

# ENDOVASCULAR THERAPY FOR INTRACRANIAL ANEURYSMS: A HISTORICAL AND PRESENT STATUS REVIEW

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Beginning in the 1960s, neurosurgeons and radiologists have made attempts to treat intracranial aneurysms using nonclip techniques. The evolution of such therapy has included acrylics, metallic particles, balloons, electric current, and nondetachable and detachable coils. This article will chronologically review these various techniques and the papers that reported their results so that the reader can understand how endovascular therapy developed and the position it currently holds in the treatment of intracranial aneurysms. © 2002 by Elsevier Science Inc.

## KEY WORDS

*Intracranial aneurysms, endovascular therapy, history, coils.*

As we prepare to enter the new millennium and exit the Decade of the Brain, neurosurgeons treating neurovascular disease must be acutely aware of the changing landscape of aneurysm therapy. As new interventional procedures develop, traditional concepts of aneurysm treatment are being challenged by a group of radiologists and neurosurgeons who seek to occlude these lesions through endovascular routes. Familiarity with early works relating to endovascular and non-traditional exovascular aneurysm therapy is important if we are to understand the foundation on which the growing specialty of endovascular neurosurgery is built. Such knowledge also provides practitioners with a

new view of past ideas that may become pertinent in the future. The goal of this review is not to include all papers published on the topic of endovascular aneurysm therapy, but rather to provide the reader with a chronological framework for understanding the field's evolution to its current status so that future treatment can be anticipated and proposed.

## 1960s

In 1964 Luessenhop and Velasquez tried to occlude an aneurysm by advancing a silicon balloon into a supraclinoid carotid lesion. Although this treatment was unsuccessful, it represented the first attempt by a neurosurgeon to treat an aneurysm using an endovascular technique [44]. In 1965 Alksne and Fingerhut reported their experimental findings using a magnet and 3 micron diameter carbonyl iron spheres suspended in 25% polyvinyl pyrrolidone to occlude arteries and aneurysms [2]. Using a magnet applied to the external surface of a dog femoral artery and an aneurysm pouch made on a dog femoral artery these authors injected their iron particle suspension into the descending aorta via a catheter and occluded the vessel beneath the magnet in one experiment and the aneurysm pouch in another. In 1969, Alksne and Rand published their results relating to metallic thrombosis of aneurysms in 9 patients [3]. Three patients had partial aneurysm occlusion. In one of these, the aneurysm reruptured; another suffered a middle cerebral artery occlusion secondary to an embolus. Six patients had complete aneurysm occlusion. Three Hunt and Hess

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Grade 1 patients did well. One Hunt and Hess Grade 3 patient failed to recover and two Hunt and Hess Grade 4 patients suffered posterior cerebral artery strokes secondary to vessel thrombosis after aneurysm occlusion. While Alksne experimented with iron as an embolic agent to occlude aneurysms, Mullan in Chicago concentrated on the concept of aneurysm thrombosis using electric current. In 1964 and 1965 he and others in his group reported their initial work involving the direct and stereotactic insertion of needles and copper wires transfundally into ruptured and unruptured aneurysms [51, 52]. Once the aneurysm was punctured, 200 to 2,000 milliamps would be applied to the electrode for 1 to 2 hours. Arteriograms performed every 30 minutes charted the progress of thrombus formation within the fundus. Of 12 patients reported in the 1965 paper, one worsened after the procedure (8.3%). No rebleeding occurred at 6 to 14 months follow-up, although 3 patients required surgical clipping for aneurysm recurrence. While this therapy offered an alternative to surgical clipping, the authors felt that control of the degree of thrombosis was exceedingly difficult.

## 1970s

In 1973 Serbinenko expanded Luessenhop and Velasquez's concept and selectively obliterated an aneurysm using a latex balloon. In 1974 he reported two additional cases of aneurysm treatment using detachable balloons [68]. While Sebinenko continued his pioneering balloon work in Russia, Mullan in 1974 reported his additional experience using electrothrombosis to treat 61 aneurysms [53]. In this series he reported a 6.5% procedural death rate secondary to bleeding or excessive thrombosis and a 3.2% stroke rate. In 1977, Alksne and Smith described their experience embolizing a posterior communicating artery aneurysm with carbonyl iron and methylmethacrylate introduced stereotactically into the aneurysm fundus [4]. This report provided no details regarding the procedure itself or the patient outcome. While Alksne used iron as an embolic agent, Sheptak reported a series of 20 patients whose aneurysms were treated by injecting isobutyl-2-cyanoacrylate into the fundus under direct visualization or using stereotactic technique [69]. Sixteen patients achieved good to excellent results, 2 worsened, and 2 died (1 death occurred 3 years after the procedure). Eighteen patients had follow-up arteriography 10 to 14 days after the procedure. Seven had complete occlusion and 11 had incomplete occlusion. Two patients rehemorrhaged

within 1 month of treatment and were found at surgery to have bled from an unoccluded portion of the lesion. Both recovered in good to excellent condition. In 1978, Debrun described his results using balloons to treat 14 carotid siphon aneurysms [13]. Eight lesions were successfully treated, with parent vessel preservation in 5. Three patients died and 2 suffered post-procedural hemiplegia.

