Feasibility, Procedural Morbidity and Mortality, and Long-Term Follow-Up of Endovascular Treatment of 321 Unruptured Aneurysms

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BACKGROUND AND PURPOSE: The purpose of our study was to evaluate the technical feasibility, morbidity and mortality, and durability of occlusion of unruptured aneurysms treated with Guglielmi detachable coils (GDCs) with a long-term follow-up.

MATERIALS AND METHODS: Between January 1998 and January 2005, we treated 321 unruptured aneurysms with GDCs in 5 neuroradiologic institutions. During this period, 63% of unruptured aneurysms were treated by endovascular technique. Procedural feasibility, technical complications, morbidity and mortality, and acute and long-term angiographic occlusion were assessed.

RESULTS: Overall technical feasibility of coiling treatment was 94%; 302 aneurysms were treated by endovascular technique. At the end of the initial procedure, acute occlusion was classified as complete in 207 cases (70%), subtotal in 84 cases (26.1%), and incomplete in 11 cases (3.9%). Ischemic complications were observed in 28 patients (9%); 8 patients (2.6%) had perforation of their aneurysms. Treatment-related morbidity was 14.4%, and morbidity with clinical complications was evaluated at 7.7% (n = 23 patients). Five patients (1.7%) died as a result of aneurysm perforation. Final follow-up angiograms, after 9 secondary treatments, demonstrated complete occlusion in 193 patients (69.5%), subtotal in 80 aneurysms (28.5%), and incomplete occlusion in 5 (1.8%). Nineteen patients were lost to follow-up (6.3%).

CONCLUSION: Endovascular coiling with detachable coils is an attractive option for treatment of unruptured aneurysms. This method of treatment is safe with a low rate of complications. Prospective studies with longer follow-up periods are needed to assess the long-term durability of occlusion in unruptured aneurysms.

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symptomatic aneurysms may be defined as incidental aneurysms found in patients with a symptomatic aneurysm (which are not responsible for the clinical presentation), patients imaged for reasons unrelated to aneurysms who happen to have an incidental aneurysm that was completely unexpected, and those found in patients investigated because they are at risk of harboring an aneurysm (familial aneurysm disease, polycystic kidney disease).1-3 Incidental unruptured aneurysms are defined as those found unexpectedly in patients undergoing investigation for other suspected pathology.

The management of unruptured aneurysms may include observation, surgery, endovascular embolization, or a combination of these. Since 1991 and the introduction of detachable coils and more recently the results of the International Subarachnoid Aneurysm Trial,4,5 endovascular treatment is an accepted alternative to surgical treatment of intracranial ruptured aneurysms. The question remains, however, as to which treatment offers the better outcome and what risks are involved. Surgical treatment, which has been in use for more than 40 years, has fairly clearly defined risks and morbidity.6 Endovascular treatment appears to offer lower risks but is still developing. Most recent evidence on the relative risks of treatment and of observation comes from the International Study of Unruptured Intracranial Aneurysms (ISUIA).7 The treating physician must weigh the natural history of aneurysms and the potential consequences of subarachnoid hemorrhage (SAH) with the efficacy, morbidity, and mortality of the intervention. Ideally, the morbidity and mortality rate of endovascular treatment should be lower than that of the natural history rupture rate. A measure of complications caused by the treatment itself would be ideal so that the impact of therapy could be isolated from other aspects of presentation or medical care.

Materials and Methods

From January 1998 to January 2005, we prospectively collected the results of nonruptured aneurysms treated with Guglielmi detachable coils (GDCs; Boston Scientific/Neurovascular, Fremont, Calif) in 5 neuroradiologic centers. During this period, 480 patients with unruptured aneurysms were referred to our institution. The decision to treat, especially in small aneurysms (<5 mm), depended on a full assessment of the patient (including life expectancy and their wishes) and an assessment of the risks and efficacy of the intervention. The selection criteria included the size, shape, location of aneurysms, and the patient’s clinical condition and wishes. The assignment of patients to methods of treatment was made in a joint meeting of neurosurgeons and neuroradiologists. In this population of patients, 321 aneurysms (63%) in 290 patients were considered for endovascular treatment.

Endovascular treatment was performed by 5 experienced physicians. Each physician had at least 5 years’ experience with endovascular coiling. Endovascular management for all patients treated as part
of this study series was similar in technique and approach. All aneurysms were embolized with the same type of coils (GDC 10 or 18). We have used GDC 18 for aneurysms >15 mm and for giant aneurysms. In this study, only GDC coils were used. Sometimes, in cases in which the balloon remodeling technique was used, a nondetachable balloon was placed at the aneurysm neck. At this time, we did not use the intracranial stent-assisted coil packing technique.

