Neurosurg Focus 17 (5):E5, 2004

Current treatment options for unruptured intracranial aneurysms

Peng Roc Chen, M.D., Kai Frerichs, M.D., and Robert Spetzler, M.D.

Barrow Neurological Institute, Phoenix, Arizona; and Brigham and Women's Hospital, Boston, Massachusetts

A patient with an unruptured intracranial aneurysm has three options: surgical clip placement, endovascular coil occlusion, and observation. The decision making about management of these lesions should be based on the risk of aneurysm rupture and the risks associated with surgical or endovascular intervention. For patients who require interventions, factors such as aneurysm recurrence rate, its location, surgical or endovascular accessibility, the patient's general medical condition, and the individual's treatment preference should be taken into account to determine the choice of therapies. Currently, a team approach by neurosurgeons and endovascular interventionists is recommended to evaluate each patient and to tailor the best treatment plan.

Key Words • **unruptured intracranial aneurysm** • **subarachnoid hemorrhage** • **endovascular coil occlusion** • **aneurysm clip occlusion**

Major advances in microsurgery, skull base surgery, and particularly endovascular neurosurgery, along with neuroanesthesia and intraoperative neuroelectrophysiological monitoring, have increased the safety and feasibility of treatments to obliterate intracranial aneurysms. In this paper the authors discuss the current treatment options for unruptured intracranial aneurysms: surgical obliteration, endovascular embolization, and conservative management. Special consideration is given to the idea of the team approach in which all available modalities are used to treat these patients optimally.

SURGICAL TREATMENT

If one decides to treat an unruptured intracranial aneurysm, the risks of the intervention must be thoroughly considered. Surgical aneurysm clip occlusion has been the favored treatment method for approximately 40 years, since the operating microscope was introduced in neurosurgery, and is considered the time-tested treatment for aneurysms.[2,24,51] As with any other procedure, high-volume centers and experienced surgeons appear to offer better outcomes and fewer complications.[3]

Risks Associated With Surgical Treatment

In a systematic metaanalysis of surgical treatment for unruptured aneurysms, Raaymakers, et al.,[43] identified 61 studies published between 1966 and June 1996. These series included a total of 2460 patients (57% female, mean age 50 years) and at least 2568 unruptured aneurysms (27% > 25 mm, 30% located in the posterior circulation) with a mean follow-up duration of 24 weeks (range 2–234 weeks). The mortality rate was 2.6% (95% CI 2–3.3%), and permanent morbidity occurred in 10.9% (95% CI 9.6–12.2%) of patients. Postoperative mortality and morbidity rates were significantly lower in more recent years for nongiant aneurysms and lesions with an anterior location. The lowest morbidity and mortality levels were found in small anterior circulation aneurysms (mortality 0.8%, morbidity 1.9%), and the highest levels were in large posterior fossa lesions (mortality 9.6%, morbidity 37.9%).

In the prospective arm of the ISUIA,[21] investigators found the surgery-related mortality rate at 1 year to be 2.7% in patients with no prior SAH and 0.6% in patients who had previously suffered a rupture. Morbidity rates were 9.9 and 9.8%, respectively, in these two groups. Unlike most of the previous studies, patients' cognitive impairment had been included as morbidity. These results are similar to the in-hospital mortality rates of 2.5 and 3% in a statewide analysis of discharge data in New York[5] and California,[26] respectively. A similar result was obtained through the Nationwide Inpatient Sample hospital discharge database (1996–2002).[3] Of 3498 patients who were treated at 463 hospitals, with 585 surgeons identified in the database, 2.1% died and 16.1% were discharged to skilled-nursing facilities or other institutions rather than home after repair surgery for an unruptured intracranial aneurysm. Nevertheless, the mortality rate was lower at high-volume hospitals (1.6% compared with 2.2%), and discharge other than to home occurred in 15.6% of patients after surgery at high-volume hospitals (those with ≥ 20 cases/year) compared with 23.8% at low-volume hospitals (those with < four cases/year).