## 1980s

In 1981, Debrun reported 9 cases of aneurysms treated using detachable balloons placed in proximal parent vessels [15]. In 1982 Romodanov and Shcheglov reported 137 intravascular occlusions of saccular aneurysms using detachable balloons [25]. Fifteen patients had parent vessel occlusion and 93 had selective fundal obliteration with parent vessel preservation. Three patients were reported to have aneurysm recanalization and 3 patients died from vessel thrombosis. In 1984 Berenstein described 9 cavernous aneurysms, one vertebral aneurysm and 1 posterior inferior cerebellar artery aneurysm that were treated with proximal vessel balloon occlusion [7]. One embolic complication was reported. Hieshima and Higashida reported cases of balloon embolization of aneurysms in 1987 and 1988 [25]. In 1989 these authors published their group's experience with 26 aneurysms treated using balloon embolization [27]. Sixty-five percent of the cases had selective aneurysm occlusion with parent vessel sparing while the remainder had parent vessel sacrifice. Complications included an 11% incidence of transient ischemic events, 11% incidence of stroke, and 20% incidence of death secondary to immediate or delayed aneurysm rupture.

## 1990s

The use of balloons for aneurysms was again reported by Higashida in 1990. In this paper the author described his group's use of balloons to manage 87 cavernous carotid artery aneurysms between 1981 and 1989 [28]. Seventy eight percent of these patients had their internal carotid artery occluded across or just proximal to the aneurysm neck while 22% had selective aneurysm occlusion and vessel preservation. All patients who had vessel sacrifice had partial or complete symptom alleviation and aneurysm thrombosis. Sixty-three percent of selectively embolized aneurysms were occluded at follow-up and 37% had more than 85% thrombosis. Stroke rate was 4.6%. Other reports from the 1990s regarding the use of detachable

balloons included Scheglov's 725 cases, Serbinenko's 267 cases, George's 92 cases, and Hodes' 16 cases [25]. Good results in these series ranged from 43–80%. Mortality rates were 5–8% and neurologic morbidity was less than 10%. In 1991 Moret also reported his results with attempted balloon treatment of 128 aneurysms. Of 101 treated lesions 91 had selective placement of the balloon within the fundus and 10 had aneurysm and parent vessel occlusion. Eighteen recurrences were recorded in the selective group (20%). Six of these were successfully retreated. Four patients died from post-procedural hemorrhage and 10 patients suffered neurologic deficits secondary to thrombi and emboli [49].

Endovascular therapy for aneurysms shifted focus in the 1990s from balloon occlusion to platinum coil occlusion. This shift grew out of dissatisfaction with the ability of balloons to adequately fill a complex geometrical shape without either leaving unprotected fundus or creating a ball valve system of aneurysm refilling. It was also spurred on by the development of catheters and guidewires that allowed safe, selective catheterization of the neck and fundus, thus permitting delivery of highly pliable coils that easily and atraumatically assumed the shape of the aneurysm thus permitting more complete occlusion. In 1990 and 1991 Dowd, Arnaud and Higashida selectively embolized intracranial aneurysms using platinum coils [16,25,29]. The single greatest problem with platinum minicoil insertion, however, remained the inability to control the embolic agent once it was pushed out of the catheter and into the aneurysm. Inadvertent migration of these highly thrombogenic devices into distal vasculature made their use for embolization of aneurysms a dangerous procedure.

In 1991 Guido Guglielmi, an Italian neurosurgeon revolutionized the endovascular treatment of aneurysms by introducing a device that permitted introduction of platinum coils into the aneurysm fundus with relative security [22]. Guglielmi's invention of Guglielmi detachable coils (GDC) permitted the interventionalist to place a coil attached to a stainless steel guide wire into an aneurysm and consider its position and effectiveness. Once the physician was satisfied with the coil's position an electric current was applied to the portion of the guide wire that remained in the operator's hand outside the femoral sheath. The electric current would electrolytically dissolve the connection between the guide wire and the platinum coil, thus separating the two and releasing the coil from its tether. Once this was achieved the guide wire was removed and another coil advanced into the aneurysm fundus. The pro-

cess was repeated until the aneurysm no longer opacified on follow-up arteriograms. In addition to electrolytically releasing the coil, Guglielmi felt that the positive current promoted thrombosis within the fundus by attracting negatively charged blood elements such as red blood cells, white blood cells, platelets, and fibrinogen. He based this belief on earlier work by Mullan (see previous section) and Araki [29]. In the same journal issue in which Guglielmi published his experimental work on GDC he published his group's results in 15 patients treated in 1990 [22]. The new system achieved immediate 70 to 100% intra-aneurysmal occlusion. There were no peri-procedural strokes or deaths and only one case of transient aphasia. In 1992 Guglielmi's group published the first multicenter results of GDC treatment [23]. The results in 43 posterior fossa aneurysms with 1 to 18 month follow-ups showed 81% immediate complete occlusion in small-necked lesions and 15% immediate complete occlusion in wide-necked aneurysms. Eighty-five percent of wide-necked aneurysms and 19% of small-necked aneurysms demonstrated 70 to 98% thrombosis. Procedure related morbidity and mortality were 4.8% and 2.4%, respectively.

