Intradural Saccular Aneurysms Treated by Guglielmi Detachable Bare Coils at a Single Institution Between 1993 and 2005
Clinical Long-Term Follow-Up for a Total of 1810 Patient-Years in Relation to Morphological Treatment Results

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Background and Purpose—The aim of this study was to analyze the clinical results of Guglielmi detachable bare coil (GDC) embolization of intradural saccular aneurysms (AAs) at a single center and to relate the morphological results at various time points to the clinical situation.

Methods—All intradural saccular AAs treated with GDCs between 1993 and April 2005 were prospectively entered into a database completed by retrospective analysis of charts and images and a long-term clinical outcome questionnaire. In 413 consecutive patients, there were 466 treated AAs, of which 68.7% were ruptured and 31.1% were unruptured.

Results—The periprocedural thromboembolic event rate, retreatment procedures included, was 5.4%, causing permanent neurologic deficits in 2.2% of patients. One patient (0.2%) bled during a mean±SD clinical follow-up of 64.3±39.9 months (93 AAs were followed up for >8 years and 45 AAs were followed up for >10 years) for a total of 1810 patient-years. The modified Rankin Scale score was 0 in 54.7%, 1 in 21.0%, 2 in 12.1%, 3 in 7.1%, 4 in 2.1%, 5 in 0.3%, and 6 (death from unrelated causes) in 2.7% of patients. If an aneurysm, with or without a remnant, was unchanged for 12 months, then the risk for future morphological loss was 4.8%, whereas if an aneurysm showed a morphological loss during the earlier 12-month interval, the risk for additional late loss was 38.3% (P<0.001, odds ratio=12.4).

Conclusions—Embolization of saccular AAs entails a prolonged management period. A stable angiographic result during a 12-month interval predicts a low risk for morphological deterioration. This regimen, aiming for a stable angiographic result rather than complete aneurysm occlusion, gives a low rebleed rate and excellent clinical long-term results. (Stroke. 2008;39:2288-2297.)

Key Words: aneurysm ■ coiling ■ long-term clinical follow-up

Endovascular embolization is accepted as a primary treatment for intracranial saccular aneurysms (AAs) in many countries and particularly in France since the early 1990s. The main concern still remains as to whether the relatively high early minor recanalization rates, 11.9% to 33.6%,1–8 and the “stable” AA remnants that are found in 16.2% to 26% of Guglielmi detachable bare coil (GDC)–treated patients3–6,8,9 inflect a threat to the long-term clinical results in this patient group. In addition, long-term clinical results for completely occluded AAs are still lacking.

Embolization of AAs implies a prolonged management period with control angiograms and possible retreatment before a presumed stable result is obtained. Therefore, combined clinical and morphological follow-up studies are crucial to understand the role and strategy for embolization in the treatment of these patients and prevention of rebleeding. In the present single-institution series, since 1993 we have treated and continue to treat “berry AAs” uniquely with GDCs, and in only a few cases have we used balloon-assisted remodelling techniques. Intracranial stents have not been used, and the basic protocol for endovascular embolization of AAs has remained the same throughout the study period. The present retrospective study adds important information about clinical outcomes in the long term and compares the long-
term aneurysmal morphological outcome in subgroups of previously GDC-treated AAs.

Patients and Methods

Referral, Selection, and Inclusion of Patients

Referral to our institution for nearly all acutely symptomatic aneurysm patients is sent via the “Grande Garde” in Paris and Ile de France region, which encompasses 10 million inhabitants. This is a general combined neurosurgical/neurointerventional on-call service that is split among 6 hospitals in the region, meaning that referral is completely unbiased. In the early years, patients were selected for endovascular treatment if the aneurysm was thought easy to treat by an endovascular approach, considered difficult to treat surgically, or after a previously failed surgical treatment. Since ≈1995, endovascular coiling is the first choice of treatment at our center, resulting in 79% of ruptured AAs being referred to treatment with this method today.

All consecutive patients treated in the Neurovascular Unit of Hospital Bicêtre in Paris were prospectively entered into a database that has been maintained since 1993. For the present study, the patient files in the database were individually examined, and in every case where information was unclear or missing, the original clinical file and angiograms were scrutinized and the missing data were added to the database. The present study therefore includes all consecutive ruptured and unruptured berry, intradural AAs treated solely by endovascular GDCs since 1993 until the beginning of March 2005.

A total number of 466 intradural berry AAs in 413 consecutive patients were GDC coiled between 1993 and March 2005, of which 31.3% (146/466) were unruptured and 68.7% (320/466) were ruptured. Patients with fusiform, giant, dissecting, arteriovenous malformation–associated, partially thrombosed, infectious, inflammatory, mycotic, or extradural AAs were excluded from the study even if treated with the same coils.

