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## **Recommendations for the Management of Patients With Unruptured Intracranial Aneurysms : A Statement for Healthcare Professionals From the Stroke Council of the American Heart Association**

Joshua B. Bederson, Issam A. Awad, David O. Wiebers, David Piegras, E. Clarke Haley, Jr, Thomas Brott, George Hademenos, Douglas Chyatte, Robert Rosenwasser and Cynthia Caroselli

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## Recommendations for the Management of Patients With Unruptured Intracranial Aneurysms

### A Statement for Healthcare Professionals From the Stroke Council of the American Heart Association

Joshua B. Bederson, MD, Chair; Issam A. Awad, MD; David O. Wiebers, MD; David Piepgras, MD; E. Clarke Haley, Jr, MD; Thomas Brott, MD; George Hademenos, PhD; Douglas Chyatte, MD; Robert Rosenwasser, MD; Cynthia Caroselli, RN, Members

**A**neurysmal subarachnoid hemorrhage (SAH) has a 30-day mortality rate of 45%, with approximately half the survivors sustaining irreversible brain damage.<sup>1</sup> On the basis of an annual incidence of 6 per 100 000, ≈15 000 Americans will have an aneurysmal SAH each year. Population-based incidence rates vary considerably from 6 to 16 per 100 000, with the highest rates reported from Japan and Finland.<sup>2-5</sup> Approximately 5% to 15% of stroke cases are secondary to ruptured saccular aneurysms. Although the prevention of hemorrhage has been advocated as the most effective strategy aimed at lowering mortality rates,<sup>6</sup> the optimal management of patients with unruptured intracranial aneurysms (UIAs) remains controversial. Management decisions require an accurate assessment of the risks of various treatment options compared with the natural history of the condition.

The natural history of UIAs and treatment outcomes are influenced by (1) patient factors, such as previous aneurysmal SAH, age, and coexisting medical conditions; (2) aneurysm characteristics, such as size, location, and morphology; and (3) factors in management, such as the experience of the surgical team and the treating hospital. These many influences have contributed to considerable variability in the reported risks for aneurysmal SAH and the treatment of UIAs. There are no prospective randomized trials of treatment interventions versus conservative management to date, and it is possible that no such studies will be carried out in the future.

According to a classification system suggested by Cook et al,<sup>7</sup> randomized clinical trials with low likelihoods of false-

positive and false-negative errors provide the highest level of evidence (level I) that can be applied to a clinical recommendation. Randomized trials with high likelihoods of false-negative and positive errors provide level II evidence. Level III evidence is generated with nonrandomized concurrent cohort comparisons between contemporaneous patients who did and those who did not receive treatment. Level IV evidence is generated with nonrandomized historical cohort comparisons between current patients who are receiving therapy and former patients who did not. Level V evidence is generated with case series without control subjects. For UIAs only, level IV and level V evidence exists, and these can support grade C recommendations. Grade C recommendations often present an array of potential clinical actions, any of which could be considered appropriate.<sup>7</sup>

The Stroke Council of the American Heart Association formed a task force to develop practice guidelines for the management of UIAs. A consensus committee reviewed the existing data in this field and prepared recommendations. The database for this review was the existing literature in the English language regarding UIAs assembled by the committee.

These guidelines are intended to serve as a framework for the development of treatments for individuals and as a basis for future research regarding UIAs. It is recognized that these recommendations may not apply to all situations. Further anticipated epidemiological research during the next few years,<sup>8</sup> as well as possible subsequent randomized trials for appropriate subgroups of patients with UIAs, will be useful for confirmation or modification of the guidelines in this document.

#### Natural History

Few systematic studies of natural history had been performed until the recent International Study of Unruptured Intracranial Aneurysms (ISUIA).<sup>8</sup> This study provided compelling evidence that natural history is different for patients with UIAs who have no history of SAH than it is for patients with a history of prior SAH due to a separate aneurysm. In consideration of the natural history of intracranial aneurysms, it is therefore important to distinguish between these 2 groups.

