Treatment of Intracranial Aneurysms by Embolization with Coils
A Systematic Review
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Background—Embolization with coils is increasingly used for the treatment of intracranial aneurysms. To assess the percentage of complications, the percentage of aneurysm occlusion, and the short-term outcome, we performed a systematic review of studies on embolization with controlled detachable or pushable coils.

Summary of Review—To find studies on embolization with coils, we performed a MEDLINE search from January 1990 to March 1997, checked all reference lists of the studies found, performed a Science Citation Index search on Guglielmi, and hand searched recent volumes of 25 journals. Two authors independently extracted data by means of a standardized data extraction form from 48 eligible studies totalling 1383 patients. Permanent complications of embolization with controlled detachable coils occurred in 46 of 1256 patients (3.7%; 95% CI, 2.7% to 4.9%); 400 of 744 aneurysms (54%; 95% CI, 50% to 57%) were completely occluded. By means of weighted linear regression, no relation between baseline characteristics and outcome measurements was found. The results in the prespecified subgroups of patients with a ruptured aneurysm, an unruptured aneurysm, or a basilar bifurcation aneurysm were essentially the same as the overall results.

Conclusions—Short-term results indicate that embolization with coils is a reasonably safe treatment for patients with an unruptured aneurysm and for patients with aneurysmal subarachnoid hemorrhage. The effectiveness in terms of complete occlusion of the aneurysm is moderate. Randomized trials are warranted to compare surgical clipping with embolization with coils. (Stroke. 1999;30:470-476.)

Key Words: cerebral aneurysm • embolization, therapeutic • endovascular therapy • treatment outcome

The standard method of treatment for intracranial aneurysms is surgical clipping. Until recently, endovascular treatment was restricted to patients in whom the aneurysm was unsuitable for clipping because of the size or location of the aneurysm or in whom surgical clipping was contraindicated. Since the introduction of controlled detachable coils for endosaccular packing of aneurysms, embolization is increasingly used; in some institutes embolization is now proposed as the initial method of treatment.1–3

Many reports on embolization with coils of intracranial aneurysms have been published, but a general overview on the existing body of knowledge is lacking. The collective information from observational studies is pivotal in the planning of randomized trials and for informing patients who cannot be treated surgically.

We performed a systematic review to assess the proportion of complications, the degree of aneurysm occlusion, and the short-term outcome of treatment of intracranial aneurysms by embolization with controlled detachable coils and with pushable coils without a system for controlled detachment.
rysm associated with an arteriovenous malformation; and patients with an aneurysm in the cavernous sinus were not eligible. Non–English language use was not an exclusion criterion. Studies without data on coil type, aneurysm type, or complications of the embolization procedure were excluded.

Data Extraction
Two authors (E.H.B. and G.J.E.R.) independently extracted data from eligible studies by means of a standardized data extraction form. In case of disagreement, both observers reviewed the article in question together. If necessary, we had data extracted by a translator. The following data were extracted for (1) study design, (2) baseline characteristics, (3) procedure, and (4) outcome. Data extracted for study design included prospective or retrospective data collection, study period, criteria for inclusion, outcome assessor, and definition of outcome.

Data extracted for the baseline characteristics category included number of patients, mean age, number of ruptured aneurysms and unruptured aneurysms (subdivided into symptomatic aneurysms, asymptomatic aneurysms additional to a ruptured aneurysm, and asymptomatic incidental aneurysms), clinical condition before embolization, time interval between subarachnoid hemorrhage (SAH) and embolization (for patients with a ruptured aneurysm), aneurysm location, aneurysm size, and aneurysm neck size. Initially we intended to present data on clinical condition before embolization for patients with SAH using the World Federation of Neurological Surgeons grading scale. Because almost all studies still used the Hunt & Hess grading system, we were forced to use this scale. For the classification of aneurysm size, we used the categories small, large, and giant and registered how these categories were defined in each study.