While Guglielmi and others focused on GDC, other individuals continued to work with alternative methods. In 1992 and again in 1994 Kinugasa published preliminary experience with the embolization agent cellulose acetate polymer [33,34]. Nine aneurysms were filled with this agent. One patient suffered a transient neurologic deficit and one patient bled 3 months after treatment. In 1993 Casasco reported results of nonretrievable fibered platinum coils in 71 aneurysms [11]. With mean angiographic follow-up of 13 months, immediate complete occlusion was achieved in 84.5% of cases with the remainder showing more than 90% occlusion. Clinical follow-up at 6 months revealed 85% good outcome. A 3% procedural subarachnoid hemorrhage rate, 3% delayed bleed rate, and 6% procedural stroke rate were recorded. In 1994 Halbach investigated the role of embolization in alleviating the effects of mass effect from large aneurysms compressing brain parenchyma and cranial nerves [26]. Of 26 aneurysms located both inside and outside the cavernous sinus presenting with symptoms from mass effect, 50% had symptom resolution, 43.3% improved, and 7.7% demonstrated no change. The authors felt that the improved group tended to have less calcium in the aneurysm wall and had symptoms for a shorter period of time.

Since 1994 the vast majority of published work on endovascular aneurysm therapy has centered on the GDC system. In 1994 Zubillaga reported 79 GDC

cases with 85% complete occlusion in small-necked aneurysms and 15% complete occlusion in wide-necked aneurysms [77]. This paper pointed out the difficulty of achieving complete obliteration of wide-necked aneurysms with GDC alone. In 1995 Byrne reported two GDC series. The first involved 50 GDC embolized aneurysms. Immediate complete obliteration was achieved in 100%, 95%, and 85% of small, large, and giant aneurysms, respectively [9]. Follow-up in 42 aneurysms at 6 months demonstrated recanalization of 17% of small aneurysms, 19% of large aneurysms, and 50% of giant aneurysms. Procedure-related morbidity and mortality were 18% and 4%, respectively. The second series involved 69 lesions. Morbidity and mortality in that study were 4.3% and 1.4% [10]. Richling also published a series of 74 GDC cases in 1995 with a greater than 90% occlusion rate of 76% at 8 months in 40 patients eligible for follow-up [64]. In 1996 McDougall's series of 33 coiled basilar apex aneurysms demonstrated that 84% had greater than 90% obliteration at a mean follow-up of 12 months with a 3% stroke rate and 3% delayed rebleed rate. Pierot's 1996 series of 35 basilar aneurysms included 74% with immediate complete occlusion and 27% with greater than 90% occlusion [47]. There was a 3% procedure-related death rate and no delayed hemorrhages, although the follow-up period was less than 2 years [59].

For publications of case series relating to GDC aneurysm embolization, 1997 was a banner year. Nichols' 6-month results of 28 ruptured posterior circulation aneurysms showed a 90% rate of 99 to 100% obliteration and 5% rate of 90% obliteration [57]. Treatment-related mortality was 3.8%, and serious procedure-related morbidity was 0%. Roy's group reported their results with 28 ophthalmic segment aneurysms [65]. At a mean follow-up of 15 months, 50% complete occlusion was achieved while 39% of cases were classified as having small residual necks. Procedural stroke rate was 3.5%. There were no deaths and no cases of rebleeding. Vinuela, in 1997, reported the results of an 8-center series of 403 coiled aneurysms treated between 1990 and 1995 [74]. Small-necked small aneurysms showed 71% complete occlusion, large aneurysms showed 35% complete occlusion and giant aneurysms achieved 50% complete occlusion. Complications included aneurysm perforation (2.7%), unintended parent vessel occlusion (3%), embolization (2.48%), and procedure-related death (1.74%). Because this series included patients treated from the initial use of first-generation GDC to more current use of improved coils in more experienced hands it is difficult to determine the true current status of

GDC procedures from such an extended study. The UCLA group, in this same year, published their mid-term clinical results in 100 consecutive patients [46]. Seventy-five percent of patients achieved excellent clinical status and 11% achieved good status at a mean follow-up of 3.5 years. Rehemorrhage rate was 0% with small aneurysms, 4% with large aneurysms, and 33% with giant aneurysms. Of note, 20 of the 100 coiled cases were referred for interventional therapy because of initial failed surgical clipping. In 1997 Raymond added to his group's reporting of location specific results of aneurysm coiling by publishing findings in 31 embolized basilar apex lesions [61]. Forty-two percent of cases had immediate complete obliteration while 52% had small residual necks or dog ears. There were no incidences of postcoiling subarachnoid hemorrhage over a short follow-up period. Repeat angiography at six months in 27 cases revealed 30% complete obliteration and 59% with residual necks. Seven recurrences over 42 months required retreatment. Death and stroke rate related to therapy were each 3%. Raymond and Roy in this same year described a series of 75 treated ruptured aneurysms (likely including cases from their two previous series on ophthalmic and basilar lesions) in which 40% had complete occlusion, 37% had residual neck or dog ear, and 16% had fundal opacification [62]. Follow-up angiography in 50 cases at 6 months demonstrated 46% complete occlusion and 42% residual neck or dog ear. Good to excellent outcomes were achieved in 72% of cases. Klein also contributed to the 1997 literature with a series of 21 basilar aneurysms [35]. Immediate complete and greater than 90% occlusion were achieved in 67% and 33% of patients, respectively. Fourteen patients underwent repeat arteriography after 6 months. Three patients with partially occluded wide-necked aneurysms showed recanalization. All three were retreated without incident. No episodes of rebleeding occurred. While 24% of patients had one posterior cerebral artery occluded only one patient suffered a permanent neurologic deficit. Overall morbidity and mortality were 5% each.