Abbreviations used in this paper: CI = confidence interval; GDC = Guglielmi detachable coil; ICA = internal carotid artery; ISUIA = International Study of Unruptured Intracranial Aneurysms; MCA = middle cerebral artery; NSAID = nonsteroidal anti-inflammatory drug; SAH = subarachnoid hemorrhage.

Conditions Influencing Surgical Outcome

There are various risk factors that are potential predictors of surgical outcome besides hospital case volume or the experience of surgeons, and these are age of a patient and size and location of an aneurysm.[11,21,48] The surgical outcome is independently associated with the age of patients, the size of the aneurysm, and its location.

Aneurysm Size. Solomon, et al.,[48] found that aneurysm size had an important influence on surgical outcome. The morbidity and mortality rate for unruptured aneurysms was 0% for aneurysms less than or equal to 10 mm in diameter, 6% for aneurysms between 10 and 25 mm, and 20% for aneurysms greater than 25 mm. Drake[11] reported a 15% morbidity and mortality rate in nongiant posterior circulation aneurysms compared with 39% for giant posterior circulation lesions, although ruptured aneurysms were also included in his series. In the ISUIA,[21] investigators revealed a 2.6 relative risk of poor surgical outcome for aneurysms larger than 12 mm in diameter.

Aneurysm Location. Aneurysm location within the posterior circulation is associated with an increased incidence of poor outcome in the ISUIA.[21] Solomon, et al.,[48] observed a 50% morbidity and mortality rate after surgery in unruptured giant basilar aneurysms compared with a 13% rate for anterior circulation giant aneurysms. Drake[11] found a 14.3% morbidity rate after surgical treatment of unruptured asymptomatic aneurysms in the posterior circulation, compared with 0% morbidity in the anterior circulation. Other locations such as posterior–superior projecting anterior communicating artery aneurysms[41] and clinoidal segment and cavernous portion ICA aneurysms are also associated with higher levels of morbidity and mortality due to technical difficulties involved in achieving adequate intracranial exposure and proximal control.[17,18]

Patient Age. In the prospective arm of the ISUIA,[21] an increase of 2.4 in relative risk was observed in patients who were older than 50 years of age. Takahashi[50] found the worst surgical outcome in patients at 80 years of age or older. Khanna, et al.,[34] stated a sixfold higher risk of a poor outcome in a 70-year-old patient after surgery compared with a 30-year-old patient, if aneurysm size and location are constant. This could be due to an increased incidence of atherosclerotic and/or calcified aneurysm necks and domes, in addition to medical comorbidities in the older patients.

How do Statistics Influence the Decision to Operate?

Despite all the risks associated with surgical treatment for unruptured intracranial aneurysms, the decision to proceed does require mathematical calculation. For instance, in the study published by Juvela,[28] the group of patients with the longest follow-up duration (23.4 years) had a cumulative rate of bleeding of 10.5% at 10 years after diagnosis of an unruptured aneurysm, 23% at 20 years, and 30% at 30 years. If the patient's age is 50 years or younger at the time of diagnosis, and their projected life expectancy is 80 years, the risk of a devastating SAH in the next 30 years will outweigh the surgical risks. In many situations, however, a high-risk natural history is associated with a high surgical risk. For example, a 30-mm unruptured basilar apex aneurysm would have a 5-year rupture risk of approximately 50 to 60% and a 40 to 50% risk of death or severe disability, and a postoperative risk of death approaching the same range if surgical clip occlusion was the only option.[21] In such a situation, the patient's age, comorbidities, his or her preference, and the availability of alternative treatment modalities will influence the decision-making process.