Data extracted for the procedures category included type of coils used, number and type of complications, and degree of aneurysm occlusion. We classified the type of coil as pushable or controlled detachable. When controlled detachable coils were used, we further specified which type was used. Procedural complications were classified as rupture of the aneurysm, cerebral ischemia, other intracranial complication, or extracranial complication. We considered any clotting or coil protrusion into the parent vessel during embolization an ischemic complication, regardless of the occurrence of clinical symptoms, because transient clinical deficits during treatment cannot be detected when the patient is under general anesthesia. Depending on the authors’ description, we classified complications as transient or permanent. The degree of aneurysm occlusion on immediate postembolization angiography was categorized as 0% to 90% occlusion, >90% to 99% occlusion, or complete occlusion. We only extracted data on the degree of aneurysm occlusion if it could be fitted into one of these categories. When an embolization procedure was discontinued and the aneurysm was occluded during a second procedure within 1 month of the first procedure, data on the degree of aneurysm occlusion after this second procedure were used. Second procedures because of recurrence of the aneurysm on follow-up angiography were not included in this review.

For the outcome category, we extracted data on rebleeds, short-term survival, and functional outcome after embolization and the time interval between embolization and outcome assessment. If outcome was assessed at more than one point, we extracted data from the assessment that was performed closest to 1 month after embolization. We used the Rankin scale for categorization of functional outcome.4 If data on functional outcome were given only in global terms, we dichotomized outcome into independent (Rankin grade 0 to 2) versus dependent (Rankin grade 3 to 5). If adjustment into 1 of these 2 categories was not possible, we excluded the study from the analysis on functional outcome after embolization. Mortality was specified as related to the procedure or to other causes.

If studies reported on embolization of aneurysms of more than one type (ruptured, unruptured, symptomatic, additional, or incidental), we collected these data per type of aneurysm separately, if possible. When patients were described twice, we extracted data from the most recent publication only.

Data Analysis
We calculated the percentage of all complications of the embolization procedure, permanent complications, aneurysm perforations during embolization, ischemic complications, aneurysms occluded >90%, completely occluded aneurysms, patients with a Rankin grade 0 to 2, patients who had died at the initial outcome assessment, and the mortality related to the procedure. These calculations were performed separately for patients treated with any type of controlled detachable coil, patients treated with Guglielmi detachable coils, and patients treated with pushable coils.

For patients treated with controlled detachable coils, we decided in advance to perform subgroup analyses for patients with an aneurysm located at the basilar bifurcation, those with a ruptured aneurysm, and those with an unruptured aneurysm (symptomatic or asymptomatic).

We included case reports but performed recalculations after exclusion of studies reporting on <5 patients. Our eligibility criteria permitted inclusion of studies that did not provide data on all baseline characteristics or on the degree of aneurysm occlusion or functional outcome. To assess the results in patients from studies of high methodological quality, we performed another analysis including only those studies that were prospective and reported on ≥5 patients treated with controlled detachable coils, in which data on aneurysm type, location, and size; complications of the embolization procedure; degree of aneurysm occlusion; and functional outcome were all available.

By weighted linear regression analyses, in which the number of patients was taken as weight, we quantified the relationship of aneurysm type (ruptured, unruptured symptomatic aneurysms, additional, and incidental), clinical condition before embolization, aneurysm location, and aneurysm size with percentages of permanent complications, of aneurysms occluded >90%, and of patients with a Rankin grade 0 to 2 at follow-up. We also performed weighted linear regression analyses to quantify the relationship of Hunt & Hess grade before embolization or time interval between SAH and embolization on the one hand with percentage of permanent complications, degree of aneurysm occlusion, and functional outcome in the subgroup of patients with a ruptured aneurysm on the other.

Studies that reported on <5 patients and studies on embolization with pushable coils were excluded from the regression analyses.