Beginning in 1997 papers began to be published about the management of wide necked aneurysms. It was clear from previous reports that larger aneurysms with larger necks were not being satisfactorily obliterated over the short or long term. The difficulty in managing these lesions was devising a means of keeping the coils within the aneurysm fundus and neck during and after deployment. In 1997 and 1998 Moret, Levy, Mericle, and Sanders each published their experiences using Moret's balloon remodeling technique [41,42,48,50,66]. These

authors demonstrated excellent short-term results with lesions that were previously untreatable using endovascular methods. Surprisingly, the morbidity and mortality rates in this small number of cases was no higher than with routine GDC embolization. Taking advantage of the availability of new, highly flexible coronary stents, Higashida in 1997 took an alternative approach to the treatment of previously endovascularly unapproachable fusiform aneurysms. The author's group placed a stent across the lesion and then advanced coils through the stent's walls to thrombose the aneurysm outside the stent while maintaining a patent lumen [30]. The use of stents to maintain a parent vessel lumen while at the same time provide a buttress that keeps coils within the aneurysm was expanded upon by Lanzino and Sekhon in 1998 [37,67]. Five lesions were treated in all, 4 of them in combination with GDC embolization. Results over the short term have been favorable.

Some of the first medium-term outcome studies began to surface in 1998. In a series by Leber et al, the medium-term results of endovascular treatment of intracranial aneurysms was compared to open surgery [38]. These authors examined the results of 162 aneurysms treated microsurgically and 134 aneurysms treated by endovascular embolization with GDC. The mean follow-up was 2.6 years (range, 1.5 to 4.5 years). Each group was well matched for age, sex, and location of aneurysms. These authors reported no significant difference between the patient outcomes of surgically or endovascularly treated aneurysms. Most importantly, they concluded that endovascular surgery was not associated with a higher risk of morbidity and mortality than surgical clipping of aneurysms, but cautioned that the results have to be confirmed by longer follow-up.

Collice et al attempted to develop a multidisciplinary approach to aneurysm management [12]. Using a team of neurosurgeons, neuroradiologists, and neurointerventionalists, aneurysms were selected for either endovascular coiling or surgical clipping. Their patients were stratified into four groups: Group 1 consisted of 104 surgically treated patients with ruptured aneurysms; Group 2 of 27 patients with ruptured aneurysms treated with GDC; Group 3 of 7 patients who were untreated; Group 4 of 26 patients with unruptured aneurysms treated with either modality. These authors suggested that aneurysms should be surgically clipped if they occur in patients less than 65 years old in good condition and with a Hunt-Hess Grade I-III, except if it is a basilar apex aneurysm. Patients in poor health or older than 65 should be treated

endovascularly regardless of Hunt-Hess grade, except if the aneurysm is in the MCA distribution. Giant aneurysms should be treated on a case-by-case basis. Though the number of cases treated with coils was too small to derive statistical significance for their proposed management scheme, patient outcomes were comparable with many purely surgical series.

In 1998 additional series were published with longer-term GDC results. Debrun's series of 152 aneurysms contained two important observations [14]. The first was that when a coiled aneurysm had a dome-to-neck ratio greater than or equal to 2 there was a 72 to 80% incidence of complete occlusion. The second was that operator experience counted. In their last 123 cases there was no procedural mortality, 1% morbidity and a 2.5% incidence of procedure-related transient ischemic events. While the authors describe using balloon remodeling in selected cases it is not clear how often this technique was utilized with those aneurysms having a dome:neck ratio <2. Turjman seconded Debrun's statement concerning the importance of experience in achieving better results with GDC embolization [72]. In his paper factors predicting incomplete occlusion were larger aneurysm size, more direct inflow, and earlier chronological treatment. Keuther's 1998 series of 77 aneurysms also provided some additional longer-term evaluation of the GDC technology [36]. Average angiographic and clinical follow-up in this study were 1.4 and 2.2 years, respectively. Initial angiographic results demonstrated 40% complete occlusion, 52% near complete occlusion (90-99%), and 8% incomplete occlusion (less than 90%). Procedure-related morbidity was 9.1%. No completely occluded lesions hemorrhaged over 1.9 years of follow up while 2.6% of incompletely occluded lesions bled in a delayed fashion (1.4%/year). Follow-up angiograms in 45 patients revealed 41% complete occlusion, 46% near complete occlusion, and 13% incomplete occlusion. Of those patients presenting with mass effect, 35% had complete resolution of their symptoms after embolization, 40% improved, and 25% were either unchanged or worsened. Eskridge's report on basilar apex aneurysms in the Food and Drug Administration's multicenter trial revealed greater than 90% occlusion in 75% of cases [17]. Mortality, however, in the unruptured group was 12% while rebleeding rates for unruptured and ruptured aneurysms ranged from 3.3-4.1%. Permanent neurologic deficits in cases of unruptured aneurysms occurred in 9%. Why unruptured aneurysms did so poorly in this study requires further investigation. In 1999 Murayama reported results of GDC