Procedure

Once endovascular treatment was determined as the best treatment alternative, patients were placed under general anesthesia. A femoral puncture was used as the first choice in all patients except 2, in whom a direct carotid puncture was used due to vessel tortuosity. A 6F introducer was placed in the femoral artery by using the Seldinger technique and bilaterally when the remodeling technique was used. Heparin was administered as an intravenous bolus to achieve an activated clotting time approximately 2 times that of normal (perfusion of heparin 20 × International units per kilogram of body weight divided by height) with intravenous infusion of 250 mg of aspirin.

Prevention of proximal vasospasm was done by perfusion of papaverine through a guiding catheter into the carotid or vertebral artery (240 mg of papaverine diluted into 500-mL physiologic serum). A 6F guiding catheter was selectively placed in the artery supplying the aneurysm. Once the optimal angiographic projection was defined, aneurysm catheterization was performed by advancing a microcatheter over a microwire. Coils were placed through the microcatheter into the aneurysm and detached under fluoroscopy. This process was repeated until the aneurysm was occluded as densely as possible.

In all cases, coil size, coil type, and the total number of coils used were recorded. Procedural complications were also recorded. Anticoagulation was routinely continued for the first 48 hours postprocedure.

Immediately after the procedure, digital subtraction angiography was performed to assess the degree of aneurysmal occlusion. Angiograms were collected prospectively in all patients. The degree of aneurysmal occlusion was scored by 2 independent neuroradiologists: each doctor independently evaluated and graded each angiogram into the aneurysm sac (and neck were densely packed, subtotal occlusion when a neck remnant appeared, and an incomplete occlusion when loose packing and partial opacification were noted.

Since 2002, all aneurysm measurements were performed on diagnostic angiograms that best displayed the neck region in relation to the parent artery and the 3D projection.

Follow-Up

Each patient was scheduled for follow-up angiography by digital subtraction angiography (DSA) and by MR imaging at 3–6 months, 12 months, and yearly thereafter with MR angiography (MRA).10 Multiple projections with selective injections served to define any residual lesions. When DSA and MRA were twice subsequently concordant, the patient would undergo an annual MRA and control DSA every 2 years. In the case of discordance of results or in patients with a potential risk of coil compaction, additional follow-up angiography was performed. All angiograms were evaluated by 2 neuroradiologists independent of the treating neuroradiologists.

The qualitative and quantitative variables tested included patient baseline characteristics, aneurysm variables, and therapeutic and posttherapeutic factors. Patients were characterized by age, sex, initial symptoms, aneurysm morphology (size, location), and number of aneurysms. Treatment feasibility was assessed and included coil characteristics such as total number of coils used, coil size, use of a nondetachable balloons, technical complications, and immediate posttreatment aneurysm occlusion.

Results

Patients and Clinical Data

Patients ranged in age from 18 to 77 years (mean age, 49 years), and 63% were female (sex ratio, 2/1). Clinical presentation and symptoms, aneurysm location, size and shape of the aneurysm sac, and patient age were considered before treatment. The location of treated aneurysms is detailed in Table 1. Aneurysms located in the anterior circulation represented 90% of all aneurysms treated (n = 292). Patients were classified into 2 groups: Group 1 consisted of patients in whom previous treatment of SAH was performed, and group 2 consisted of patients with no prior history of SAH (Table 1). Within this population, distinction was assessed between incidental formation, mass effect, familial form, dysplastic disease, stroke, and association with brain disease. One hundred seventy-nine patients (55%) had aneurysms discovered incidentally during MRA for unrelated medical conditions. Forty-seven (14.6%) had a previous history of SAH, with treatment of the ruptured aneurysm during the acute phase.

Size of Aneurysms. Aneurysms <5 mm (n = 99) represented 31% of all patients, 46% (n = 149) of patients had aneurysms measuring between 5 and 9 mm, 11.8% (n = 38) of aneurysms measured between 10 and 14 mm, 7% (n = 24) of aneurysms measured between 15 and 19 mm, and 3% were considered giant (n = 11). Aneurysms <10 mm represented 77% of all aneurysms in this series. Dome-to-neck ratios were not noted for all aneurysms; the balloon remodeling technique was used in the treatment of 54 aneurysms (17%).