Results
Study Characteristics
We included 48 studies in 6 languages (9 articles were non-English) that described endovascular treatment in 1383 patients.1–3,5–49 Fourteen studies (798 patients; 58% of all patients included in the review) were prospective, and 18 studies (39 patients; 3%) were retrospective; the method of data collection was unknown for 16 studies reporting on 546 patients (39%). Nineteen studies (31 patients; 2%) reported on <5 patients per study. Thirty-six studies (831 patients; 60%) included only patients in whom the aneurysm was unsuitable for surgical clipping or in whom surgical clipping was contraindicated. In 9 studies (578 patients; 42%), well-defined outcome measurements were used; 1 study reported outcome assessment by an independent observer. Two studies specified the level of experience of the endovascular team. The period of follow-up was <1 month in 9 studies (82 patients; 6%), ranging from 1.5 to 24 months in 14 studies (593 patients; 43%), and was not reported in 13 studies (95 patients; 7%). Twelve studies (613 patients; 44%) provided no data on functional outcome or provided data that could not be categorized into the dichotomy of independent (Rankin grade 0 to 2) or dependent (Rankin grade 3 to 5).
Table 1 shows the baseline characteristics of patients treated with controlled detachable coils (Guglielmi detachable coils, mechanical detachable spirals, or interlocking detachable coils), patients from methodologically high-quality studies, patients in each prespecified subgroup, and patients treated with pushable coils. Because many studies provided data on baseline characteristics for the entire series of patients and not by subgroup, we could not extract details on all eligible patients for all of our prespecified subgroups. The numbers of patients included in these subgroups are therefore much smaller than the total number of patients eligible for the subgroups. High-quality studies are those prospective studies that provided detailed data on baseline characteristics and outcome.

**Baseline Characteristics**

Controlled detachable coils were used in 1256 patients with 1310 aneurysms: Guglielmi detachable coils for 1184 aneurysms in 1136 patients, mechanical detachable spirals for 122 aneurysms in 116 patients, and interlocking detachable coils for the treatment of 4 aneurysms in 4 patients. Pushable coils were used in 127 patients with 129 aneurysms.

Twenty-eight patients may have been double-counted, because it was not possible to exclude patients that were described twice in some overlapping studies, in which no individual patient data were provided.

### Table 1. Baseline Characteristics of All Patients Treated With Controlled Detachable Coils (Guglielmi Detachable Coils, Mechanical Detachable Spirals, or Interlocking Detachable Coils), All Patients Treated With Pushable Coils, and Patients Included in the Prespecified Subgroups*

<table>
<thead>
<tr>
<th></th>
<th>Controlled Detachable Coils</th>
<th>High-Quality Studies</th>
<th>Ruptured Aneurysms</th>
<th>Unruptured Aneurysms</th>
<th>Basilar Bifurcation</th>
<th>Pushable Coils</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>1256</td>
<td>204</td>
<td>509</td>
<td>90</td>
<td>185</td>
<td>127</td>
</tr>
<tr>
<td>No. of studies</td>
<td>37</td>
<td>7</td>
<td>14</td>
<td>18</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>No. of aneurysms</td>
<td>1310</td>
<td>209</td>
<td>509</td>
<td>92</td>
<td>185</td>
<td>129</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>51 (p=1246)</td>
<td>49 (p=204)</td>
<td>56 (p=506)</td>
<td>48 (p=83)</td>
<td>49 (p=165)</td>
<td>47 (p=127)</td>
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<tr>
<td>Aneurysm type</td>
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<tr>
<td>Ruptured aneurysms</td>
<td>(a=1236)</td>
<td>(a=209)</td>
<td>(a=509)</td>
<td>(a=92)</td>
<td>(a=177)</td>
<td>(a=129)</td>
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<tr>
<td>Unruptured symptomatic</td>
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<td>Unruptured additional</td>
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<td>Unruptured incidental</td>
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<td>Clinical condition before embolization</td>
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<td>Unruptured</td>
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<tr>
<td>Hunt &amp; Hess 1 to 3</td>
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<td>Hunt &amp; Hess 4 to 5</td>
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<td>Time interval between embolization and SAH</td>
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<td>Embolization within 3 d</td>
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<td>Embolization within 3 to 14 d</td>
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<td>Embolization within 14 to 30 d</td>
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<td>Embolization after 30 d</td>
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<td>Size of aneurysm neck &gt;4 mm</td>
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<td>Aneurysm location</td>
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<tr>
<td>Anterior communicating artery</td>
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<tr>
<td>Pericallosal artery</td>
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<td>Carotid artery</td>
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<tr>
<td>Medial cerebral artery</td>
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<td>Basilar artery</td>
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<td>Vertebral artery</td>
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<tr>
<td>Aneurysm size</td>
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<td>Small</td>
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<td>Large</td>
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<td>Giant</td>
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*p* = number of patients; a, number of aneurysms.