embolization of 120 incidental aneurysms. Initial complete or near complete occlusion was achieved in 91% of cases. Ninety-five percent of patients had no neurologic change following their procedure. Delayed bleed rate was 0.8% and average hospital stay was 3.3 days [54].

In 1999 Byrne et al published their results over the previous 5 years of 317 GDC-treated patients who were followed a median of 22.3 months (6-65 month range) [10]. Stable occlusion was found in 86% and 85% of small and large aneurysms, respectively, while recurrent filling was identified in 14.7%. Rebleeding secondary to recurrence was 0.8% in year 1, 0.6% in year 2, and 2.4% in year 3. Excellent or good outcomes at 6 months were achieved in 87.8% of patients with Hunt-Hess Grades 1 and 2, 71.4% of patients with Hunt-Hess Grade 3, and 48.5% of patients with Hunt-Hess Grades 4 and 5.

In 1999, Vanninen et al published their group's 3-month results in the first prospective, randomized study comparing GDC with surgery [73]. Aneurysms thought by a group of neurosurgeons and radiologists to be good candidates for either therapy were randomized to one treatment arm and matched for age, Hunt-Hess score, Fischer grade, site, and size. With the exception of posterior communicating artery aneurysms, angiographic results were equivalent between the two modalities, with better results in the endovascular group for posterior circulation lesions. One rebleed occurred in an incompletely coiled lesion. Technique-related mortality was 4% and 2% for the surgical and endovascular groups, respectively. The 3-month angiograms demonstrated 95% of coiled aneurysms to be 95% or more occluded (67% complete occlusion, 28% small neck remnant). Immediate postsurgical angiograms demonstrated 74% complete ligation. Small-neck remnants were visible in 16% and fundal filling was visible in 9%. Follow-up studies for the surgical group were not performed. Functional outcome in the two groups was not revealed in Vanninen's paper but will, according to the authors, be disclosed after 1 year follow-up.

Gruber et al revealed their 1999 findings relating to basilar apex aneurysms and demonstrated what they felt were comparable if not better results with endovascular therapy [21]. Forty-one patients with equivalent aneurysms (from an anatomic standpoint) were compared retrospectively. Overall outcomes, while better for GDC, are difficult to interpret because more patients in the surgical group were treated after SAH. However, when the SAH group was looked at separately the authors found the following trends. Despite a mean Hunt and Hess score of 3 in the GDC group and 1 in the surgical

group, GOS at discharge was identical, mean length of stay was 60% shorter in the GDC group, and hospital charges were on average 36% lower for embolized patients. Initial anatomic outcomes were better in the surgical group with a 20% incidence of aneurysm remnant in the exovascular group and 34% incidence of less than 95% obliteration in the endovascular group. Shortcomings of this paper include no long-term follow-up and poor angiographic follow-up. Although lower initial hospital costs were lower for embolized patients, the authors fail to take into consideration the expense of repeat imaging studies in both groups. Another report by Steiger et al compared surgical versus endovascular management of 100 posterior circulation aneurysms [71]. The authors utilized surgical clipping as treatment of choice in good-grade patients, while endovascular therapy was preferred for patients in poor clinical grade or if the aneurysm was judged difficult to access surgically. Complications resulting in significant morbidity or mortality occurred following 5 surgical and 1 endovascular procedure. These authors concluded that decision-making regarding treatment modalities should be based on aneurysm location, rather than size and shape. Additionally, it was the authors' opinion that endovascular treatment for small, narrow-necked aneurysms on proximal arteries of the posterior circulation should be considered, whereas large, distal, and broad-necked aneurysms should be managed with surgery.

In a larger series of 395 aneurysms, Lot et al attempted to compare results of endovascular and microsurgical aneurysms management [43]. One hundred and two aneurysms were surgically clipped, and 293 were coiled. Management decisions were based on the shape of the aneurysm as follows: aneurysms with narrow neck and ratio of neck diameter to sac diameter less than one-third were selected for coiling. Satisfactory results with complete or subtotal obliteration and no recanalization were obtained in 92% before retreatment and in 98.8% after retreatment. For both clipped and coiled aneurysms, good and excellent clinical outcomes were achieved in 90% of small aneurysms and in 86.5% of larger ones. These authors' results are comparable to those of large series of microsurgical management alone. Hence, with appropriate patient selection, Lot et al demonstrated that endovascular management is an excellent alternative for many aneurysms with suitable anatomy.