Feasibility and Efficacy of Treatment. Treatment was successful in 302 aneurysms. In 19 aneurysms (6%), treatment failed due to tortuosity of cerebral anatomy (n = 5) or instability of coil deployment (n = 6) and a large neck with a small sac (n = 8). Some patients were referred to a neurosurgeon for surgical clipping (n = 16), and the others were followed with MRA. The procedural feasibility of occlusion with coils was 94% in our study.

Table 1. Clinical presentation of patients

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<th>Diagnosis</th>
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| Incidental dysplastic disease     | 179| 55.76%
| Vascular dysplasia                | 3  | 0.93%
| Polycystic kidney disease         | 7  | 2.18%
| Familial                          | 10 | 3.12%
| Mass effect                       |    |       |
| Headache                          | 47 | 14.64%
| Nerve compression                 | 11 | 3.43%
| Eye pain                          | 1  | 0.31%
| Vertigo                           | 2  | 0.62%
| Brain disease                     |    |       |
| Stroke                            | 8  | 2.49%
| Tumor                             | 4  | 1.25%
| Arteriovenous malformation        | 2  | 0.62%
| History of SAH                    |    |       |
| Another aneurysm                  | 47 | 14.64%

SAH indicates subarachnoid hemorrhage.
**Immediate Posttreatment Results.** At the end of the initial procedure, occlusion was classified as complete or total occlusion in 207 patients (68.5%), subtotal in 84 patients (27.8%), and incomplete in 11 patients (3.7%). During follow-up, a second coil intervention was performed in 9 aneurysms because of an initial incomplete occlusion or secondary coil compaction.

**Complications and Technical Failure**

We make a distinction between treatment-related morbidity (ie, clotting, rupture, device abnormalities, hemorrhagic shock) and the overall morbidity including the permanent neurologic sequelae after treatment.

The most significant complication of endovascular therapy is technical failure, which exposes the patient to the risks of the procedure without offering any benefit of aneurysmal occlusion.

Ischemic complications were observed in 28 patients (9%) during embolization. Twelve patients experienced coil migration into the parent vessel, inducing a thromboembolic event resulting in ischemic disease in 5 patients (Glasgow Outcome Scale [GOS] 2 for n = 3, and GOS 3 for n = 2). Seven patients had a good recovery (GOS 1).

Fifteen patients had angiographic evidence of clotting without protrusion of a coil, 7 of them recovered after fibrinolysis perfusion, 2 had artery occlusion (GOS 3 for 2 patients), and 6 had small cerebral infarcts seen at 3-month MR imaging (GOS 2). In our experience, the balloon remodeling technique was used in 17% of the patients. We did not observe more complications with this technique of treatment.

One patient had a carotid dissection with occlusion of the artery; 1 carotid stent (Wallstenst; Boston Scientific, Natick, Mass) was rapidly deployed into the artery. Arterial polygon was not sufficient to assure the cerebral perfusion, and the patient had an serious cerebral infarct with clinical hemiplegia (GOS 3).

Perforation of the targeted aneurysm occurred in a total of 8 patients (2.6%), 3 of which occurred during catheterization and 5 of which occurred during deployment of the first coil. The coil was pushed rapidly into the aneurysm. All intraprocedural ruptures were managed with a systemic protamine injection for heparin reversal, and coils were pushed rapidly into the aneurysms. Perforation is the most serious complication that may occur during embolization. Total procedural deaths occurred in 5 patients, and 3 ruptures had no clinical consequence for patients (GOS 1). We did not observe any rupture during the procedure with the balloon. Coil stretching occurred in 5 patients without clinical complication in all. Morbidity of technique was evaluated at 14.4% for all procedures performed. Permanent neurologic morbidity was evaluated at 7.7% (n = 23 patients). One patient had an ophthalmic artery spasm with transient visual symptoms caused by a microguidewire. One patient had an important orbital neuroglia because of a giant carotid ophthalmic aneurysm with mass effect.

**Mortality of Endovascular Treatment.** Five patients (1.7%) died as a result of aneurysm perforation. Three had hematoma and SAH during the procedure. Coils were rapidly deployed, and heparin was immediately reversed. However, the hematoma was extensive, and the patients died of intensive increase of intracranial pressure. One patient had a hemorrhagic shock with tachycardia, adrenergic reaction, and serious arrhythmic trouble. He was shocked on the table, but all reanimation was unsuccessful. One patient had a perforation of lenticulostriatal artery, due to the microguidewire, during the procedure without change of arterial blood pressure or arrhythmic trouble. Complete embolization was achieved, and an immediate CT was performed showing a hematoma. Despite immediate surgical evacuation, the patient died in the intensive care unit 5 days later. Overall mortality of endovascular treatment was 1.7% for our series of unruptured aneurysms.