#### Patients Without Prior History of SAH

Natural history studies in patients without a history of SAH include the Cooperative Aneurysm Study, in which 32 of 165

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For comments or questions about this statement, contact Joshua Bederson, MD, One Gustave L. Levy Place, New York, NY 10029; e-mail [jbederson@mssm.edu](mailto:jbederson@mssm.edu)

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patients with symptomatic UIAs were selected for conservative management and 8 (25%) died from SAH at 3 months to 3 years after diagnosis. The 8 patients who died had aneurysms of 7 to 10 mm in diameter or larger; no UIAs of <7 mm ruptured. Three of 9 patients with 7- to 10-mm aneurysms bled; however, the precise sizes of these aneurysms were not stated.<sup>9</sup> In a study from Japan, Inagawa et al<sup>10</sup> studied 47 patients with 55 UIAs for a mean duration of 5.1 years. During follow-up, 1 rupture occurred in a patient without prior SAH who had a giant ( $\geq 25$  mm) basilar aneurysm. In another Japanese study, Asari and Ohmoto<sup>11</sup> reported on 54 patients followed up for 43.7 months and found subsequent rupture in 11 patients, including 8 of 39 patients without prior SAH. The average aneurysm size in those who bled was 13.1 mm. However, 4 patients (10%) with 4- to 5-mm aneurysms bled.

In a study by Yasui et al,<sup>12</sup> 234 patients with and without SAH were evaluated during a period of 6.25 years. Thirty-four patients (14.5%) bled, with an average annual rupture rate of 2.3%. In a separate study, these authors evaluated aneurysm size in 25 patients with or without prior SAH and rupture of a previously unruptured aneurysm.<sup>13</sup> Twenty-two of the newly ruptured aneurysms were <9 mm in diameter at initial diagnosis and 16 were <5 mm in diameter. Aneurysm size increased in 19 of 20 patients who were reassessed angiographically after rupture. Despite aneurysm growth in the majority of patients who bled, aneurysm size was <9 mm in 11 patients and <5 mm in 5 patients at the time of rupture. Although the authors concluded that even the smallest UIAs require "radical treatment or careful follow-up," the methods used in these retrospective studies substantially limit the strength of any conclusions about aggressive treatment.

In a study by Wiebers et al<sup>14</sup> that included 130 patients with a mean follow-up interval of 8.3 years, 15 of 130 patients had a subsequent intracranial hemorrhage. Of the 102 aneurysms <10 mm in diameter at the time of discovery, none ruptured, whereas of the 51 aneurysms  $\geq 10$  mm in diameter, 15 ruptured during a mean follow-up of 8.3 years. A multivariate discriminant analysis of the relationship of several independent variables to aneurysm rupture revealed that the only variable of independent statistical significance for the prediction of aneurysmal rupture was aneurysm size.<sup>14,15</sup> Only 36 aneurysms were in the 6- to 9-mm category and only 10 were in the 8- to 9-mm category, leaving considerable doubt about the use of 10 mm as a critical size below which the risk of rupture would be negligible.

ISUIA is the largest, most systematic natural history study performed to date. The investigators used predefined criteria for patient entry and aneurysmal rupture across multiple centers, remeasurement of all aneurysms with hard-copy films that involved a defined system for magnification correction, and a published methodology for in-depth detection, review, and adjudication of detailed data regarding outcome events.<sup>8</sup> This study also had sufficient numbers of patients to allow secondary subgroup analysis according to aneurysm size, location, and history of SAH from a different aneurysm.

ISUIA researchers retrospectively identified 727 patients with UIAs followed up for an average of 7.5 years, reporting a rupture rate of 0.05%/y in patients with aneurysms <10 mm

in diameter and of  $\approx 1\%/y$  for those with aneurysms  $\geq 10$  mm in diameter.<sup>8</sup> The rupture rate was 6% in the first year among patients with giant ( $\geq 25$  mm) UIAs. Aneurysm location also predicted future rupture (posterior communicating, vertebrobasilar/posterior cerebral, and basilar tip UIAs were more likely to rupture). However, aneurysm size was the best predictor of future rupture. Multiple other patient demographic characteristics, aneurysmal symptoms other than rupture, aneurysmal characteristics, behavioral factors, and associated medical conditions did not independently predict future rupture. Among the patients without prior SAH with posterior communicating, vertebrobasilar/posterior cerebral, and basilar tip UIAs  $\geq 25$  mm in diameter, the risk of rupture was  $\approx 45\%$  at 7.5 years; 10- to 24-mm UIAs and <10-mm UIAs in the same locations carried rupture risks of  $\approx 15\%$  and  $\approx 2\%$  over 7.5 years, respectively. In all other locations, the rupture risks at 7.5 years for  $\geq 25$ -mm, 10- to 24-mm, and <10-mm UIAs were  $\approx 8\%$ ,  $\approx 3\%$ , and  $\approx 0\%$ , respectively.