Endovascular Treatment

All aneurysm clipping procedures in this single-institution series were performed by 3 senior neurointerventionalists (P.L., G.R., H.A.). The basic protocol for endovascular clipping of aneurysms at our institution has not changed since introduction of the method. The procedures were performed via a femoral approach with 6F guiding catheters. Heparinization was routinely used to reach an activated clotting time of twice the baseline value. For ruptured aneurysms, heparin was started after detachment of the first coil within the aneurysm sac. The aneurysms were embozized exclusively with bare GDCs (Boston Scientific Neurovascular). Balloon remodelling was used in 13.7% for unruptured and in 5.6% for ruptured AA coiling procedures. From the start, we tried to avoid overpacking of the ruptured AA because it may include packing of a false sac with its risk of early rerupture or periprocedural rupture. Heparinization was usually maintained for 24 hours. Since 2005, heparin is no longer maintained for 24 hours if the procedure is uneventful and the neck small. In ruptured AAAs, intensive care support always included calcium channel blockers, control of arterial pressure and, if needed, triple-H treatment. Since 1996, 3-dimensional functionality was added to the angiosuite, and since then, it has been routinely used when analyzing the lesion and surrounding vasculature before and after the embolization procedure.

Clinical Follow-Up

The short-term clinical follow-up was performed by registering all complications during the first hospitalization period. The complications were divided into those caused by or as a direct consequence of the initial hemorrhage and those caused by the endovascular treatment. The long-term clinical follow-up was performed by first sending a letter with a questionnaire to the patients and/or their relatives. The questionnaire consisted of questions regarding new intracranial hemorrhagic episodes, functional status according to the modified Rankin Scale (mRS), gross neurologic symptoms, other diseases or diagnoses, ability to work, details regarding cranial imaging after a possible second intracranial hemorrhage or other recent cranial imaging studies, and details regarding treatment of a possible new intracranial hemorrhage.

Slightly more than one third (34.7%) responded to the questions by mail, and 57.1% of patients/relatives gave clinical information when contacted by telephone by 1 of the French-speaking coworkers. The patients/relatives were then asked the same questions that had been sent out by mail previously. A small number (8.2%) of patients/relatives preferred that we contact their general practitioner to obtain the information required. This strategy for long-term data retrieval resulted in a total long-term clinical response rate of 89.1% (342/384) of all patients surviving the initial hospitalization period (29 patients died of complications of the initial subarachnoid hemorrhage or from other medical complications). A total of 4 of the patients responding to the questionnaire did not provide their mRS information. The clinical follow-up rate for the aneurysms was 90.1% (394/437).

Angiographic Follow-Up

The treated aneurysms were included in a routine follow-up program consisting of angiography at 3 months, 15 months, and 4 to 5 years after the coiling procedure. If an aneurysm remnant or a change in treatment result was detected on any of the follow-up angiograms, additional angiograms were obtained at shorter intervals. The treatment results were classified as occluded (100%), neck remnant (90% to 100%), or incomplete occlusion (<90%). If the treatment result was “incomplete occlusion,” the patient could be retreated and then reentered into the standard angiography follow-up program. From previous assessment, a treatment result was considered stable if 2 consecutive angiograms, within a minimum 12-month interval, were identical.

We excluded patients who had not yet had the possibility to achieve an angiographically confirmed stable treatment result, ie, patients who were treated during the last 15 months before the start of data analysis. Any special feature encountered at the time of the first treatment, or multifocality, could alter the frame described.

Statistical Analysis

In patients with multiple treated AAs, each treated aneurysm was separately analyzed for angiographic result. Untreated AAs were not included in the statistical analysis. For the clinical results, analysis was based only on the individual patient and not each AA. Continency table data were analyzed with Fisher’s exact test.

Results

Demographics and Techniques

Ruptured and Unruptured AAs

Angiographic analysis and clinical data were obtained for a total of 466 GDC-treated intradural sacular AAs in 413 patients. The patient cohort had a mean ± SD age of 47.2 ± 14.2 years and consisted of 64.6% females and 35.4% males. Multiple AAs were found in 33.6% of all patients, resulting in a total of 806 AAs in this patient cohort. The distribution of AA frequencies was as follows: 66.4% of patients had 1 aneurysm, 20.1% had 2, 10.2% had 3, 2.1% had 4, and 1.2% had 5 AAs. The prevalence of multiple AAs significantly differed between males and females: 38.6% of females and 25.4% of males had multiple AAs (P = 0.01; odds ratio [OR] = 1.86; 95% CI: 1.18 to 2.89). There was a nonsignificant difference between patients with ruptured and unruptured AAs: 34.1% of patients with ruptured and 43.8% of patients with unruptured AAs had multiple AAs (P = 0.08, OR = 1.48). However, among males, there was a significant difference between ruptured and unruptured AAs: 24.8% of males with ruptured and 41.9% of males with unruptured AAs had multiple AAs (P < 0.05; OR = 2.18; 95% CI 1.05 to 4.57). Among females, there was a nonsignificant
Table 1. Location of 466 Intradural, Saccular AAs