Advantages of Surgical Clip Occlusion

It is widely accepted that surgical clip occlusion yields longstanding aneurysm obliteration and extremely low rates of subsequent SAH from a completely obliterated lesion. In a recent study, Lozier, et al.,[36] reported an annual rate of postoperative SAH of 0.18% for all clip-occluded aneurysms and 0% for completely obliterated lesions during 7.4 ± 3.7 years of follow up. Asgari, et al.,[2] reported a rebleeding incidence of 0.4% in 1170 patients with completely clip-occluded aneurysms during a 12-year follow-up period. In a study of long-term (2.6–9.6 years) angiographic outcome in surgically treated aneurysms, David, et al.,[8] demonstrated 1.5% recurrence in 135 aneurysms in which clips were placed with no residual neck. Of 12 aneurysms with known residual necks, 25% enlarged. Therefore, the long-term result of surgical clip occlusion is reliable, although periodic follow-up review may also be necessary in surgically treated patients.

ENDOVASCULAR TREATMENT

In 1991, Guglielmi and colleagues[15,16] introduced the detachable coil for treatment of intracranial aneurysms. Their technique revolutionized the endovascular treatment of intracranial aneurysms. In 1995, the GDC system (Boston Scientific/Target, Inc., Fremont, CA) received US Food and Drug Administration approval. At that time, aneurysms considered unsuitable for surgery were candidates for GDC embolization. In subsequent years, however, the criteria for endovascular treatment broadened and GDCs are now approved for the treatment of all aneurysms. In 1999, Guglielmi's group was the first to report a large series of 115 patients in whom 120 intracranial aneurysms were incidentally identified.[38] The efficacy of coil occlusion in preventing subsequent hemorrhage of intracranial aneurysms is based on mechanical hemodynamic exclusion of intraaneurysm flow by the GDCs.[49] Currently available data on endovascular treatment of intracranial aneurysms with GDCs are derived mostly from relatively small series composed of several hundred patients.

There are two metaanalyses of the outcomes of coil placement for aneurysm occlusion. Brilstra, et al.,[7] reviewed 48 studies including 1383 patients. Permanent complications (death/disability) of embolization with GDCs occurred in 3.7% of cases, and 54% (95% CI 50–57%) of aneurysms were completely occluded after one procedure. The other review,[35] which focused on GDC embolization of posterior circulation aneurysms, showed procedural complication and morbidity rates of 12.5 and 5.1%, respectively. Procedural and 30-day mortality rates were 1.4 and 6.7%, respectively, and the overall mortality rate was 9.8%. Complete aneurysm occlusion was achieved in 47.6%, near-complete occlusion (90–99%) in

43.4%, and incomplete occlusion in 9% of cases. The annual risk of SAH after embolization was 0.8%.

These data indicate that coil embolization is a reasonably safe treatment for patients with unruptured or ruptured aneurysms. The effectiveness of coils in terms of complete occlusion of the lesion after the first procedure is moderate. There are also concerns about recurrences in 20.7% of treated aneurysms,[44] and there is a higher rebleeding rate (0.9%) for completely coil-occluded aneurysms than for completely clip-occluded lesions (0.4%).[2]

Nevertheless, it is important to understand that these case series are based on retrograde data analysis of a technology in flux and that patient selection bias may have skewed the results as follows. 1) There was a learning curve for using GDCs and related catheter-based techniques. For instance, in 324 patients in the endovascular series reported by Debrun, et al.,[9] the first 25 patients, who were seen between May 1994 and February 1995, were treated without taking into account the geometry of the aneurysms as an important criterion for coil insertion. This led to high morbidity and mortality rates, and angiographically confirmed occlusion was found in less than 50% of these aneurysms at 6-month follow-up review. 2) Endovascular treatment has been offered as the alternative option for patients who are too sick or simply too old to tolerate surgical clip occlusion for aneurysms. 3) Unlike microsurgery, which is stable technologically after 40 years of development, endovascular techniques continue to evolve rapidly. For instance, in the not too distant past broad-necked aneurysms were considered unsuitable for GDC treatment. Lately, with newly emerging modalities such as remodeling techniques in which balloons or stents are used, these aneurysms have become suitable targets for endovascular treatment.[19] The introduction of a specific microcatheter-deliverable, self-expandable stent designed exclusively for the intracranial circulation (Neuroform; BSCI, Natick, MA) has further augmented the endovascular armamentarium.