Additional 1999 manuscripts by Bavinski, Solander, and Yamaura point out the utility of using GDC in the management of basilar aneurysms, multiple intracranial aneurysms, and dissecting aneurysms

[6,70,76]. Each of these works documents excellent short-term clinical outcomes following endovascular therapy. As with all recent publications, longer-term results relating to rebleeding are not yet available.

In 1999, Kahara et al examined an often overlooked aspect of aneurysm management, that of postoperative psychosocial sequelae. Postprocedural clinical, emotional, and social (CES) outcome on a disability scale was reported for 44 GDC-treated patients and 106 surgically treated patients. In 75% of the embolized aneurysms successful occlusion was achieved; procedural mortality was 2.3%, and morbidity 18.2%. Clinical status of all 15 patients with unruptured aneurysms was preserved. Of the surviving 29 patients with ruptured aneurysms 12 improved and the rest preserved their clinical status. In 91% of the embolized patients and in 85% of the operated patients CES outcome was categorized as good or excellent (not statistically significant) [32].

An earlier paper by Bavinski et al during the same year reported 4 patients with 3 recurrent and 1 residual aneurysm after surgical clipping. Each was retreated using GDCs. Three aneurysms were totally occluded and the other had greater than 90% occlusion, suggesting that treatment with GDC is a viable alternative to reoperation in all patients with recurrent or residual aneurysms after a failed attempt at surgical obliteration [7].

Also during 1999 Regli et al examined the angiographic and anatomic features that determine whether a patient with an unruptured middle cerebral artery aneurysm is treated using endovascular coil placement or surgical clipping. They attempted prospective management of their patients, with endovascular management as the first line treatment, and surgical clipping reserved only for those aneurysms that could not be coiled. Thirty consecutive patients harboring 34 unruptured MCA aneurysms were evaluated. Of 34 unruptured MCA aneurysms, only 2 (6%) were successfully embolized and 32 (94%) were clipped. Of these 32 surgically treated aneurysms, in 11 (34%) an attempt at GDC embolization had failed, whereas in 21 (66%) primary clipping was performed because of unfavorable anatomy. GDC treatment failed in 11 (85%). An unfavorable dome/neck ratio ( $<2$ ) and an arterial branch originating at the aneurysm base were the reasons for embolization failure. These authors concluded that for unruptured MCA aneurysms, surgical clipping appears to be the most efficient treatment option. It is clear that larger studies in centers with significant endovascular and surgical experience need to conduct similar studies [63].

In 1999, Gruber et al reported their experience with coiling of giant and very large wide-necked aneurysms. To evaluate prevention of aneurysmal rebleeding, relief of aneurysmal mass effect, and prevention of embolic complications, they studied 30 patients with 31 giant or very large aneurysms that were considered to have unacceptable risk/benefit ratios for open surgery and were treated with GDCs. With GDC treatment, 73.3% of the population experienced excellent to good recoveries (Glasgow Outcome Scale scores of 4 or 5), with a 13.3% procedure-related morbidity rate and a 6.7% procedure-related mortality rate. Two hemorrhaging episodes occurred after GDC treatment (annual bleeding rate, 2.5%; 2 hemorrhaging episodes/79.2 patient-year). Symptoms related to aneurysmal mass effect were improved in 45.5% of the patients presenting with signs of neural compression. Among 23 patients with 24 aneurysms with angiographic follow-up, complete or nearly complete occlusion was observed in 17 aneurysms (71%) over an angiographic follow-up period of  $24.3 \pm 19.6$  months. A single total embolization served as definitive treatment for only 12.5% of the giant aneurysms and 31% of the very large aneurysms, with the remaining aneurysms requiring repeat coiling. Gruber's report demonstrates that endovascular treatment of giant aneurysms may be an attractive option with procedure-related morbidity and mortality rates comparable to (or lower than) those of open surgery [20]. Retreatment, however, should be anticipated.

The evolution of stent technology now allows for the endovascular treatment of previously untreatable aneurysms. Wilms et al described a case of a superior hypophyseal aneurysm of the left supraclinoid carotid artery that could not be treated with GDC, even in combination with a supporting non-detachable balloon. After an unsuccessful attempt at surgical clipping, treatment consisted of the placement of a stent over the neck of the aneurysm, advancement of a microcatheter through the stent mesh, and subsequent embolization with a GDC resulting in an excellent outcome [75]. Additional recently reported applications of stent technology include rescue from procedural complications and the solving of complex clinical problems. Pride et al described 3 patients who underwent unplanned placement of intravascular stents. In 2 patients a stent was used to provide stabilization of irretrievable unraveled fragments of a GDC and a partially deployed coronary stent. No periprocedural neurologic complications were encountered and 6-month follow-up angiography in 1 patient showed only minimal myointimal hyperplasia induced by stent-

stabilized GDC fragments adjacent to the internal carotid vessel wall [60]. Similarly, Fessler et al described the use of a low-profile, navigable stent to trap an extruded GDC during treatment of an internal carotid artery cavernous segment aneurysm [18]. A paper by Johnston et al in 1999 retrospectively compared matched groups of coiled and clipped unruptured aneurysms treated at university hospitals. This paper demonstrated a significant reduction in adverse outcomes, in patient deaths, length of stay, and mean charges when aneurysms were treated with endovascular techniques [31].