**Evolution of Occlusion (Table 2)**

**Evolution of the 207 Aneurysms with Total Occlusion.** At follow-up angiographic examination, 160 aneurysms (77.2%) remained completely occluded with no modification of the initial packing observed. A small recurrence was observed in 28 patients (13.5%) between 3 months and 2 years after initial treatment. A coil compaction with a remnant was observed in 4 cases (1.9%). These patients underwent a second embolization. Thirteen patients (6.2%) were lost to follow-up. Two patients died as consequences of aneurysm rupture during the embolization procedure.

**Evolution of 84 Aneurysms with Subtotal Occlusion.** In 45 patients (53.5%), no modification of the initial occlusion was noted. In 30 patients, spontaneous thrombosis (35.7%) of the sac of the aneurysm resulting in a total occlusion was observed. A coil compaction with a remnant was observed in 2 patients. Four patients were lost to follow-up, and 3 died.

**Evolution of 11 Aneurysms with Incomplete Occlusion.** In the 11 initial incompletely occluded aneurysms, 3 patients received a second embolization to ameliorate coil packing in the sac. Three aneurysms had spontaneous amelioration of packing due to thrombosis, and 2 patients were lost to follow-up. In 3 patients, multiple angiogram follow-ups were performed, and no modification of occlusion was observed. These patients did not undergo a second procedure because the procedure was considered more “dangerous” than the natural evolution. These patients were scheduled for regular follow-up.

**Second Procedures.** Despite an initial total occlusion, rechannelization-inducing second procedures were performed in

![Table 2. Evolution of occlusion during follow-up](image-url)
4 aneurysms totally occluded and in 2 aneurysms with subtotal initial occlusion. In our series, a second treatment was performed in 9 (3.2%) patients (6 recanalizations and 3 initial incompletely occluded aneurysms) between 3 months and the 2 first years’ post-initial treatment. Retreatment in this series is calculated at 3.2%, considering all follow-up procedures. Of these, total occlusion was achieved in 2; subtotal, in 5 aneurysms; and incomplete, in 2 cases.

**Discussion**

**Natural History of Unruptured Aneurysms**

Results from ISUIA² represent the largest study of the natural history of unruptured aneurysms to date and include 2621 patients from 53 centers. In patients without a history of hemorrhage, aneurysms <10 mm have an annual 0.05% rupture rate, those >10 mm have an approximate 1% rupture rate, and giant aneurysms have a 6% rupture rate. This rate may increase in patients with a SAH from a different aneurysm; this rate is 0.5% for small aneurysms and 1% for those >10 mm. The overall mortality rate is 66% when aneurysms rupture. Five-year cumulative rupture rates for patients who did not have a history of SAH with aneurysms located in the internal carotid artery, anterior communicating, or anterior cerebral artery or middle cerebral artery were 0%, 2.6%, 14.5%, and 40% for aneurysms <7 mm, 7–12 mm, 13–24 mm, and 25 mm or greater, respectively. For the same size categories involving posterior circulation, the rates were 2.5%, 14.5%, 18.4%, and 50%, respectively. In 2003, Wiebers et al¹¹ reported that aneurysm size and location are important predictors of rupture risk: The overall rupture rate was 0.8% per year. For Juvela et al,¹² the constant rupture rate was 1.3% annually during 30 years of follow-up, and there was a 52% mortality rate with aneurysmal rupture.

Surgical management of aneurysms is the traditional gold standard intervention because it completely excludes aneurysms from the circulation, with little possibility of recurrence. Evaluating the efficacy and utility of endovascular treatment for unruptured aneurysms is challenging because of the inherent selection bias in reports and different management across institutions. Furthermore, evaluating an unruptured aneurysmal population treated by endovascular approach is the better way to precisely define the efficacy, morbidity, and mortality of the technique.