Advantages of Endovascular Coil Occlusion

In 2002, the International Subarachnoid Aneurysm Trial Collaborative Group[23] published the first prospective randomized trial in which outcomes after endovascular coil occlusion or surgical clip placement were compared in 2143 patients with ruptured intracranial aneurysms. In the endovascularly treated group, 23.7% of patients were either dependent or dead at 1 year, compared with 30.6% of those who underwent surgical clip occlusion. Despite some shortcomings, including only 1 year of follow up so far, the relative and absolute risk reductions for dependency or death in patients undergoing endovascular compared with surgical treatment were 22.6 and 6.9%, respectively. Enrollment in the study was halted early because significance was reached prior to attaining the target enrollment number. The risk of rebleeding from the ruptured aneurysm after 1 year was 2 per 1276 and 0 per 1081 patient-years for individuals allocated to the endovascular and surgical treatment groups, respectively. The results in this trial indicate that if a ruptured aneurysm is suitable for both treatments, endovascular coil occlusion is significantly more likely to result in disability-free survival 1 year after SAH, although the long-term durability of coil treatment remains to be discovered.

For unruptured aneurysms, the prospective ISUIA data on treatment outcomes make direct comparisons of clip placement and coil occlusion difficult because patient characteristics were different. There were disproportionately more elderly patients and more posterior circulation and large aneurysms (which predispose patients to worse outcomes) in the endovascular cohort. Nevertheless, patients in Group 1 (those with no history of SAH from a different aneurysm) had a combined morbidity and mortality rate at 1 year of 12.6% for clip placement and 9.8% for coil occlusion, a 22.3% relative risk reduction for coil placement. For patients in Group 2 (those with a history of SAH from a different aneurysm that had been repaired), the numbers were 10.1% for clip placement and 7.1% for coil occlusion, with a relative risk reduction of 29.7% for coil insertion at 1 year.[21]

Long-term follow-up data after coil occlusion of an unruptured aneurysm will be needed to prove not just the short-term efficacy but also the long-term durability of this new treatment. This is the subject of current and future studies,[42] including the long-term follow up from the International Subarachnoid Aneurysm Trial.

Conditions Influencing the Feasibility of Endovascular Treatments

Advances in endovascular technology have made possible the treatment of increasingly complex aneurysms over time. Prohibitive tortuosity in the access vessels may make an endovascular approach impossible. Combining an open surgical approach to provide access closer to the lesion may be suitable in rare cases. Incorporation of a daughter dome in the aneurysm neck may make it unlikely that an endovascular cure can be achieved. Incorporation of the parent artery into the aneurysm may mean that the artery is more suitable for surgical reconstruction, unless it is readily amenable to stent or balloon remodeling techniques and reconstruction. Partial thrombosis of the aneurysm makes recurrence of the lesion due to shifting and compaction of the coil mass very likely. The role of endovascular treatment in the management of mass effect–producing aneurysms is controversial. Intuitively, only an open surgical approach would have a reasonable chance to relieve the symptoms of mass effect. On the other hand, some evidence exists that cranial neuropathies also improve after endovascular coil occlusion.[6] The mechanism of recovery in cranial nerve function after endovascular aneurysm occlusion is unclear. It has been speculated that recovery occurs due to reductions in the aneurysm's size, its degree of pulsatility, and adjacent cerebral edema.

TEAM APPROACH

Combining Surgical and Endovascular Modalities to Treat Unruptured Aneurysms

It has become clear that surgical clip placement is no longer the only treatment option for obliteration of cerebral aneurysms; surgical and endovascular modalities have become complementary technologies in the treatment of these patients. As part of a multidisciplinary team, cerebrovascular surgeons who use open approaches and endovascular surgeons evaluate every aneurysm case together to decide on the optimal treatment modality; observation, surgical clip placement, endovascular coil occlusion, or a combination of these approaches. This could include surgical reconstruction of parent arteries or bypass procedures followed by coil insertion, and vice versa. For the optimal treatment plan, practitioners would strive to find the delicate balance between maximizing aneurysm obliteration and minimizing treatment-related morbidity to optimize the benefit to the patient.