## 2000s

In 2000, an excellent retrospective analysis of 112 patients with ruptured posterior circulation aneurysms was reported by Lempert et al. The Hunt-Hess grade at presentation of treated patients was I in 26 patients (24%), II in 24 (22%), III in 27 (25%), IV in 24 (22%), and V in 8 (7%). Clinical follow-up for the total population was achieved in 104 of 109 patients (96%), with a mean duration of 13.1 months. Angiographic follow-up for the subset excluding parent vessel occlusion cases was obtained in 93% of cases, with a mean duration of 7.2 months. 109 of 112 cases (97%) were successfully embolized. The mean projected area of the aneurysm occlusion was 94.6%. At latest clinical follow-up, 81 of 109 patients (74%) achieved good recovery with GOS score of I, 10 of 109 (9%) were moderately disabled (GOS II), and 5 of 109 (5%) were severely disabled (GOS III), 1 of 109 (1%) remained in a vegetative state (GOS IV), and 12 of 109 (11%) were dead. Of the subset of 77 patients with Hunt-Hess grades I to III, 68 (88%) achieved good clinical outcomes (GOS I-D). Procedure-related permanent morbidity was 2.8%, and one patient had a second SAH following a partial coiling [40]. The observed favorable outcome and low morbidity in this group of high-risk patients suggest that GDC embolization may be a first-line intervention for the management of patients with ruptured posterior circulation aneurysms.

As we begin on the new millennium, we will appreciate novel advances in basic science as it directly enhances our surgical devices. One example is the report by Murayama et al [56]. This study describes a porcine model in which ion implanted surface-modification technology creates a borderless surface on protein-coated platinum GDCs. GDCs were coated with either type I collagen, fibronectin, vitronectin, laminin, or fibrinogen. A to-

tal of 56 experimental aneurysms were constructed microsurgically in the common carotid arteries of 28 swine. These experimental aneurysms were embolized with standard GDCs ( $n = 23$ ), collagen GDC-Is ( $n = 11$ ), vitronectin GDC-Is ( $n = 6$ ), laminin GDC-Is ( $n = 4$ ), fibrinogen GDC-Is ( $n = 6$ ), or fibronectin GDC-Is ( $n = 6$ ). They found no evidence of increased coil friction/stiffness during delivery of GDC-Is through microcatheters in this aneurysm model. Interestingly, more scar formation and neointothelium at the neck of the aneurysms were observed macroscopically when GDC-Is were used. Perhaps most importantly, differences in the proportion of neck coverage between standard GDCs ( $48.3\% \pm 20.5\%$ ) and all GDC-I groups were observed (collagen GDC-I- $89.4\% \pm 14.9\%$ ,  $p < .01$ ; vitronectin GDC-I- $71.5\% \pm 7.0\%$ ,  $p < .05$ ; laminin GDC-I- $76.5\% \pm 11.0\%$ ,  $p < .05$ ; fibrinogen GDC-I- $74.8\% \pm 13.9\%$ ,  $p < .05$ ; fibronectin GDC-I- $87.5\% \pm 15.0\%$ ,  $p < .01$ ). Histopathology demonstrated well-organized fibrous tissue bridging the aneurysms' necks when using GDC-Is, whereas only a fibrin-like thin layer covered the standard GDC surfaces. Another article by Murayama et al in 2001 demonstrated the efficacy of treating experimental porcine aneurysms with a coil coated with bioabsorbable polymeric material [55]. These coils led to improved formation of neointima across aneurysm necks when compared to standard platinum coils. This promising data may decrease the chances of coil compaction and aneurysm recanalization in future years.

## SUMMARY AND CONCLUSION

The use of endovascular therapy for cerebral aneurysms has grown exponentially over the last few years owing to the development of new technologies that have made aneurysm occlusion safer and more effective. With the advent of new catheters, wires, balloons, flexible stents, aneurysm neck occlusion devices, and embolic agents the field of endovascular neurosurgery will continue to make inroads into aneurysm treatment.

We continually look to past series to compare the results of open surgical and endovascular aneurysm therapy. Comparisons, however, are difficult for a number of reasons. Many surgical series have poor angiographic follow-up, thus making it hard to ascertain the true complete occlusion rate of open surgical clipping. Those studies that do provide follow-up have often depended upon low-resolution limited-view intraoperative angiography. Nevertheless, studies that have specifically examined the role of post surgical angiography have pointed out