<table>
<thead>
<tr>
<th>Location</th>
<th>% of AAs</th>
<th>No. of AAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior circulation</td>
<td>85.9</td>
<td>275</td>
</tr>
<tr>
<td>Anterior communicating artery</td>
<td>34.7</td>
<td>111</td>
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<tr>
<td>Posterior communicating artery</td>
<td>26.3</td>
<td>84</td>
</tr>
<tr>
<td>Carotid/ophthalmic artery</td>
<td>10.6</td>
<td>34</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td>6.6</td>
<td>21</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>4.7</td>
<td>15</td>
</tr>
<tr>
<td>Anterior cerebral</td>
<td>3.1</td>
<td>10</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>14.1</td>
<td>45</td>
</tr>
<tr>
<td>Vertebrobasilar</td>
<td>11.6</td>
<td>37</td>
</tr>
<tr>
<td>Posterior inferior cerebellar artery</td>
<td>1.9</td>
<td>6</td>
</tr>
<tr>
<td>Anterior inferior cerebellar artery</td>
<td>0.3</td>
<td>1</td>
</tr>
<tr>
<td>Posterior cerebral</td>
<td>0.3</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location</th>
<th>% of AAs</th>
<th>No. of AAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior circulation</td>
<td>87.7</td>
<td>128</td>
</tr>
<tr>
<td>Carotid/ophthalmic artery</td>
<td>35.6</td>
<td>52</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td>14.4</td>
<td>21</td>
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<tr>
<td>Posterior communicating artery</td>
<td>13.0</td>
<td>19</td>
</tr>
<tr>
<td>Anterior communicating artery</td>
<td>10.3</td>
<td>15</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>7.5</td>
<td>11</td>
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<tr>
<td>Anterior cerebral</td>
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<tr>
<td>Posterior circulation</td>
<td>12.3</td>
<td>18</td>
</tr>
<tr>
<td>Vertebrobasilar</td>
<td>10.3</td>
<td>15</td>
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<tr>
<td>Posterior cerebral</td>
<td>2.1</td>
<td>3</td>
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<td>0</td>
</tr>
<tr>
<td>Anterior inferior cerebellar artery</td>
<td>0</td>
<td>0</td>
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</table>

The difference between ruptured and unruptured AAs: 42.1% of females with ruptured and 53.5% of females with unruptured AAs had multiple AAs (P=0.09; OR=1.58). Eighty-eight percent (410/466) of AAs were <10 mm, and 12.0% (56/466) of AAs were between 10 and 25 mm.

The neck was considered narrow (&lt;=4 mm) in 71.5% (333/466) and broad in 28.5% of AAs. Anterior circulation AAs constituted 87.1% (406/466) and posterior circulation AAs, 12.9% of all AAs (Table 1). We found 3 angiographically confirmed de novo aneurysms. A balloon remodelling technique was used in 8.15% of all aneurysm coiling procedures. Endovascular retreatments were performed for 15.2% of AAs with a total of 90 retreatment procedures.

Ruptured AAs

The clinical status of patients with ruptured AAs was defined according to the Hunt and Hess (H&H) grading system; thus, 13.7% (42/307) of patients were in grade 1, 53.7% (165/307) were in grade 2, 15.0% (46/307) were in grade 3, 14.0% (43/307) were in grade 4, and 3.6% (11/307) were in grade 5. Balloon remodelling was used in 5.63% (18/320) of procedures.

Unruptured AAs

Among patients with unruptured AAs, 45.9% (67/146) presented incidentally, 30.8% (45/146) with headache, 21.9% (32/146) with a neurologic deficit, and 1.4% (2/146) with epilepsy. Balloon remodelling was used in 13.7% (20/146) of procedures.

Early Clinical Results and Procedural Complications

Ruptured and Unruptured AAs

The total periprocedural complication rate was 6.44% (30/466 AAs) for the initial treatment and 5.94% (33/556) with the 90 embolization retreatment procedures included. The thromboembolic event rate, retreatment procedures included, was 5.40% (30/556), causing permanent neurologic deficits in 2.16% (12/556). The total periprocedural mortality was 0.36% (2/556).

Ruptured AAs

Twenty-nine of 307 patients (9.45%) died of complications of the initial hemorrhage, such as vasospasm and pneumonia, or of an early rebleed before or after endovascular treatment. Three of 307 (0.98%) patients rebled within a week after the coiling procedure. All 3 patients had multiple AAs with 5, 3, and 2 AAs, respectively. In 2 patients, only the 2 AAs most likely to have bled were initially treated; due to the blood distribution of the rehemorrhage, it was concluded that they bled from 1 of the untreated AAs. In the patient with 2 AAs, only the 1 most likely to have bled was treated, and it could not be decided which 1 rebled. Two of the 3 patients died of the early rebleed and 1 survived with an mRS score of 2. In this series, 34.1% of patients with ruptured AAs had multiple AAs. The management of multiple AAs was discussed by Porter et al10 in 2001, when they showed that despite these early rebleeds, the overall selection of the AA to be treated emergently in multiple location was satisfactory; the long-term follow-up in this series with a high number of untreated AAs associated with coiled ruptured ones confirms the choice of the target in the prevention of rebleeding.

Among the primary treatment procedures for 320 ruptured AAs, the total periprocedural complication rate was 6.56% (21/320 AAs). Eighteen of 320 (5.63%) were thromboembolic events producing neurologic deficits in 2.81% (9/320), of which 1.88% (6/320) were permanent and 0.94% (3/320) were transient. Included in these thromboembolic complications were dissections in 0.94% (3/320) and parent-vessel occlusions in 0.63% (2/320). In addition, perimembolization aneurysm rupture occurred in 0.94% (3/320) of procedures.

Unruptured AAs

Mortality in the unruptured aneurysm group was 0%, and the total periprocedural complication rate for the primary treatment was 6.16% (9/146 AAs). All of these were thromboembolic events producing neurologic deficits in 4.11% (6/146), of which 3.42% (5/146) were permanent and 0.68% (1/146) were transient. No dissections or parent-vessel occlusions occurred. Periembolization aneurysm rupture occurred in 0.68% (1/146) of procedures.