Factors in Treatment Selection

No formal or generally accepted guidelines exist to facilitate the choice between the various treatment modalities. This choice would also be influenced by the available expertise of practitioners for each modality. The following six factors, however, certainly influence the selection of treatment modalities: 1) location of the aneurysm; 2) relationship of the aneurysm to its parent vessels and other branches; 3) aneurysm dome/neck ratio; 4) surgical and endovascular accessibility of the lesion; 5) age and general medical condition of the patient; and 6) patient's treatment preference.

Aneurysm Location. For unruptured MCA aneurysms, surgical clip placement may still be the most efficient treatment option.[45,46] The two major anatomical features responsible for failure of endovascular procedures are a dome/neck ratio of 1.5 or less and an arterial branch (proximal [M_2] segment) originating from the aneurysm neck. These features are frequently seen in MCA aneurysms. In contrast, surgical clip placement in MCA aneurysms results in a very low rate of morbidity. For anterior cerebral artery aneurysms, especially superior–posterior projecting lesions, endovascular coil occlusion avoids brain retraction and septal branch injury.[41] Aneurysms in the cavernous or paraclinoidal ICA are associated with higher surgical risk, and an endovascular approach may be the more appropriate treatment option.[37,40] For aneurysms in the posterior circulation, especially basilar apex lesions, endovascular treatment offers lower procedure-related morbidity and mortality rates.[12,14]

Relationship to Parent Vessel. Aneurysms with parent vessels incorporated into the neck or dome are generally unsuitable for endovascular coil occlusion, although remodeling techniques have created new opportunities for an endovascular option.[45,46] In this situation, however, strong consideration should be given to an open surgical approach unless it is contraindicated.

Aneurysm Dome/Neck Ratio. An aneurysm neck size less than 4 mm or a dome/neck ratio of 2 or higher are favorable parameters for coil occlusion; otherwise, surgical clip placement is the better option.[9,10,13] One should bear in mind, however, that the new endovascular remodeling techniques (that is, stent- or balloon-assisted coil placement), have created new opportunities for endovascular treatment.[4,19,20]

Surgical and Endovascular Accessibility. Intracavernous ICA aneurysms are difficult to access surgically. Direct clip placement, ipsilateral ICA occlusion, or external carotid–internal carotid bypass followed by ICA occlusion have been used as treatment options. Because of the high morbidity and mortality rates related to these procedures, they may not be the primary treatment for this type of aneurysm. Endovascular coil occlusion, on the other hand, may provide a safer alternative.[40] Conversely, extreme tortuosity of the aortic arch, carotid artery, or vertebral artery, and chronic carotid or vertebral artery occlusion can be obstacles that prohibit catheter access to these aneurysms.

Patient Age and Medical Condition. Elderly patients and those with comorbidities tolerate endovascular approaches better than open surgery and craniotomy.[37]

In summary, it is likely that a combined microsurgical–endovascular team approach will provide the means to achieve the best outcomes for patients with unruptured intracranial aneurysms.

Patient Preference. When it is technically feasible to treat an aneurysm either surgically or endovascularly, the patient's preference regarding therapy modality should be considered, despite the possibility of different long-term outcomes.

Conservative Management

If conservative management is chosen for a newly found unruptured aneurysm, it is crucial to reduce the risks of rupture, which concomitantly can have a useful effect. Questions such as the following may arise: should these patients be placed on a regimen of anticoagulant drugs or aspirin to treat other comorbidities (for example, pulmonary embolism, deep venous thrombosis, mechanical cardiac valves, stroke, and so forth)?

Reduction of Risk Factors

Cessation of Tobacco Smoking. In the ISUIA retrospective data, 60.6% of patients with aneurysms were current smokers.[22] In their long-term follow-up data, Juvela and colleagues[28,29,33] revealed a prevalence of active smoking ranging from 45 to 75% in patients with SAH, whereas in the general adult population in Finland it is only 20 to 35%. It is likely that smoking is associated with an increased risk of SAH by contributing to formation of an aneurysm and increasing its rate of growth. Among smokers, the number of cigarettes smoked daily seems to be more significantly associated with aneurysm growth than the duration of or age at start of smoking. Those who had quit smoking had no increased risk of aneurysm growth. Therefore, cessation of cigarette smoking may help reduce both the risk of formation of aneurysms and the risk of rupture.