*Because many studies provided data on baseline characteristics for the entire series of patients as a whole and not categorized per subgroup, we could not extract details on all patients eligible for one of our prespecified subgroups. The numbers of patients included in these subgroups are therefore much smaller than the total number of patients eligible for the subgroups. High-quality studies are those prospective studies that provided detailed data on baseline characteristics and outcome.
smaller than the total numbers of patients eligible for the subgroups. In some studies aneurysms <10 mm but in other studies aneurysms <12 or 15 mm were considered small. In all studies, aneurysms >25 mm were considered giant.

**Percentage of Complications, Degree of Aneurysm Occlusion, and Functional Outcome**

Table 2 shows for each patient and treatment group the percentage and type of complications, the degree of aneurysm occlusion, and the functional outcome. Data on permanent complications related to the procedure were available for all patients, but data on the degree of aneurysm occlusion and on functional outcome were not provided for all patients.

There were no statistically significant differences in percentages of permanent complications between the different patient and treatment groups. Treatment with controlled detachable coils resulted in a smaller percentage of aneurysm occlusion but better functional outcome than treatment with pushable coils. Patients with a ruptured aneurysm had a higher percentage of aneurysm occlusion but a worse functional outcome than patients with an unruptured aneurysm. Results in patients with a basilar bifurcation aneurysm were in the same range as those in patients with an aneurysm located elsewhere. Six of 200 patients (3%) with an aneurysm not located at the basilar bifurcation and 10 of 185 patients (5.4%) with a basilar bifurcation aneurysm had a complication resulting in a permanent deficit. Basilar bifurcation aneurysms were less often completely occluded (45%; 95% CI, 37% to 52%) than aneurysms not located at the basilar bifurcation (59%; 95% CI, 50% to 68%). There were only minor differences between basilar and other aneurysms with respect to the proportion of patients with a Rankin grade 0 to 2 at the initial outcome assessment and the proportion of aneurysms occluded >90%.

Exclusion of studies reporting on <5 patients did not essentially alter the results, nor did exclusion of patients treated with controlled detachable coils other than Guglielmi detachable coils.

**Weighted Linear Regression**

Table 3 shows the results of the weighted linear regression analyses. No relation was found between outcome measures and aneurysm size, the aneurysm being ruptured or unruptured, or any other baseline characteristic.

In the subgroup of patients with a ruptured aneurysm, no relation was demonstrated between Hunt & Hess grade before embolization or time interval between SAH and embolization on the one hand with the rate of permanent complications, degree of aneurysm occlusion, or functional outcome on the other.

**Rebleeding After Embolization**

In 16 patients who had presented with SAH before treatment, the aneurysm rebled after embolization. Two patients rebled after an embolization that had been complicated by perforation of the aneurysm; these rebleeds occurred 12 hours and 2 weeks after the procedure.17,13 Two patients had a rebled after incomplete but >90% occlusion at 7 and 20 days after treatment.12 Twelve other patients with incompletely occluded aneurysms (degree of occlusion not reported) had a rebled (3 patients at 4, 10, and 19 days after embolization and 9 patients between 6 and 36 months).29,45

Three patients with unruptured aneurysms had a SAH after embolization. One patient refused further treatment despite major refilling of the body of the aneurysm at 4 months and bled 7 months after treatment.46 In another patient the aneurysm ruptured 24 hours after partial occlusion.19 A patient with an incompletely treated giant aneurysm had a SAH 18 months after embolization.8

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**Table 2. Complication Rate, Degree of Aneurysm Occlusion, and Functional Outcome**