the relatively high incidence of unexpected findings. Macdonald found unexpected residual aneurysms, unexpected completely unclipped aneurysms, and unexpected major vessel occlusions in 4%, 4%, and 12% of his group's cases, respectively [45]. The same investigator in another study found unexpected arterial occlusions in 6% of cases and unexpected persistently filling aneurysms in 10% of cases studied after clipping [1]. A study of 597 clipped aneurysms by Le Roux revealed a 5.7% incidence of aneurysm remnants and a 5.7% incidence of vessel occlusion [39]. Payner, likewise, identified a 3.2% incidence of unexpected residual aneurysm and a 1.9% incidence of parent vessel stenosis [58]. In all of these series the operative word is "unexpected." The post surgery angiography papers and other surgical series do not take into consideration and rarely report the cases of expected and accepted residual aneurysm neck or fundus opacification following clipping. While residual neck is not necessarily reported as a failure of surgical treatment in cases of wide-necked, calcified, or atherosclerotic aneurysms located throughout the cerebral arterial tree, it is invariably viewed as an example of technical failure in endovascular series. All neurosurgeons who treat aneurysms are aware that preservation of afferent and efferent vessels often necessitates incomplete aneurysm clipping. Nevertheless, such remnants are rightfully viewed as surgical necessity rather than failure. A second reason comparisons are difficult is the length of time it will take to determine rehemorrhage rates from coiled lesions. Perhaps the best paper relating to the topic of rerupture of aneurysm rests is by Feuerberg [19]. The author followed 28 residual aneurysms after clipping and found a rebleed rate of 0.38 to 0.79% per year during the observation period (4-13 years). It is difficult to conceive of a study involving endovascular cases that will be able to follow patients with residual necks and small dog ears long enough to determine the rebleed rate in view of the small rebleed rate observed by Feuerberg. While we know from past experience that continued fundal filling puts patients at high risk for rebleeding, as endovascular devices improve fundal filling will become a rare entity. As a result, comparisons between exo and endovascular surgery will rest on the true incidence of and risk posed by residual aneurysm neck.

Having viewed the extent of retrospective literature available on endovascular aneurysm treatment, many will propose a large, multicenter prospective randomized trial comparing embolization with open surgery. The limitations of such a study, however, are obvious. We already know from most

published papers that the short term (less than 5 years) rehemorrhage rate, stroke rate, procedural death rate, and 1-year clinical outcomes of endovascular therapy compare favorably with open surgical clipping. What we do not know is the long-term durability of endovascular aneurysm occlusion. In an ever-changing field with new devices being released on an almost monthly basis, at what point do we feel comparisons are justified? Likewise, what group will fund a study that runs long enough to detect the true rebleed rate from residual necks and dog ears? By the time such a study could be completed, the technology used to conduct its endovascular arm would be obsolete, thus depreciating the study's value. Such questions and dilemmas are ones endo/exovascular neurosurgeons will face for years to come. Only with continued observation can we hope to come up with an ultimate answer.

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## COMMENTARY

This article is a thorough and exhaustive review of the data regarding the historical development as well as the present development of intravascular treatment of intracranial aneurysms. We believe, as the authors do, that this is an important review and that it represents a thorough study of the developments leading up to our present day treatment of intracranial aneurysms. We all must constantly look back at the development of existing technology as we plan the future so as to take lessons from the past as we move forward in developing future therapies. The authors clearly point this out and we congratulate them on their meticulous review.

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This article, authored by two experienced interventionalists, promises in its title to update readers on the historical development and current status of the endovascular treatment of intracranial aneurysms. It accomplishes the first portion of that goal with remarkable thoroughness, detailing in cogent fashion the sequential technical refinements and innovative conceptual approaches that together have resulted in the widespread acceptance of endovascular coiling as an acceptable treatment option for intracranial aneurysms. Unfortunately, the authors provide us no pragmatic synthesis of the diverse information presented from more than 70 clinical series, and mention only that direct comparison of endovascular and microsurgical treatments is "difficult," primarily because of the low incidence and poor quality of angiographic follow-up in many surgical series. Other than a solemn prediction that "in the new millennium" novel technical developments will enable "the field of endovascular neurosurgery to continue to make inroads into aneurysm treatment," readers are left to drawn their own conclusions as to the present status of interventional therapy.

More disappointing is the authors' reticence as regards a potential randomized comparative trial of endovascular versus microvascular aneurysmal therapy. The reasons they cite (continued evolution of technology, necessity for protracted long-term angiographic and clinical follow-up) are unconvincing to the other neurosurgeons, interventionalists, and neurologists who have supported the formulation of the 3 clinical trials now proposed for NIH funding. Without question, at least one of these multi-center prospective studies will be funded and carried to completion. Hopefully, the authors will overcome their stated reluctance and lend their individual expertise to a well-designed effort that should better define the individual applicability, risks, efficacy, and durability of each of these therapeutic modalities.

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Dr Horowitz and his colleagues have produced a very interesting review of endovascular therapy for intracranial aneurysms. Their review of the literature is pertinent for modern clinical decision-making. The manuscript appears to be complete and nicely analyzed. However, I would like to add one historical point. In the 1980s, the first coiling of an intracranial aneurysm was carried out by Dr Sadek Hilal at The Neurological Institute in New York. The report was published as an abstract and presented at a national meeting [1]. Unfortunately, shortly after that report Dr Hilal became very ill and could not continue his work. Others used the platinum coils that he developed to begin coiling aneurysms. However, frustration with the Hilal mini-coils led to the discovery in 1991 by Dr Guglielmi of the coils that are now in popular use.

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## REFERENCE

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Horowitz and co-authors have written an excellent review of the different endovascular techniques used in the treatment of cerebral aneurysms since 1960. I share their skepticism about the soundness of a double-blind trial of surgical or GDC treatment