Control of Hypertension and Risk Factors for Atherosclerosis. The risk factors for SAH and for growth of an aneurysm are very similar. Hypertension, alcohol consumption (particularly binge drinking),[27,31–33] cocaine and amphetamine abuse,[39] oral contraceptive use,[25] and cholesterol level higher than 6.3 mmol/L,[1] in addition to cigarette smoking, may all be associated with an increased risk of aneurysm formation and SAH. Controlling hypertension and the risk factors for atherosclerosis may reduce the risks of aneurysm formation and rupture.

Anticoagulation Drug and Aspirin/NSAID Use in Patients With Unruptured Cerebral Aneurysms. There is no evidence of an increased risk of SAH in patients with unruptured aneurysms who are given anticoagulating agents. Nevertheless, avoidance of anticoagulant drugs in patients known to harbor an unruptured aneurysm may reduce the risk of a poor outcome if the aneurysm ruptures. There is evidence of worse outcomes after aneurysmal SAH in patients who use anticoagulating agents; the mortality rate in this group is at least twice as high.[47]

Use of aspirin or other NSAIDs preceding aneurysmal SAH does not significantly affect outcome, however. Interestingly, an NSAID given after SAH might actually reduce morbidity by reducing the risk of secondary ischemic events.[30]

CONCLUSIONS

Treatment options for an intracranial aneurysm are no longer limited to craniotomy with aneurysm clip occlusion. The field of endovascular neurosurgery continues to evolve rapidly and provides an excellent alternative as well as a complementary treatment option. This emphasizes the need for a center-based approach in the management of cerebral aneurysms. Continuous improvements in endovascular techniques and material provide a great opportunity to integrate microsurgery and endovascular treatment to assess each aneurysm and to provide the best treatment option and ultimately the best outcome.

