 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>59 (47.2)</td>
<td>52 (52.0)</td>
<td>25 (47.2)</td>
<td>18 (48.6)</td>
</tr>
<tr>
<td>Class 2</td>
<td>53 (42.4)</td>
<td>41 (41.0)</td>
<td>23 (43.4)</td>
<td>14 (37.8)</td>
</tr>
<tr>
<td>Class 3</td>
<td>6 (4.8)</td>
<td>7 (7.0)</td>
<td>5 (9.4)</td>
<td>5 (13.5)</td>
</tr>
<tr>
<td>Failure</td>
<td>7 (5.6)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>125 (100)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total (actually treated)</td>
<td>118 (94.4)</td>
<td>100 (84.7)</td>
<td>53 (44.9)</td>
<td>37 (31.4)</td>
</tr>
</tbody>
</table>

Values are number (percentage).

†Surgically treated lesions or lesions treated by parent vessel occlusion were excluded from angiographic follow-up.

‡Numbers include 5 patients in whom a second GDC procedure was performed.

For the statistical analyses, a p value of less than 0.05 was considered significant.

**Note:** The table above represents the morphological results of the study, categorized by class and follow-up period, showing the percentage of patients in each category. The table also includes a section on recurrences and clinical follow-up details.
Characteristics of Patients and Aneurysms
This series is by definition a selected one because patients were referred by neurosurgeons who did not believe that surgical or conservative treatment was the best options for these patients. We excluded giant aneurysms from the study because they represent a specific subgroup at high risk\(^1\) of hemorrhage, often requiring combined treatments. We also excluded lesions for which our primary intention was parent vessel occlusion since the recurrence issue does not apply to this group. The location of aneurysms differs from surgical series with a higher incidence of ophthalmic and basilar aneurysms and a comparatively low incidence of MCA and posterior communicating aneurysms. This selection bias reflects the reality that the former 2 locations are often considered surgically more difficult.\(^2\)\(^,\)\(^3\) This selection may also have an impact on treatment efficacy since carotid-ophthalmic aneurysms are often underrepresented in ruptured aneurysm series, an observation that suggests a lesser tendency to bleed. Conversely, basilar tip aneurysms, overrepresented in the present series, showed the highest rupture rate in the ISUIA report.\(^4\) The small number of MCA aneurysms is related to selection bias by the endovascular team. The anatomic characteristics of these lesions have led to more frequent complications when they are treated by coiling.\(^2\)\(^,\)\(^3\) They were consequently more frequently excluded. Patients with multiple aneurysms (50%) are also more frequent than in most surgical series.\(^5\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^8\) Although the risk of hemorrhage is higher in patients with multiple aneurysms,\(^1\)\(^4\)\(^,\)\(^3\) the morbidity and mortality related to multiple craniotomies also increase.\(^9\) Many patients have been managed by a combination of open surgery, endovascular treatment of larger aneurysms, and observation of smaller additional lesions. These latter aneurysms were either very small or had an unfavorable morphology for endovascular treatment. Some of these patients are thus still theoretically at risk of bleeding from untreated aneurysms.

Complications Related to Endovascular Treatment
We found that procedure-related morbidity and mortality were decreased compared with a synchronous observational study performed in our institution on endovascular treatment of acutely ruptured aneurysms.\(^2\)\(^1\) Perioperative ruptures were less frequent (2.4% compared with 8%), which may be self-explanatory because of a less fragile wall. Thromboembolic events, however, remained a significant problem (7.8%). While these events may be managed by therapeutic thrombolysis,\(^3\) they account for the majority of permanent complications. We observed a morbidity of 4.3% (with good outcome in all patients) or 5.2% if we include the complication related to a follow-up angiogram (endovascular management morbidity), with no mortality in 116 patients. These figures compare favorably with the results of surgical series.\(^3\)\(^,\)\(^4\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^8\) Furthermore, if surgical results are stratified to take into account lesions in more difficult locations (54.4% of patients of this series), the morbidity significantly increases to 18.7%.\(^3\)\(^6\) We did not find a relationship between age and complication rate, as reported by the ISUIA for surgery, but numbers are much smaller in the present study. Another endovascular series\(^2\) reported results almost identical to the present one. In this context, in which procedure-related morbidity should be low, endovascular treatment of unruptured aneurysms is an attractive alternative. However, future multicentric studies should be performed to confirm that the safety levels reported here can be reproduced in nonselected patients.