### Patients With Prior History of SAH

In consideration of patients with UIA and a prior history of SAH from another source, 1 series involved 142 patients who harbored 181 UIAs who were followed up until death, SAH, or  $\geq 10$  years for a mean of 13.9 years.<sup>16</sup> Nearly all (131) of the 142 patients had prior SAH from a separate aneurysm that was repaired. The annual rupture rate from UIAs was 1.4% for the entire group. Aneurysm size was the only variable studied that predicted future rupture. However, the strength of the predictive value of size was marginal for the entire population ( $P=0.036$ ) and was not statistically significant for the 131 patients with prior SAH.

Review of other data from studies of patients with SAH and multiple aneurysms includes an evaluation of 182 patients followed up for a mean of 7.7 years, of whom 50 had the ruptured aneurysm treated surgically. Ten patients subsequently had intracranial hemorrhage, of which 3 were believed to have bled from a previous intact aneurysm. There was no clear relationship between the size of the aneurysm and propensity for rupture. However, the group with late rebleeding included a significantly greater proportion with aneurysms  $\geq 10$  mm in diameter.<sup>17</sup> In another study of 61 patients with SAH and 2 intracranial aneurysms in whom only the ruptured aneurysms had been clipped, 7 patients bled from a previously unruptured aneurysm, and 3 additional patients experienced fatal hemorrhage during a 10-year follow-up period. However, aneurysm sizes were not reported.<sup>18</sup>

The ISUIA<sup>8</sup> identified 722 patients with a prior history of SAH followed up for 7.5 years and reported rupture rates for patients with UIAs <10 mm in diameter that were 11 times higher (0.5%/y) than for patients without prior SAH with the same size aneurysms. Rupture rates for patients with prior history of SAH with UIAs  $\geq 10$  mm in diameter were 0.65%/y. The only clear predictor of future rupture among these patients was basilar tip location. Size alone did not predict future rupture. Among the patients with prior history of SAH with basilar tip UIAs of <10 mm, the rupture risk was  $\approx 12\%$  at 7.5 years compared with 3% for <10-mm UIAs in other locations.

The ISUIA findings differ from those of previous studies, which have shown (1) the mean diameter of aneurysms of patients who present with SAH to typically be <10 mm,<sup>19–22</sup> (2) the surgical morbidity and mortality rates to be significantly lower (see later),<sup>21,23</sup> and (3) a considerably higher annual rupture rate than that reported by ISUIA.<sup>21</sup> Like all natural history studies to date, ISUIA was based on retrospectively identified patients, which has raised controversy about patient selection. Population-based studies of SAH demonstrate a mortality rate for first SAH of 45%.<sup>1</sup> However, the mortality rate after a first SAH in the ISUIA was 83%, and in a previous study by the same authors with similar patient selection criteria, the rate was >90%.<sup>4</sup> This suggests that selection bias for inclusion in these studies resulted in the high mortality rates after rupture but could also be attributed to wide confidence intervals or a true higher mortality rate in this population. Selection criteria could also alter the apparent rupture rates. Because patients with factors that favor surgery are more likely to be excluded from analysis, a systematic error could be introduced that excludes aneurysms more likely to bleed. Apparent inconsistencies may also be attributable to actual differences between patients whose aneurysms are discovered before or after rupture. Although significant questions remain, ISUIA still represents the most comprehensive effort to date in documentation of the natural history of UIAs.

Spontaneous SAH is most frequently caused by 7- to 10-mm aneurysms.<sup>9,14,24</sup> This observation has led to the suggestion that 7 to 10 mm is a critical size for rupture of an unruptured aneurysm and is seen as an apparent contradiction of ISUIA, in which 10 mm was a critical size for rupture. However, alternative hypotheses could account for this observation, including a much higher prevalence of 7- to 10-mm aneurysms, a decrease in aneurysm size at the time of rupture, or a smaller critical size for aneurysms that rupture at the time they form or soon after they form. Current evidence does not conclusively support one explanation over the others, and further work will be needed to address this issue.