References

1. Adamson J, Humphries SE, Ostergaard JR, et al: Are cerebral aneurysms atherosclerotic? **Stroke 25:**963–966, 1994
2. Asgari S, Wanke I, Schoch B, et al: Recurrent hemorrhage after initially complete occlusion of intracranial aneurysms. **Neurosurg Rev 26:**269–274, 2003
3. Barker FG II, Amin-Hanjani S, Butler WE, et al: In-hospital mortality and morbidity after surgical treatment of unruptured intracranial aneurysms in the United States, 1996–2000: the effect of hospital and surgeon volume. **Neurosurgery 52:** 995–1009, 2003
4. Bendok BR, Hanel RA, Hopkins LN: Coil embolization of intracranial aneurysms. **Neurosurgery 52:**1125–1130, 2003
5. Berman MF, Solomon RA, Mayer SA, et al: Impact of hospital-related factors on outcome after treatment of cerebral aneurysms. **Stroke 34:**2200–2207, 2003
6. Birchall D, Khangure MS, McAuliffe W: Resolution of third nerve paresis after endovascular management of aneurysms of the posterior communicating artery. **AJNR 20:**411–413, 1999
7. Brilstra EH, Rinkel GJ, van der Graaf Y, et al: Treatment of intracranial aneurysms by embolization with coils: a systematic review. **Stroke 30:**470–476, 1999
8. David CA, Vishteh AG, Spetzler RF, et al: Late angiographic follow-up review of surgically treated aneurysms. **J Neurosurg 91:**396–401, 1999
9. Debrun GM, Aletich VA, Kehrli P, et al: Aneurysm geometry: an important criterion in selecting patients for Guglielmi detachable coiling. **Neurol Med Chir 38 (Suppl):**1–20, 1998
10. Debrun GM, Aletich VA, Kehrli P, et al: Selection of cerebral aneurysms for treatment using Guglielmi detachable coils: the preliminary University of Illinois at Chicago experience. **Neurosurgery 43:**1281–1297, 1998
11. Drake CG: Progress in cerebrovascular disease. Management of cerebral aneurysm. **Stroke 12:**273–283, 1981
12. Eskridge JM, Song JK: Endovascular embolization of 150 basilar tip aneurysms with Guglielmi detachable coils: results of the Food and Drug Administration multicenter clinical trial. **J Neurosurg 89:**81–86, 1998
13. Fernandez Zubillaga A, Guglielmi G, Viñuela F, et al: Endovascular occlusion of intracranial aneurysms with electrically detachable coils: correlation of aneurysm neck size and treatment results. **AJNR 15:**815–820, 1994
14. Gruber DP, Zimmerman GA, Tomsick TA, et al: A comparison between endovascular and surgical management of basilar artery apex aneurysms. **J Neurosurg 90:**868–874, 1999
15. Guglielmi G, Viñuela F, Dion J, et al: Electrothrombosis of saccular aneurysms via endovascular approach. Part 2: preliminary clinical experience. **J Neurosurg 75:**8–14, 1991
16. Guglielmi G, Viñuela F, Sepetka I, et al: Electrothrombosis of saccular aneurysms via endovascular approach. Part 1: electrochemical basis, technique, and experimental results. **J Neurosurg 75:**1–7, 1991
17. Guidetti B, La Torre E: Carotid-ophthalmic aneurysms. A series of 16 cases treated by direct approach. **Acta Neurochir 22:** 289–304, 1970
18. Guidetti B, La Torre E: Management of carotid-ophthalmic aneurysms. **J Neurosurg 42:**438–442, 1975
19. Han PP, Albuquerque FC, Ponce FA, et al: Percutaneous intracranial stent placement for aneurysms. **J Neurosurg 99:**23–30, 2003
20. Henkes H, Fischer S, Weber W, et al: Endovascular coil occlusion of 1811 intracranial aneurysms: early angiographic and clinical results. **Neurosurgery 54:**268–285, 2004
21. The International Study of Unruptured Intracranial Aneurysms Investigators: Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. **Lancet 362:**103–110, 2003
22. The International Study of Unruptured Intracranial Aneurysms Investigators: Unruptured intracranial aneurysms—risk of rupture and risks of surgical intervention. **N Engl J Med 339:** 1725–1733, 1998
23. The International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. **Lancet 360:**1267–1274, 2002
24. Jane JA, Winn HR, Richardson AE: The natural history of intracranial aneurysms: rebleeding rates during the acute and long term period and implication for surgical management. **Clin Neurosurg 24:**176–184, 1977
25. Johnston SC, Colford JM Jr, Gress DR: Oral contraceptives and the risk of subarachnoid hemorrhage: a meta-analysis. **Neurology 51:**411–418, 1998
26. Johnston SC, Zhao S, Dudley RA, et al: Treatment of unruptured cerebral aneurysms in California. **Stroke 32:**597–605, 2001
27. Juvela S: [Alcohol and the prognosis of subarachnoid hemorrhage.] **Duodecim 109:**355–357, 1993 (Fin)
28. Juvela S: Natural history of unruptured intracranial aneurysms: risks for aneurysm formation, growth, and rupture. **Acta Neurochir Suppl 82:**27–30, 2002
29. Juvela S: Risk of subarachnoid hemorrhage from a de novo aneurysm. **Stroke 32:**1933–1934, 2001
30. Juvela S, Hillbom M, Numminen H, et al: Cigarette smoking and alcohol consumption as risk factors for aneurysmal subarachnoid hemorrhage. **Stroke 24:**639–646, 1993
31. Juvela S, Porras M, Heiskanen O: Natural history of unruptured intracranial aneurysms: a long-term follow-up study. **J Neurosurg 79:**174–182, 1993
32. Juvela S, Porras M, Poussa K: Natural history of unruptured intracranial aneurysms: probability of and risk factors for aneurysm rupture. **J Neurosurg 93:**379–387, 2000
33. Juvela S, Poussa K, Porras M: Factors affecting formation and growth of intracranial aneurysms: a long-term follow-up study. **Stroke 32:**485–491, 2001
34. Khanna RK, Malik GM, Qureshi N: Predicting outcome following surgical treatment of unruptured intracranial aneurysms: a proposed grading system. **J Neurosurg 84:**49–54, 1996