Angiographic Follow-Up

Ruptured and Unruptured AAs

Angiographic follow-up was performed at 3 months in 78.7%, at 15 months in 71.4%, and at 4 to 5 years in 47.1% of all AAs. Subgroup analysis showed that if an aneurysm, with or without
a remnant, was unchanged for 12 months, then the risk for future “morphological loss” was 4.8%, whereas if an aneurysm showed a worsened morphology during the earlier 12-month interval, the risk for additional late loss was 38.3% (P<0.001; OR=12.4; 95% CI, 4.52 to 34.1). The last available angiogram for each aneurysm showed that 63.3% were completely occluded, 28.5% had a neck remnant, and 8.2% were incompletely occluded.

### Ruptured AAs

The initial post-GDC embolization angiograms showed complete aneurysm obliteration in 55% (176/320 AAs), a neck remnant in 37.5% (120/320), and incomplete occlusion in 7.50% (24/320) of treated AAs. Because 29 patients died during the initial hospitalization period, follow-up was possible in 291 ruptured AAs. Of the AAs in the surviving patient group, 85.9% (250/291 AAs) had at least 1 follow-up angiography and 76.3% (222/291) had at least 2 follow-up angiographies with a 12-month interval. Follow-up angiography 4 to 5 years after the last embolization was performed in 47.4% (138/291) of aneurysms.

Follow-up angiography was performed at 3 months in 77% (224/291) of AAs, and when compared with the immediate postembolization control, 41.1% (92/224) of AAs were unchanged without a remnant, 20.0% (45/224) were unchanged with a remnant, 17.0% (38/224) showed morphological improvement, and 21.9% (49/224) showed “morphological loss.” Forty-two of 291 (14.4%) AAs were retreated early after the first follow-up angiography. A follow-up angiography at 12 months after the last angiography or retreatment was performed in 72.9% (212/291) of AAs, and morphological status at that time was compared with either the initial treatment result or the retreatment result. Thus, with 14.4% of AAs being retreated early, 32.1% (68/212) of AAs were unchanged without a remnant, 26.4% (56/212) were unchanged with a remnant, 25.0% (53/212) showed morphological improvement, and 16.5% (35/212) showed “morphological loss” 12 months after the preceding angiography or retreatment.

Two hundred twenty-two AAs had at least 2 follow-up angiograms in a 12-month interval. Of these 222 AAs, 138 also had a late follow-up digital subtraction angiography 4 to 5 years after the latest treatment. To better predict which AAs were at risk for future morphological deterioration, we analyzed the late morphological outcome of AAs that showed unchanged, improved, or “worsened” morphology during the earlier 12-month follow-up interval. We found that if an aneurysm was unchanged, with or without a remnant, during the 12-month interval, the risk for late morphological loss was 5.1% (4/79 AAs). On the other hand, if an aneurysm showed worsened morphology during the earlier 12-month interval, the risk for late morphological loss was 37.1% (13/35) (P<0.001; OR=11.1; 95% CI, 3.3 to 37.4; Table 2).

To illustrate the general management of aneurysm treatment at our institution, including retreatments and various follow-up times, we also present the last angiographic result obtained for each aneurysm: 61.6% (197/320) were completely occluded, 30.3% (97/320) had a neck remnant, and 8.1% (26/320) were incompletely occluded. With these angiographic results, excellent long-term clinical results were achieved (see following sections).

### Table 2. Morphological Outcome in Embolized AAs With 4 to 5 Years of Angiographic Follow-Up

<table>
<thead>
<tr>
<th>Previous 12-month Interval</th>
<th>Ruptured, n=138</th>
<th>Unruptured, n=68</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unchanged without remnant</td>
<td>6.3% (3/48)</td>
<td>5.3% (2/38)</td>
</tr>
<tr>
<td>Unchanged with remnant</td>
<td>3.2% (1/31)</td>
<td>0% (0/9)</td>
</tr>
<tr>
<td>(Unchanged with or without remnant inclusive)</td>
<td>5.1% (4/79)</td>
<td>4.3% (2/47)</td>
</tr>
<tr>
<td>Improved morphology</td>
<td>4.2% (1/24)</td>
<td>0% (0/9)</td>
</tr>
<tr>
<td>Unchanged or improved</td>
<td>4.9% (5/103)</td>
<td>3.6% (2/56)</td>
</tr>
<tr>
<td>Loss in morphology</td>
<td>37.1% (13/35)</td>
<td>41.7% (5/12)</td>
</tr>
</tbody>
</table>

### Unruptured AAs

The initial post-GDC embolization angiograms showed complete aneurysm obliteration in 52.7% (77/146 AAs), a neck remnant in 37.7% (55/146), and incomplete occlusion in 9.59% (14/146) of treated AAs. One hundred twenty-nine of 146 AAs (88.3%) had at least 1 follow-up angiography, and 71.9% (105/146) had at least 2 follow-up angiographies within a 12-month interval. A follow-up angiography 4 to 5 years after the last embolization was performed in 46.6% (68/146) of AAs.