<table>
<thead>
<tr>
<th></th>
<th>Controlled Detachable Coils</th>
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<th>Unruptured Aneurysms</th>
<th>Basilar Bifurcation</th>
<th>Pushable Coils</th>
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<tbody>
<tr>
<td>Complications</td>
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<tr>
<td>Aneurysm perforations</td>
<td>151 (12%)</td>
<td>31 (15.4%)</td>
<td>49 (9.6%)</td>
<td>18 (20%)</td>
<td>30 (16.2%)</td>
<td>25 (19.7%)</td>
</tr>
<tr>
<td>Ischemic perforations</td>
<td>30 (2.4%)</td>
<td>9 (4.5%)</td>
<td>14 (2.8%)</td>
<td>. .</td>
<td>5 (2.7%)</td>
<td>6 (4.7%)</td>
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<tr>
<td>Ischemic complications</td>
<td>107 (8.5%)</td>
<td>17 (8.5%)</td>
<td>34 (6.7%)</td>
<td>15 (16.7%)</td>
<td>18 (9.7%)</td>
<td>17 (13.4%)</td>
</tr>
<tr>
<td>Permanent complications</td>
<td>46 (3.7%)</td>
<td>11 (5.5%)</td>
<td>12 (2.4%)</td>
<td>6 (6.7%)</td>
<td>10 (5.4%)</td>
<td>9 (7.1%)</td>
</tr>
<tr>
<td>Aneurysm occlusion</td>
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<tr>
<td>&gt;90%</td>
<td>654 (87.9%)</td>
<td>182 (87.1%)</td>
<td>477 (93.7%)</td>
<td>72 (82.8%)</td>
<td>151 (87.8%)</td>
<td>85 (97.7%)</td>
</tr>
<tr>
<td>100%</td>
<td>400 (53.8%)</td>
<td>127 (60.8%)</td>
<td>264 (51.9%)</td>
<td>39 (44.8%)</td>
<td>77 (44.8%)</td>
<td>68 (78.2%)</td>
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<tr>
<td>Follow-up</td>
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<tr>
<td>Independent (Rankin grade 0 to 2)</td>
<td>510 (89.6%)</td>
<td>175 (89.7%)</td>
<td>83 (89.2%)</td>
<td>71 (97.3%)</td>
<td>105 (90.5%)</td>
<td>89 (76.7%)</td>
</tr>
<tr>
<td>Dependent (Rankin grade 3 to 5)</td>
<td>29 (5.1%)</td>
<td>7 (3.6%)</td>
<td>3 (3.2%)</td>
<td>1 (1.4%)</td>
<td>4 (3.4%)</td>
<td>11 (9.5%)</td>
</tr>
<tr>
<td>Deceased</td>
<td>30 (5.3%)</td>
<td>13 (6.7%)</td>
<td>7 (7.5%)</td>
<td>1 (1.4%)</td>
<td>7 (6.0%)</td>
<td>16 (13.8%)</td>
</tr>
<tr>
<td>Procedure related</td>
<td>6 (1.1%)</td>
<td>4 (2.1%)</td>
<td>1 (1.1%)</td>
<td>0 (0%)</td>
<td>1 (0.9%)</td>
<td>4 (3.4%)</td>
</tr>
</tbody>
</table>

p indicates number of patients; a, number of aneurysms.
The results in the prespecified subgroups indicate that embolization with coils is a reasonably safe procedure with a low complication rate not only in patients with a ruptured aneurysm but also in patients with an unruptured aneurysm and in patients with a basilar bifurcation aneurysm.

Weighted linear regression analyses of outcome measures with aneurysm type, clinical condition before embolization, aneurysm size, and aneurysm neck size did not show any relation that was statistically significant, but the limited numbers of patients included in these analyses preclude definite conclusions. We studied only short-term results. Larger aneurysms with wider necks may show a higher rate of recanalization and therefore more often need an additional treatment to prevent rupture in the long-term, but this topic was beyond the scope of our study.