Accumulating evidence points to an influence of aneurysm size on the risk of rupture in patients with UIAs and no history of SAH from another aneurysm, with larger lesions more likely to hemorrhage. Although the underlying pathophysiology remains uncertain, ISUIA indicates that incidental aneurysms in patients with prior SAH from another intracranial aneurysm carry a higher risk for future rupture.

Thus far, all natural history studies have been performed on patients selected for conservative management, which may influence the results. Although the natural history of UIAs could be revealed in a prospective study with no treatment and long-term follow-up, it may be unrealistic to expect that such a study will be conducted.

## Diagnostic Evaluation

### Computed Tomography

Most CT scanners obtain slice thicknesses of 5 to 10 mm, and small aneurysms may not be visible, even with intravenous contrast agents; therefore, standard CT with or without contrast agents cannot adequately define the presence or

absence of an intracranial aneurysm, particularly if an unruptured lesion is suspected.<sup>25,26</sup>

### CT Angiography

CT angiography is performed by obtaining images acquired during the arterial phase of contrast opacification. CT angiography may demonstrate aneurysms as small as 2 to 3 mm with sensitivities of 77% to 97% and specificities of 87% to 100%.<sup>27</sup> This modality of imaging may be useful when patients with identified UIAs are given conservative follow-up, in patients with partially clipped aneurysms, or in those who have undergone treatment with endovascular techniques.<sup>28–31</sup> CT angiography has been used as a screening tool in populations at high risk for intracranial aneurysms.<sup>25,32–34</sup>

### MRI/Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) axial source images may undergo computer reformation to display several vessels in multiple projections<sup>35–37</sup> and can provide additional views that cannot be obtained with intra-arterial catheter angiography. MRA is useful as a screening modality, with sensitivity rates of 69% to 93%, and is particularly useful for aneurysms of >3 to 5 mm.<sup>32,38–41</sup> MRA may be less useful in the detection of subtle changes in aneurysm size or as a screening tool in patients with previously treated intracranial aneurysms and should be restricted to patients with magnetic resonance-compatible clips.

### Intra-Arterial Angiography

Intra-arterial catheter angiography continues to be the “gold standard” in the diagnostic evaluation of intracranial aneurysms. Transcatheter studies provide the most information about small perforating vessels and produce higher-resolution images than other imaging modalities.<sup>42–44</sup> However, catheter angiography is a more invasive procedure. Recent studies of experienced neuroradiological centers demonstrate a risk of local catheter-related complications of ≈5%, total neurological morbidity rate of ≈1%, and permanent neurological morbidity rate of ≈0.5%.<sup>45,46</sup>

## Screening for UIAs

### Theoretical Rationale for Screening

Because of the poor prognosis from SAH and the relatively high frequency of asymptomatic intracranial aneurysms, the role of elective screening has been a subject of discussion in the literature. Until recently, the only effective screening procedure was intra-arterial catheter angiography, a procedure both costly and invasive. Noninvasive imaging techniques now exist, such as MRA and CT angiography, which are less expensive and noninvasive and have a high degree of sensitivity and specificity as outlined here.

### Populations at Increased Risk of Harboring an Intracranial Aneurysm

Certain genetic syndromes have been associated with an increased risk of aneurysmal SAH, such as autosomal dominant polycystic kidney disease and type IV Ehlers-Danlos syndrome. These syndromes support the theory of inherited susceptibility to aneurysm formation.<sup>8,9,18,25,29,47</sup>

The familial intracranial aneurysm (FIA) syndrome occurs when 2 relatives, third degree or closer, have radiographically proved intracranial aneurysms.<sup>2,7,11,14,28,30,48</sup> Cohorts with this syndrome have SAH at a younger age than in the general aneurysm population, are more likely to harbor multiple aneurysms, and have more hemorrhages among siblings and mother-daughter pairings.<sup>2,16,30</sup> In family members with  $\geq 2$  first-degree relatives with SAH, the risk of harboring an unruptured aneurysm was found to be 8% in 1 study,<sup>32</sup> whereas another study reported a relative risk of 4.2.<sup>45</sup> Family members with only 1 affected first-degree relative have a higher relative risk of harboring an unruptured aneurysm than the general population but less than those with the FIA syndrome.<sup>44,49</sup> In patients who have been treated for a ruptured aneurysm, the annual rate of new aneurysm formation is 1% to 2%.<sup>17,46,50,51</sup> Patients with multiple intracranial aneurysms may be particularly susceptible to new aneurysm formation.<sup>50</sup>