Follow-up angiography was performed at 3 months in 82.2% (120/146) of AAs, and when compared with the immediate postembolization control, 49.2% (59/120) of AAs were unchanged without a remnant, 16.7% (20/120) were unchanged with a remnant, 23.3% (28/120) showed morphological improvement, and 10.8% (13/120) showed “morphological loss.” Nine of 146 (6.2%) AAs were retreated early after the first follow-up angiography.

A 12-month follow-up angiography after the last treatment was performed in 68.5% (100/146) of AAs, and morphological status at that time was compared with either the initial treatment result or the retreatment result. Thus, with 6.2% of AAs being retreated early, 39.0% (59/150) of AAs were unchanged without a remnant, 18.0% (27/150) were unchanged with a remnant, 9.0% (14/150) showed morphological improvement, and 42.0% (62/146) showed morphological loss 12 months after the preceding angiography or retreatment.

One hundred five AAs had at least 2 follow-up angiograms within a 12-month interval. Of these 105 AAs, 68 also had a late follow-up digital subtraction angiography 4 to 5 years after the last treatment. To better predict which AAs were at risk for future morphological deterioration, we analyzed the late morphological outcome of AAs that showed unchanged, improved, or “worsened morphology” during the earlier 12-month follow-up interval. We found that if an aneurysm was unchanged, with or without a remnant, during the 12-month interval, the risk for a late morphological change was 4.3% (2/47 AAs). On the other hand, if an aneurysm showed worsened morphology during the earlier 12-month interval, the risk for late loss was 41.7% (5/12; P<0.01; OR=16.1; 95% CI, 2.6 to 99.5; Table 2).

To illustrate the general management of aneurysm treatment, including retreatments and various follow-up times, we also present the last angiographic result obtained for each
aneurysm: 67.1% (98/146) were completely occluded, 24.7% (36/146) had a neck remnant, and 8.2% (12/146) were incompletely occluded. With these angiographic results, excellent long-term clinical results were achieved (see following sections).

Retreatments

Ruptured and Unruptured AAs

Retreatments were performed if there was a significant morphological loss during angiographic follow-up or if the initial treatment result was unsatisfactory. Sixty-seven of 437 (15.3%) AAs were retreated 1 or more times with a total of 95 procedures, of which 5 were open surgical and 90 were embolization procedures. Among the embolization retreatment procedures, there were 3.3% (3/90) technical complications, producing neurologic deficits in 1.1% (1/90) of procedures.

Ruptured AAs

The retreatment rate was 17.2% (50/291 AAs) with a total of 73 procedures, of which 4 were open surgical and 69 were endovascular procedures. Thromboembolic complications occurred in 2.9% (2/69) of the endovascular procedures, but none of these produced any permanent neurologic deficit. Thirty-four (11.7%) AAs were retreated once, 10 (3.4%) were retreated twice, 5 (1.7%) were retreated 3 times, and 1 (0.3%) was retreated 4 times.

Unruptured AAs

The retreatment rate was 11.6% (17/146 AAs) with a total of 22 procedures, of which 1 was open surgical and 21 endovascular. Thromboembolic complications occurred in 4.8% (1/21) of the endovascular procedures, and that thromboembolic complication produced a permanent neurologic deficit. Twelve (8.2%) of the AAs were retreated once, and 5 (3.4%) were retreated twice.

Late Rebleeding

The database and long-term clinical follow-up information were scrutinized for rebleeds or suspected rebleeds, and in those cases, the files and images from the hospital of admission were collected and examined. In 6 patients, there was suspicion of a late rebleed, but after careful analysis, it turned out that only 1 patient with a treated, previously unruptured aneurysm had actually bled. One patient, who had undergone previous coiling for a ruptured left posterior communicating artery aneurysm, also had 3 untreated AAs, of which 1 measured 17 mm (the Figure). Endovascular and open surgical treatment was twice recommended to the patient, but the patient refused treatment of the unruptured AA. The patient rebled from 1 of the untreated AAs.

Thus, we found only 1 patient with a confirmed late bleed from an initially clipped, unruptured anterior communicating artery aneurysm. This aneurysm recurred 9 years after clipping and was subsequently coiled (the Figure). The bleed occurred 2 months after the coiling procedure, before the usual 3-month follow-up angiography. The aneurysm was coiled a second time with a good morphological result, and the patient recovered well from the subarachnoid hemorrhage and is now graded at mRS 0.

Thus, the confirmed late aneurysmal rebleed rate was 0.21% (1/466 AAs). If one excludes AAs in patients who died of complications of the initial hemorrhage and patients for whom we did not obtain any long-term clinical follow-up, the late aneurysmal rebleed rate was 0.27% (1/364 AAs).

Long-Term Clinical Results

Ruptured and Unruptured AAs

The total AA follow-up time was 24 277 months (2018.9 aneurysm-years) with a mean of 62.4 ± 39.7 and a median of 54 months. The total patient follow-up time was 21 722 months (1810.2 patient-years) with a mean of 64.3 ± 39.9 and a median of 55 months. The percentage of coiled AAs lost to clinical follow-up was 9.87% (46/466), and the percentage of patients lost to clinical follow-up was 10.9% (45/413). Forty-five AAs were followed up for > 10 years, 93 AAs for > 8 years, and 175 AAs for > 5 years.

Among the patients with available long-term clinical follow-up data, 87.9% (297/338) had an mRS score of 0 to 2, and 12.1% (41/338) had an mRS score of 3 to 6 (Table 3). Two hundred sixty-four of 338 (78.1%) patients returned to their previous lifestyle, and 74.0% (250/338) had no persisting neurologic symptoms, including regular headache, in the long term.