The less successful aneurysm occlusion in patients with an unruptured aneurysm is probably related to the larger aneurysm size in these patients compared with the aneurysm size in patients with a ruptured aneurysm. Large or giant aneurysms have wider necks than small aneurysms, which increases the risk of coils herniating into the parent vessel and makes successful occlusion more difficult to achieve.19,23,29

Compared with patients treated with controlled detachable coils, functional outcome was worse in patients treated with pushable coils, which might be related to the higher proportion of patients with an unruptured symptomatic aneurysm. An important limitation of this study is the large number of patients treated with pushable coils, which might not be acceptable in everyday clinical practice.
and to the relatively high rate of permanent complications in these patients. Pushable coils cannot be withdrawn or repositioned when placed incorrectly and are now replaced by controlled detachable coils, which can be retrieved or repositioned if necessary. Although aneurysms were larger in patients treated with pushable coils, the rate of successful aneurysm occlusion was higher than in patients treated with controlled detachable coils. The data on patients treated with pushable coils, however, should be interpreted with some caution, because 71 of 127 patients (56%) treated with pushable coils were derived from a single center with much expertise in endovascular treatment.

In the regression analyses, we used the percentage of aneurysms occluded >90% as outcome measure and not the percentage of completely occluded aneurysms because complete occlusion was not always an aim, eg, when vessels originated from the neck of the aneurysm or when the aneurysm had a wide neck with inherent risk of herniation of coils into the parent vessel. In these instances a 90% to 99% occlusion is not a treatment failure.

Our study has some weaknesses. First, selective submission and acceptance of studies with good results over studies with poor results may have caused publication bias and an underestimation of the complication rate. To minimize publication bias, we included studies in languages other than English from all journals. Many studies included in our review were retrospective and showed methodological weaknesses. The finding that the rate of complications with a permanent deficit in the prospective high-quality studies was in the same range as the overall permanent complication rate indicates that the lower methodological quality of many studies has not introduced serious bias. Second, data on baseline characteristics and outcome were often only provided for the whole group and not per patient or per subgroup. This weakens our results for the subgroups because these are necessarily based on only a part of all patients in that subgroup. Moreover, the lack of a detailed description at baseline precluded the performance of multivariate regression analyses in which we could deal with baseline differences between groups. Third, studies reported on embolization with different types of coils. We separately analyzed results in patients treated with pushable coils and in patients treated with any type of controlled detachable coils. Exclusion of patients treated with mechanical detachable spirals or interlocking detachable coils did not essentially alter the results, which indicates that there are no gross differences between treatment with Guglielmi detachable coils or other types of controlled detachable coils with regard to complication rate, degree of aneurysm occlusion, and functional outcome. Fourth, our study concerned a newly developed treatment. During the study period of studies included in this review, many endovascular therapists probably still were on the steep part of the learning curve with regard to embolization of aneurysms with coils. With increasing experience, both completeness of occlusion and clinical results are expected to improve.

Comparisons between endovascular and surgical series should be made with caution because of the wide heterogeneity in study design, patients, and aneurysms. Most patients treated with coils were poor surgical candidates because of poor medical condition, anatomic considerations, or failed surgical exploration. If comparisons are made, both completeness of aneurysm occlusion and functional outcome should be considered. In a recent series of 66 patients with ruptured aneurysms and 12 additional aneurysms treated by surgical clipping, the total percentage of unexpected residual aneurysms and totally unclipped aneurysms on postoperative angiograms was 8%. The percentage of aneurysms occluded <90% immediately after embolization with controlled detachable coils was 13%. The long-term completeness of occlusion after coiling is still unknown.

Our review indicates that treatment with coils is worth considering for patients with an unruptured aneurysm; we found that embolization with coils has a permanent complication rate of 7%. In a recent review on operation of unruptured aneurysms, morbidity was 11% and mortality 3%. Of course, the risk of treatment must be weighed against the risk of rupture of the aneurysm.

Our study shows that embolization with controlled detachable coils is an appropriate treatment for patients with an aneurysm unsuitable for surgical clipping or in whom surgical clipping is contraindicated. For patients with aneurysms suitable for both clipping and coiling, randomized trials are warranted to assess which of these modalities should be the preferred initial treatment.

Acknowledgments
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Treatment of Intracranial Aneurysms With Coils


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