### Concepts of Cost-Effectiveness

In evaluation of the clinical efficacy of screening for asymptomatic intracranial aneurysms, the costs of screening should be weighed against the risks and consequences of SAH. Several assumptions must be made to estimate these costs, such as how an aneurysm would be managed if detected, although this unrealistically simplifies the medical decision-making process. Recent studies have found that the following factors heavily influence the analysis of cost effectiveness for asymptomatic unruptured aneurysms: aneurysm incidence, risk of rupture (natural history), and risk of treatment.<sup>32,45,49,52,53</sup> Mathematical modeling studies have demonstrated that the cost effectiveness of screening is highly sensitive to the aneurysm rupture rate, even in populations at high risk for intracranial aneurysms. For example, with the assumption that all aneurysms are surgically treated with a complication rate of 5.1%, there is no theoretical benefit of screening if the annual rupture rate is 0.05%, whereas there is a benefit when the annual rupture rate is taken as  $\geq 1\%$ .<sup>53</sup>

### Recommendations

To date, there have been no randomized controlled clinical trials that addressed the cost effectiveness of screening for intracranial aneurysms, and only grade C recommendations can be made.

Screening for asymptomatic intracranial aneurysms in the general population is not indicated. Patients with environmental risk factors such as cigarette smoking and alcohol use have an increased risk of SAH, but this has not been associated with an increased frequency of intracranial aneurysms,<sup>54–58</sup> and screening for aneurysms is not warranted in this population. Theoretical modeling suggests that screening is not efficacious in populations with the genetic syndromes mentioned here or in family members with a single first-degree relative with aneurysmal SAH or an intracranial aneurysm; the latter was recently substantiated in a study that used Markov analysis methodology.<sup>49</sup> These suggestions require confirmation in further studies.

In populations with the FIA syndrome ( $\geq 2$  first-degree relatives), screening programs have demonstrated the in-

creased incidence of intracranial aneurysms. However, cost-effectiveness has not been evaluated in clinical studies, and recommendations regarding screening in this group are controversial.<sup>52,59</sup> Further information about the natural history of UIAs will help to guide future recommendations about screening programs. Until the efficacy of screening groups with the FIA syndrome has been evaluated in a population-based clinical study, screening should be considered on an individual basis.

Because the annual rate of new aneurysm formation in patients treated for aneurysmal SAH is reported to be as high as 1% to 2%, late radiological evaluation of this population should be considered.<sup>50</sup>

## Treatment of UIAs

### Relevant Outcome Measures

Assessment of treatment outcome has focused on 30-day surgical mortality rates and various treatment morbidity rates, although the latter have not been consistently identified or reported. Studies have used the Glasgow Coma Scale score or modifications, but these scales are relatively insensitive to disabilities in good outcome strata. Functional outcome with the use of other validated scales has only recently been used in the assessment of aneurysm outcome,<sup>8</sup> although the time at assessment after therapy has not been standardized. It is not known whether documented abnormalities persist or recover over time and what their functional impact may be. The impact on quality of life of living with the diagnosis of unruptured aneurysm has not been evaluated.

A cardinal aspect of reported outcomes that is rarely emphasized is the actual rate of obliteration of the aneurysm after treatment and its durability. In the absence of long-term follow-up, apparently less invasive treatment modalities may be associated with decreased morbidity rates but without effective or durable exclusion of the aneurysm from the circulation. For example, a recent meta-analysis of the literature on coil embolization of intracranial aneurysms demonstrated a low complication rate of 3.7% but a high rate (46%) of incomplete obliteration.<sup>60</sup> Documentation of aneurysm obliteration requires postoperative angiography, and this may have to be repeated to verify durability. However, the risks and costs of such routine postoperative surveillance have not been assessed. Recent data indicate that the risk of recurrence of an aneurysm that has been completely clipped at surgery is  $\approx 1.5\%$  at 4.4 years.<sup>50</sup> Incompletely clipped aneurysms have a significantly higher recurrence rate, particularly if the residual aneurysm is broad based.<sup>50</sup> A recent Japanese study demonstrated that surgical treatment of UIAs did not provide absolute protection.<sup>61</sup>