**Comparison with Other Series**

A multicentric study¹³ including 2069 patients treated in California from 1990 through 1998 compared endovascular treatment with surgery. Morbidity was found to be less in those treated with endovascular therapy and 10% versus 25%, with surgery; and mortality was also found to be less with endovascular therapy, 0.5% versus 3.5%. In this series, all posttreatment ruptures occurred in patients who were surgically clipped during 6738 person-years of follow-up, for an overall annual rupture rate of 0.2% after surgery. In another comparative study presented by Johnston et al,¹⁴ the morbidity rate for the surgical group was 18.5% versus 10.6% for endovascular treatment, and the mortality rate was 2.3% and 0.4%, respectively. Moreover, the total length of the hospital stay was longer, and hospital charges were greater for surgical patients.¹³-¹⁶

“Recommendations for Endovascular Treatment of Intracranial Aneurysms” in 2002²² concluded that “endovascular occlusion is a viable treatment option for aneurysms” and results of a randomized trial are necessary to establish the relative indications of these 2 approaches. Niskanen et al¹⁸ compared results and complications of endovascular and surgical treatment and reported that complications were more common in the surgical group than in the endovascular group. One patient died postsurgery, but no death occurred after endovascular treatment. Higashida et al⁶ in a retrospective cohort study, using data from 429 hospitals in 18 states (2535 aneurysms), showed a procedural mortality <1% for the endovascular treatment (654 procedures) versus 2.5% for neurosurgical treatment.

Rafopoulos et al¹⁹ is the only one to conclude that surgery can produce better results than embolization in patients with unruptured aneurysms of the anterior location. In 38 patients treated by endovascular therapy, 10% had transient complications and 7.5% had permanent complications versus 16.3% and 1.7% for surgery. Our series does not include the same selection of aneurysms treated.

Wanke et al²⁰ reported results of 39 patients with unruptured aneurysms, in which there was only 1 case of thromboembolic vessel occlusion and no aneurysm rupture. For Park et al,²¹ in 180 consecutive patients with 79 procedures for 72 unruptured aneurysms, the rate of procedural complications was 8.3%, which resulted in thromboembolism for 5 patients, of whom 1 died and 1 had cranial nerve palsy. More recently, in the 247 aneurysms reported by Gonzalez et al,²² the technical failure rate was 5.7%, the morbidity rate was 5.5%, and mortality rate was 0.9%. Their population contained elderly patients, who are more sensitive to general anesthesia and have more clinical complications. In their study, Pouratian et al²³ observed a 4.8% technical failure rate with an overall morbidity of 8.6% at 3 months and no mortalities. In the study of Park et al,²¹ procedure-related neurologic morbidity and mortality were 1.4% and 1.4%, respectively, for unruptured aneurysms. The main cause of morbidity and mortality was thromboembolism with 60% of all complications.

In our multicentric consecutive series, overall complications were 14.4%, with 7.7% morbidity and 1.7% mortality.
The remodeling technique was used in 17% of patients without higher complication rates, unlike the rate that Sluzewski et al. had suggested in a recent published series. We reported 5 deaths with this treatment, all due to technical failure and aneurysm perforation. Our overall mortality rate was less than 2%. Our results are consistent with those reported in the literature concerning rates of complications and morbidity and mortality. Unlike the results of Park et al., our results show that thromboembolic strokes were more frequent than rupture but were considered less dangerous and could be treated by fibrinolysis. To evaluate the frequency and causes of thromboembolic events after coiling procedure, Grünwald et al. performed diffusion-weighted MR imaging before and after the procedures to compare new hyperintense lesions. New hyperintense lesions were found in 42% of patients, with no correlation with aneurysm size or location. These new lesions on MR imaging are not automatically responsible for stroke. Mortality was 0% and morbidity, 4%. Despite these complications, most authors concluded that endovascular management is a relatively safe procedure for aneurysm treatment. We agree with this opinion.

For follow-up of these aneurysms, we propose an MRA and DSA examination between 3 and 6 months and 1 year after treatment. When occlusion is considered complete and remains stable, we propose follow-up by MRA each year and by angiography at different intervals. When occlusion is considered complete and re-DSA examination between 3 and 6 months and 1 year after treatment. When occlusion is considered complete and re-

In 2003, the study by Wiebers et al. suggested that patients with unruptured cerebral aneurysms < 7 mm in diameter have a benign natural history. Weir, who is neurosurgeon, has observed a substantial proportion of patients with SAH due to small ruptured aneurysms. In a multicentric ruptured series, 50% of aneurysms were < 5 mm. In reality, it seems difficult to limit treatment to aneurysms > 7 mm.

Conclusions
Detachable coil technology has permitted the safe treatment of 321 unruptured aneurysms in our series, with low complication rates and < 2% mortality. Stability of occlusion was 71.5%, and spontaneous improvement of occlusions was 10.6%.

Endovascular therapy for all patients considering treatment of unruptured aneurysms should be offered as a viable therapeutic option. Prospective studies with longer follow-up periods are needed to assess the long-term durability of occlusion in unruptured aneurysms.

References