Ruptured AAs

For ruptured AAs, the total aneurysm follow-up time was 15 708 months (1309 aneurysm-years) with an average of 60.6 ± 37.9 and a median of 53 months. The total patient follow-up time was 14 973 months (1248 patient-years) with an average of 60.8 ± 38.0 and a median of 52.5 months.

Among patients with available long-term clinical follow-up data, 85.2% (196/230) had an mRS score of 0 to 2, and 18.6% (42/230) had an mRS score of 3 to 6 (Table 3). One hundred seventy-six of 230 (76.5%) patients returned to their previous lifestyle, and 72.6% (167/230) had no persisting neurologic symptoms, including regular headache, in the long term.

Unruptured AAs

For unruptured AAs, the total aneurysm follow-up time was 8519 months (710 aneurysm-years) with an average of 66.0 ± 42.9 and a median of 57 months. The total patient follow-up time was 6749 months (562 patient-years) with an average of 74.3 ± 42.9 and a median of 59 months.

Among patients with available long-term clinical follow-up data, 93.5% (101/108) had an mRS score of 0 to 2, and 6.5% (7/108) had an mRS score of 3 to 6 (Table 3). Eighty-eight of 108 (81.5%) patients returned to their previous lifestyle, and 76.9% (83/108) had no persisting neurologic symptoms, including regular headache, in the long term.

Discussion

The present study was undertaken to analyze the clinical and morphological long-term outcomes of intradural saccular AAs treated solely by GDCs at a single institution. The study comprises relatively high standards of combined clinical and morphological follow-up and to our knowledge presents the longest clinical follow-up time for this technique so far. The data show, in accordance with previous studies,1,2,5-8,11,12 that morphological loss after coil treatment is relatively common. The present long-term clinical follow-up data with this regimen show a very low rebleed rate despite the fact that no stents or modified coils were used and excellent clinical outcome data in
comparison with the literature. The study also adds unique information about the natural history and clinical significance of neck remnants, indicating that more important than the presence of a neck remnant is the stability of the treatment result.

**Referral, Inclusion, and Selection Bias**
There was no referral bias concerning ruptured AAs in the study population because all patients with acute subarachnoid hemorrhage in the Paris region were handled by the “Grande Garde.” For unruptured AAs, a referral bias probably existed, because those AA were referred to us from different European countries. The majority of unruptured AAs referred to us were complex and did not fall into the category of common, intradural saccular berry AAs, and those were not included in this study. Extradural, fusiform, mycotic, giant, inflammatory, dissecting, and feeder AAs were also excluded to create a homogeneous group of patients and AAs.

The boundaries of a favorable morphology for coiling have moved over the years, and today a higher proportion (79% in 2007) of all saccular intradural AAs are embolized. There-
fore, the aneurysms treated by endovascular techniques during the early years represent a somewhat different cohort from more recent ones. The clinical results with the longest follow-up times (>10 years) are thus based on patients with AAs considered favorable for coiling, difficult to treat surgically, or after previously failed surgical treatment. It is likely that longer follow-up times for the more recent group of patients will at least not show a worse clinical result than for the more difficult aneurysms treated during the early years.

It is common in the literature to combine ruptured and unruptured AAs in the analysis of long-term follow-up.\textsuperscript{1,2,5,6,8,11,12} We believe that ruptured and unruptured AAs represent different disease entities or aneurysm states with regard to its natural history and treatment strategy, and therefore, the results for these entities were separated within the article to make relevant conclusions possible.

### Demographics

The patient characteristics in our study did not differ significantly from other large series of aneurysm embolization follow-up.\textsuperscript{2,3,5,6,13–17} The mean age in those series ranged from 52 to 57 years compared with 47.2 years in our series, the percentage of females ranged from 57% to 74% compared with 64.6%, the percentage of anterior circulation AAs ranged from 66% to 97% compared with 86.4%, the percentage of AAs <10 mm ranged from 75% to 92% compared with 88%, the percentage of AAs 10 to 25 mm ranged from 8% to 25% compared with 12%, and the percentage of wide-necked AAs ranged from 27% to 28% (only indicated in a few series) compared with 28.5% in our series. Among the ruptured AAs, the percentage of patients in H&H grade 1 ranged from 21% to 30% compared with 13.7% in our series; H&H grade 2 was 19% to 36% compared with 53.7%, H&H grade 3 was 17% to 29% compared with 15.0%, H&H grade 4 was 12% to 24% compared with 14.0%, and H&H grade 5 was 3% to 8% compared with 3.6% in our series. Therefore, results of the present study can reliably be compared with outcome data from previous studies. The only parameter that differed somewhat in our series was the relatively high number of patients in H&H grade 2. We do not know the reason for this, but we had fewer patients in H&H grades 1 and 3, suggesting that a classification bias could explain the difference.

We found a higher proportion of multiple AAs in the unruptured group compared with the ruptured group. This difference was statistically significant when males were analyzed separately. The results corroborate previous findings that showed that patients with a single AA had a higher risk of subarachnoid hemorrhage than did patients harboring multiple AAs.\textsuperscript{18} The total number of intradural saccular AAs in this patient cohort was 806, among which 320 were ruptured and treated, indicating that the majority of this type of AA do not bleed, at least within the observation time frame presented here.