35. Lozier AP, Connolly ES Jr, Lavine SD, et al: Guglielmi detachable coil embolization of posterior circulation aneurysms: a systematic review of the literature. **Stroke 33:**2509–2518, 2002
36. Lozier AP, Kim GH, Sciacca RR, et al: Microsurgical treatment of basilar apex aneurysms: perioperative and long-term clinical outcome. **Neurosurgery 54:**286–299, 2004
37. Martin NA: The combination of endovascular and surgical techniques for the treatment of intracranial aneurysms. **Neurosurg Clin N Am 9:**897, 1998
38. Murayama Y, Viñuela F, Duckwiler GR, et al: Embolization of incidental cerebral aneurysms by using the Guglielmi detachable coil system. **J Neurosurg 90:**207–214, 1999
39. Oyesiku NM, Colohan AR, Barrow DL, et al: Cocaine-induced aneurysmal rupture: an emergent negative factor in the natural history of intracranial aneurysms? **Neurosurgery 32:**518–526, 1993
40. Park HK, Horowitz M, Jungreis C, et al: Endovascular treatment of paraclinoid aneurysms: experience with 73 patients. **Neurosurgery 53:**14–24, 2003
41. Proust F, Debono B, Hannequin D, et al: Treatment of anterior communicating artery aneurysms: complementary aspects of microsurgical and endovascular procedures. **J Neurosurg 99:** 3–14, 2003
42. Qureshi AI, Hutson AD, Harbaugh RE, et al: Methods and design considerations for randomized clinical trials evaluating surgical or endovascular treatments for cerebrovascular diseases. **Neurosurgery 54:**248–267, 2004
43. Raaymakers TW, Rinkel GJ, Limburg M, et al: Mortality and morbidity of surgery for unruptured intracranial aneurysms: a meta-analysis. **Stroke 29:**1531–1538, 1998
44. Raymond J, Guilbert F, Weill A, et al: Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. **Stroke 34:**1398–1403, 2003
45. Regli L, Dehdashti AR, Uske A, et al: Endovascular coiling compared with surgical clipping for the treatment of unruptured middle cerebral artery aneurysms: an update. **Acta Neurochir Suppl 82:**41–46, 2002
46. Regli L, Uske A, de Tribolet N: Endovascular coil placement compared with surgical clipping for the treatment of unruptured middle cerebral artery aneurysms: a consecutive series. **J Neurosurg 90:**1025–1030, 1999
47. Rinkel GJ, Djibuti M, Algra A, et al: Prevalence and risk of rupture of intracranial aneurysms: a systematic review. **Stroke 29:** 251–256, 1998
48. Solomon RA, Fink ME, Pile-Spellman J: Surgical management of unruptured intracranial aneurysms. **J Neurosurg 80:** 440–446, 1994
49. Sorteberg A, Sorteberg W, Rappe A, et al: Effect of Guglielmi detachable coils on intraaneurysmal flow: experimental study in canines. **AJNR 23:**288–294, 2002
50. Takahashi T: The treatment of symptomatic unruptured aneurysms. **Acta Neurochir Suppl 82:**17–19, 2002
51. Yaşargil MG, Antic J, Laciga R, et al: Microsurgical pterional approach to aneurysms of the basilar bifurcation. **Surg Neurol 6:**83–91, 1976

Manuscript received October 7, 2004.
Accepted in final form October 21, 2004.
Address reprint requests to: Robert Spetzler, M.D., Neuroscience Publications, Barrow Neurological Institute, 350 West Thomas Road, Phoenix, Arizona 85013. e-mail: neuropub@chw.edu.