### Direct Surgical Treatment

The majority of studies of outcome after surgery for UIAs involve case series of one or more neurosurgeons in which their results are evaluated. The range of mortality and morbidity rates reported in the largest series is wide, varying from 0% to 7% for death and 4% to 15.3% for complications.<sup>8,22,62–67</sup> Two meta-analyses were recently reported.<sup>22,62</sup> The first of these involved 733 patients<sup>22</sup> and reported a 1% mortality rate and a 4% morbidity rate. The second, which

encompassed 2460 patients and reported a mortality rate of 2.6% and a permanent morbidity rate of 10.9%.<sup>62</sup> also found declining morbidity and mortality rates for anteriorly located aneurysms in recent years. There has been virtually no uniformity regarding the definition of good versus poor outcomes, or even mortality rates; some have been defined at 30 days, 3 to 6 months, or 1 year after surgery. None of the studies contained a sufficient number of patients to warrant conclusive judgment regarding the predictors of outcome as outlined later.

ISUIA constitutes the most comprehensive study on this issue, as previously outlined, and is the only study to systematically assess cognitive status before and after surgery across multiple centers with a team-evaluation approach.<sup>8</sup> Although ISUIA enrolled surgeons from leading academic institutions, it did not specify outcome thresholds to credential surgeons before participation in the study. ISUIA reported on 2 groups treated with craniotomy for UIAs: patients without a history of SAH and those with such a history. In 798 patients without prior SAH, mortality rates were 2.3% at 30 days and 3.8% at 1 year, whereas in those with prior SAH from a treated aneurysm, mortality rates were 0% at 30 days and 1% at 1 year. In addition, both patient groups were found to have neurological disability rates of  $\approx 12\%$  at 1 year, which included disability due to major cognitive impairment.<sup>8</sup> The rate of cognitive deficits reported in this study was not previously included in assessment of surgical morbidity rates for UIAs. This important finding requires further investigation and must be considered in the assessment of individual patients for possible surgical treatment.

#### ***Specific Risk Factors***

Despite the lack of level I to level III studies in the literature, experienced surgeons believe that several factors significantly influence surgical outcome. These factors can be grouped into patient characteristics (age, symptoms, and medical condition), aneurysm characteristics (size, location, and morphology), and other factors (hospital and surgical team experience). These factors should also be considered in the assessment of treatment alternatives.

#### ***Patient Characteristics***

Age is clearly an important patient factor that influences surgical outcome as illustrated by ISUIA, in which the combined morbidity and mortality rate was 6.5% for patients <45 years old, 14.4% for patients 45 to 65 years old, and 32% for patients >64 years old.<sup>8</sup> Because one of the major indications for treatment of UIA is to prevent rupture and a greater age at presentation implies a shorter period of risk, the increased surgical morbidity rate for older patients is particularly important in this condition.

#### ***Aneurysm Size, Morphology, and Location***

Aneurysm factors that potentially contribute to surgical outcome include size, morphology, and specific location. Giant aneurysms (>25 mm) require specialized surgical and adjunctive techniques<sup>68,69</sup> and carry the greatest risk, with combined mortality and morbidity rates of  $\approx 20\%$  and  $\approx 50\%$  for posterior circulation aneurysms. In a study of 107 patients with incidental aneurysms, Wirth et al<sup>65</sup> reported morbidity

rates of <3% for aneurysms of  $\leq 5$  mm, <7% for 6- to 15-mm aneurysms, and 14% for 16- to 24-mm aneurysms. In the meta-analysis by Raaymakers et al,<sup>62</sup> aneurysm size correlated with morbidity and mortality rates, with smaller aneurysms associated with better rates.