### What Is ‘Long-Term Follow-Up’?

Aneurysm embolization entails a prolonged management period with control angiograms and possible retreatment before a presumed stable result is obtained. Previous reports indicate that the majority of, but not all, changes in angiographic appearance occur during the first year after embolization.\textsuperscript{1,2,5–8} Recent studies have indeed pointed to the fact that later recurrences do occur,\textsuperscript{11,12} and therefore it is of interest to identify those parameters that predict the stability of an achieved treatment result. On the basis of previous assessments, we hypothesized that an unchanged angiographic result, with or without a remnant during a 12-month interval, could predict the future morphological result. We included only patients for whom an angiographic and clinical follow-up period of at least 15 months could be achieved. Thus, all patients treated during the last 15 months before the data collection end point were excluded. We believe that such a definition of long-term follow-up better reflects the disease process, compared with the disease management process that takes place before an early stable treatment result has been obtained. The clinical results presented additionally address whether an early stable treatment result, with or without a small neck or aneurysm remnant, can be considered safe in the long term.

### Neck Remnants

Previous studies have not documented the morphological development of AA remnants because the actual long-term angiographic data are either not presented or lacking. The present protocol, with a 4- to 5-year follow-up angiography in a large group of patients, made it possible to analyze the natural history of neck remnants in a longer perspective. On the basis of our follow-up strategy, we agree that the majority of “morphological losses” or recurrences occur early, ie, within 1 year after embolization.\textsuperscript{1,2,5–8} Two recent studies using different strategies to address recurrences obtained opposite results regarding the initial angiographic result as a predictor of recurrence.\textsuperscript{11,12} With our angiographic protocol, we found that a stable morphological result, with or without a remnant, during a 12-month interval predicted a low risk (4.8%) of later morphological loss or recurrence. On the other hand, if an aneurysm did not reach an unchanged angiographic and clinical follow-up period of at least 15 months could be achieved. Thus, all patients treated during the last 15 months before the data collection end point were excluded. We believe that such a definition of long-term follow-up better reflects the disease process, compared with the disease management process that takes place before an early stable treatment result has been obtained. The clinical results presented additionally address whether an early stable treatment result, with or without a small neck or aneurysm remnant, can be considered safe in the long term.
occlusion rates ≈8% seems low when compared with other published series of GDC coils. On the other hand, complication rates, persistent neurologic deficits, and long-term mRS scores are better than those in published series with similar population groups. These differences indicate that an embolization strategy that always aims for complete aneurysm occlusion (overpacking during the late 1990s and neck reconstruction during the last 5 years) is not necessarily accompanied by improved long-term clinical results.

Procedural Complications
Nelson et al19 recently reviewed the literature and presented the collected results after stent-assisted coiling for intradural AAs between 1999 and May 2006. Among 416 AA patients, of which 35% were ruptured, stent positioning was possible in 92.7%. The overall thromboembolic complication rate was 10.3%, and the initial aneurysm occlusion rate was 57%. Among patients with angiographic follow-up (mean±SD, 6.3±2.5 months) and reported morphological results (n=172), the total aneurysm occlusion rate was 69%. The frequency of delayed in-stent stenosis was 4.5%. These results must be compared with the data presented here with a thromboembolic complication rate of 5.8% for all patients despite a considerably higher proportion of ruptured AAs in this series (68.7% ruptured). The initial total aneurysm occlusion rate in the current study is comparable with the figure reported in the series with stent-assisted coiling (54.3% vs 57%), whereas the last angiographic result showed total aneurysm occlusion in 63.3% of our patients compared with 69% in the stent series. The proportion of large AAs was, however, larger in the stent series (35% large or giant vs 12% here), and although the number of large-necked AAs was not presented, the incidence of large necks was probably significantly higher in the stent series. The quality of angiographic follow-up was generally poor in the stent series, with at least 1 angiographic follow-up in 48.3% of patients compared with 86.7% in our series. This follow-up strategy led to retreatment in 8.0% in the stent-treated patients and to 15.3% in our series.

Considering the extremely low incidence of rebleeds and the excellent long-term clinical outcome after simple GDC coiling, one must have clear indications for the use of stent-assisted coiling, given the higher complication rate and higher cost. An aneurysm neck should probably be clearly anatomically difficult to justify its use. Studies on Hydrocoils20,21 have shown that the thromboembolic event and perforation rates in ruptured AAs were higher than in our series, which could reflect the fact that Hydrocoils are somewhat stiffer than bare GDCs. In other studies, the complication rate has been similar to that of bare coils.22,23 For Matrix coils, the procedural complication rate is

Table 4. Study Characteristics in Comparison With Other Series With Long-Term Clinical Follow-Up After Coiling Of Intradural Saccular AAs