Morphological Results
Endovascular treatment is, by nature, less frequently complete than surgical clipping of aneurysms. Furthermore, recurrences are more frequent. It has been shown that exclusion of the aneurysmal sac, with or without a residual neck (class 1 and 2), is sufficient to prevent rebleeding in 98% of cases treated in the acute phase of SAH.\(^2\)\(^1\) Conversely, the presence of a residual aneurysm is associated with frequent rebleeding.\(^2\)\(^1\) By extension, when the result of endovascular treatment of unruptured aneurysms was class 3 (residual aneurysm), we considered that the patient was not protected from rupture. These considerations form the basis of our angiographic classification of morphological results. Class 1 and 2 results are protective from rebleeding after SAH, but, because class 2 results remain incompletely treated, they may, as shown by our data, be at higher risk of recurrence, and protection from rupture may not be definitive.

Our definition of recurrence may not reveal all morphological changes over time. We believe that it does reflect changes pertinent to this study. Consequently, our goal was to assess how many patients had unsatisfactory angiographic results (class 3) immediately after treatment and how often class 1 and 2 results had an evolution toward class 3 during follow-up. The true efficacy of endovascular treatment of unruptured aneurysms, which is prevention of rupture, cannot yet be determined, but it is important to assess the incidence of class 3 results immediately and over time, especially for the evaluation of this approach in the management of this population.

The failure rate (5.6%) was similar to that in the series of Murayama et al.\(^2\)\(^5\) Failure was always related to an unfavorable neck-to-dome ratio.\(^2\)^ Most of these aneurysms were treated before the advent of newer techniques such as balloon-assisted remodeling, 3-dimensional GDC, TriSpan neck bridge device, or stents. These new techniques may lower the failure rate. We report 47.2% of complete obliteration (class 1) and 42.4% of small residual necks (class 2) as initial results compared with 63.3% and 27.5%, respectively, in the series of Murayama et al.\(^2\)\(^5\) This discrepancy may be explained by differences in the criteria used for reporting anatomic results, which, unfortunately, are subjective and difficult to standardize.

All aneurysms showing immediate complete occlusion remained in the acceptable result category on late angiographic follow-up, but 4 (7.8%) went from class 1 to class 2 category. Most aneurysms (88%) with class 2 had stable results at follow-up, but 12% recurred to an unacceptable anatomic outcome (class 3). This evolution of angiographic results differs from the previous study.\(^2\)\(^5\) No recurrence was reported in the series of Murayama et al when complete obliteration was obtained immediately compared with a recurrence rate of 32% when residual necks were initially
present. Their angiographic follow-up was, however, shorter, and the number of angiograms per patient was not indicated. As we and others\textsuperscript{37} have shown, recurrences may be revealed only on the second or third follow-up angiogram.

Overall, recurrences were documented during the entire follow-up period in a total of 10 of 100 aneurysms (10\%) with initially class 1 or 2 result that had at least 1 follow-up angiogram. The recurrence rate to an unacceptable result (class 3) was 6.0\%. These recurrences led to another form of treatment, whether by recoiling (n=3) or parent vessel occlusion (n=1) in 4 patients, with another patient being planned for recoiling. At the end of angiographic follow-up, class 1 or 2 results were still observed in 91.5\% of actually treated aneurysms and 86.4\% of the total number of lesions in which treatment was attempted (including failures). According to a quality-adjusted life-years study, for surgery to be as cost-effective as endovascular treatment, the reduction of the rupture rate obtained by coiling would have to be as low as \( \leq 25\% \),\textsuperscript{31} which, owing to our morphological results, appears improbable. Thus, we believe that the incidence of class 3 results immediately and with time is not sufficient to discredit the endovascular approach as a preventive treatment against rupture.