<table>
<thead>
<tr>
<th>Study or Last Name of First Author</th>
<th>R/U (No. of Patients)</th>
<th>Mean Patient Follow-Up Time, mo (Maximum Time)</th>
<th>Initial/Latest Angiogram, Total Occlusion Rate</th>
<th>Procedural Complications (Permanent Deficit + Mortality)</th>
<th>Long-Term Clinical Outcome, mRS or GOS Score (Rebleed Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present series R+U (413)</td>
<td>64.3 (160)</td>
<td>54.3%/63.3%</td>
<td>6.4% (2.5%)</td>
<td>mRS 0–2 87.9%</td>
<td>mRS 0–2 87.9%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>mRS 3–6 12.1%</td>
<td>mRS 3–6 12.1%</td>
</tr>
<tr>
<td>Molyneaux, 2005</td>
<td>R (1063)</td>
<td>12</td>
<td>NS/66%</td>
<td>NS (NS)</td>
<td>mRS 0–2 76.5%</td>
</tr>
<tr>
<td>Multicenter</td>
<td></td>
<td></td>
<td></td>
<td>mRS 3–6 23.5%</td>
<td>mRS 3–6 23.5%</td>
</tr>
<tr>
<td>Kremer, 2002</td>
<td>R (79)</td>
<td>41 (74)</td>
<td>70.9%/NS</td>
<td>NS (NS)</td>
<td>mRS 0–2 75%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>mRS 3–6 25%</td>
<td>mRS 3–6 25%</td>
</tr>
<tr>
<td>Friedman, 2003</td>
<td>R (83)</td>
<td>19.1 (112)</td>
<td>33%/35%</td>
<td>19% (2%)</td>
<td>GOS 4–5 77%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>GOS 1–3 23%</td>
<td>GOS 1–3 23%</td>
</tr>
<tr>
<td>Yu, 2004</td>
<td>R+U (97)</td>
<td>54 (96)</td>
<td>71.1%/82.5%</td>
<td>11.3% (7%)</td>
<td>GOS 4–5 77%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>GOS 1–3: 23%</td>
<td>GOS 1–3: 23%</td>
</tr>
<tr>
<td>Kole, 2005</td>
<td>R+U (160)</td>
<td>18.2 (75)</td>
<td>16%/19.1%</td>
<td>NS/NS</td>
<td>GOS 4–5 73.3%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>GOS 1–3 26.7%</td>
<td>GOS 1–3 26.7%</td>
</tr>
<tr>
<td>Mejdoubi, 2006</td>
<td>R (222)</td>
<td>26 (69)</td>
<td>80.7%/79.2%</td>
<td>16.5% (8.1%)</td>
<td>mRS 0–2 75.3%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>mRS 3–6 24.7%</td>
<td>mRS 3–6 24.7%</td>
</tr>
<tr>
<td>Sluzewski, 2003</td>
<td>R (160)</td>
<td>37.1 (72)</td>
<td>71%/59%</td>
<td>NS (3.8%)</td>
<td>GOS 4–5 84%</td>
</tr>
<tr>
<td>Single center</td>
<td></td>
<td></td>
<td></td>
<td>GOS 1–3 16%</td>
<td>GOS 1–3 16%</td>
</tr>
</tbody>
</table>

R indicates ruptured AAs; U, unruptured AAs; and NS, not studied.
similar to that of bare coils; on the other hand, recanalizations seem more frequent.24–26

Long-Term Clinical Outcome

In previous studies, an mRS score of 0 to 2 was reported in 75% to 76.5%, and an mRS score of 3 to 6 was reported in 23.5% to 24.5% of patients (Table 4).16,27,28 With the clinical questionnaire or telephone interviews, we found an mRS score of 0 to 2 in 87.9% and an mRS score of 3 to 6 in 12.1% of patients. In other series, the Glasgow Outcome Scale (GOS) was used, and a GOS score of 4 to 5 (good recovery or moderately disabled) was found in 73.3% to 84.0% of patients (Table 4).4,7,9,29 The difference between an mRS score of 0 to 2 and a GOS score of 4 to 5 must be considered when interpreting the results, because these GOS scores also include moderately disabled patients, which the mRS score 2 does not. In previously published series with long-term clinical follow-up, the average clinical follow-up time ranged from 12 to 54 months, compared with 64.3 months in the present series, and the number of patients in each study ranged from 79 to 1063 (International Subarachnoid Aneurysm Trial with a 12-month follow-up), compared with 413 in the present series. We also had a relatively high number of true long-term follow-up cases; ie, 45 AAs were followed up for >10 years.

A weakness of this and other studies is the patient loss to follow-up. However, even if we assume that all lost patients had an mRS score of 3 to 6, 78.2% of patients would have been in the mRS 0 to 2 group and 21.8% in the mRS 3 to 6 group, ie, still comparable with or better than other published series. In the present series, most patients who were lost to follow-up had moved abroad, and therefore, the results that we present most likely represent the true situation.

Conclusions

We have shown that intradural saccular berry AAs can be managed with excellent long-term results with low morbidity and mortality, without using adjuncts such as stents, frequent balloon remodelling, bioactive coils, etc. The proportion of surgical clipping, however, remained at ≈20% to 25% at our institution, and it is possible that we could increase the number of AAs for embolization with an increased use of adjuncts, but then new comparisons with the surgical results would have to be made. Long-term clinical results are not yet available for other treatment options such as bioactive coils and stents. Basically, the aneurysms treated and followed up strictly do not rebleed within the time frame presented here. The presence of a stable neck remnant does not justify increased risks or costs during treatment or retreatment procedures, and one should aim for materials and procedures with minimal complication risk when treating this disease.

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Disclosures

None.

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anomalies and the risk of multiple aneurysms development and bleeding. 

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