Angiographic surveillance remains important. It is too soon to determine when follow-up imaging in a particular patient is no longer necessary because we have shown that recurrences may appear only on late follow-up. From our data, it is probably safe to propose follow-up angiography 1 year after treatment in case of complete obliteration and, if the result appears stable, to postpone further follow-up to 3 years later. When a residual neck is left after treatment, a 6-month follow-up is probably safe to pick up early recurrences. Until now, noninvasive imaging modalities, such as MR angiography,\textsuperscript{38} still have limitations due to artifacts produced by the platinum, but we expect significant improvement in the near future. This issue is important because a policy of multiple angiographic studies carries its own risk. Follow-up studies and the possibility of a second treatment may add to the psychological burden of management in terms of quality of life. This is difficult to quantify. We think that with the acquisition of more data over time, we will be able to have a better understanding of the evolution and propose a much lighter protocol for the patients.

Prevention of Aneurysmal Rupture

The number of patients (n=116) and the mean follow-up period (32.1 months) are insufficient to draw conclusions regarding long-term efficacy. We did not calculate the estimated number of hemorrhages that we should have encountered spontaneously during the same period without treatment because this number is highly dependent on aneurysm size, site, history of previous hemorrhage, and, above all, on a controversial natural history.\textsuperscript{5,10,29,30,36,39,40} However, it is reassuring that no bleeding episodes occurred and that 91.5\% of treated lesions still had morphological results believed to protect from rupture at 30 months. There is only 1 reported case of late rupture of an apparently completely occluded unruptured aneurysm.\textsuperscript{41,42} In the series of Murayama et al\textsuperscript{25} of 115 patients, there was 1 late rupture 3 years after an incomplete treatment.

Should Unruptured Aneurysms Be Treated?

Since the bleeding risk of unruptured aneurysms is low, one can question whether any treatment should be proposed for small lesions. Since modern imaging reveals more and more unruptured intracranial aneurysms, it is of utmost importance to identify the best management of these patients. A cost-utility analysis,\textsuperscript{31} using different theoretical models of patients with unruptured aneurysms, showed no cost-effectiveness of either surgery or endovascular treatment for the basic model, which was a 50-year-old woman with an unruptured aneurysm of <10 mm in diameter without a previous history of hemorrhage. In this basic scenario, the annual bleeding rate was fixed at 0.05\%. In all other models, treatment was cost-effective and more effective in terms of quality of life, with endovascular treatment being superior to surgery in all scenarios, even though the protection offered by endovascular treatment was fixed at 90\% compared with 100\% with surgical clipping.\textsuperscript{30}

Even if this study is a series of consecutive patients without controls, it confirms the low morbidity of endovascular treatment and adds to the bulk of evidence that this approach may become more effective in terms of quality of life than surgery for unruptured aneurysms.\textsuperscript{23,25,31,37}

Controversy will persist until a randomized study comparing conservative and active management of unruptured aneurysms is performed. Collecting prospective data in a randomized fashion is the only way to obtain true scientific evidence. We have studied various hypotheses and estimated population sizes; if safety and morphological results of the present study can be reproduced on a larger scale, such a randomized study comparing endovascular treatment and conservative management of unruptured aneurysms is feasible.

Conclusions

Endovascular treatment of unruptured aneurysms could be attempted safely in 95.7\% of patients and without major neurological deficit in 100\% of patients. Morphological results showed obliteration of the aneurysmal sac (with or without a residual neck) in 89.6\% of lesions; recurrent opacification of the aneurysmal sac was observed in 6\% of aneurysms. A longer follow-up period is necessary to determine efficacy, but there was no aneurysmal rupture during a mean period of 32.1 months. Because endovascular treatment is relatively safe and the natural history of unruptured aneurysms remains unknown, we propose to compare conservative and endovascular management of these patients in a randomized study.

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References


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