Aneurysms with large ill-defined or fusiform necks, those arising from atherosclerotic or ectatic vessels, those that incorporate major intracranial bifurcations, and those located partially within the cavernous sinus or arising from the mid portion of the basilar artery all require special techniques and may be associated with increased surgical morbidity rates.<sup>69-73</sup> The natural history of these aneurysms is also poorly defined. As a group, aneurysms arising in the posterior circulation have been thought to pose a greater surgical risk than those in the anterior circulation. Aneurysms at the basilar apex are intimately associated with midbrain perforating arteries, and these can be injured during open surgery<sup>74</sup> or with endovascular procedures.<sup>75</sup> In the meta-analysis by Raaymakers et al,<sup>62</sup> posterior aneurysm location was associated with the highest surgical risk, particularly for giant aneurysms, for which the mortality rate was 9.6% and the morbidity rate was 37.9%. Nevertheless, as experience with microsurgical techniques increases, aneurysm location may become less of a factor that influences outcome, and recent studies report little or no increase in morbidity rates due to focal neurological deficits in cases of nongiant aneurysm of the posterior circulation.<sup>66,69</sup>

#### ***Symptoms***

Symptoms such as mass effect on cerebral or brain stem structures, compression of cranial nerves, or ischemic/embolic phenomena can be effectively treated with surgical clipping and decompression and can serve as an important indication for treatment.<sup>69,76,77</sup> For example, the development of a new third nerve palsy ipsilateral to an aneurysm of the posterior communicating artery implies growth of the aneurysm. This has traditionally been regarded as an indication for urgent treatment to prevent hemorrhage and to maximize the potential for recovery of the deficit.<sup>78-81</sup>

Symptomatic unruptured aneurysms carry a greater surgical risk than do truly incidental aneurysms,<sup>66</sup> particularly when the presenting symptom is cerebral ischemia.<sup>65</sup> However, the majority of aneurysms that cause symptoms of mass effect or ischemia are large,<sup>82</sup> and the apparent relationship between symptoms and increased risk of complications may be a reflection of aneurysm size.

#### ***Surgical Experience and Patient Referral Patterns***

Surgical experience has been shown to influence outcome after intracranial aneurysm surgery. In a study of in-hospital deaths after craniotomies performed for UIA between 1987 and 1993 in New York State hospitals, there was a 53% decrease in mortality rate when the 21 hospitals that each performed >10 craniotomies per year were compared with the 89 hospitals that each performed  $\leq 10$  such operations per year (5.3% versus 11.2% mortality rate, respectively). The majority of New York State hospitals were found to rarely have aneurysm surgery performed, and those hospitals had more than twice the in-hospital mortality rate.<sup>83</sup>

## Endovascular Management of UIAs

Currently, endosaccular occlusion of intracranial aneurysms is performed with the electrolytically detachable Guglielmi detachable coil system (GDC; Target Therapeutics).<sup>84–91</sup> This is the only endovascular device currently approved by the Food and Drug Administration in the United States and Canada. It involves platinum microwires of different sizes and lengths that can form complex shapes when deployed within the aneurysm sac.

To date, >16 000 patients with ruptured and unruptured aneurysms have been treated worldwide with the GDC method.<sup>92</sup> Published reports of early clinical and angiographic results suggest that this method is associated with fewer treatment-related complications than open surgery,<sup>93,94</sup> but the long-term efficacy of the GDC method in the prevention of rupture or growth of an unruptured aneurysm is, as yet, unproved. Halbach et al<sup>87</sup> reported on the ability of coil embolization to relieve signs and symptoms of mass effect from unruptured aneurysms. Malisch et al<sup>95</sup> reported mid-term clinical results on a consecutive series of 100 patients with a follow-up of 3.5 years. Of concern was the frequency of post-GDC embolization hemorrhage in patients with large aneurysms (4% incidence of rebleeding) and giant aneurysms (33% incidence).

Another report by Eskridge and Song<sup>96</sup> evaluated endosaccular occlusion in 150 basilar tip aneurysms as part of a Food and Drug Administration Multi-Center Clinical Trial. In this group, 83 patients had a ruptured aneurysm and 67 had unruptured basilar tip aneurysms. The rebleeding rate for treated ruptured aneurysms was up to 3.3%, and the bleeding rate for unruptured aneurysms was up to 4.1%. Permanent deficits due to stroke in patients with ruptured or unruptured aneurysms occurred in 5% and 9%, respectively. The periprocedural mortality rate in this group was 2.7%, although the mortality among patients with UIAs is unclear. The authors concluded that detachable platinum coil embolization was a promising treatment for ruptured basilar tip aneurysms that are not surgically clippable but that the role of this procedure in unruptured basilar tip aneurysms was unclear.

In a recent meta-analysis that encompassed 1383 patients treated with endovascular coils for (ruptured or unruptured) intracranial aneurysms, Brilstra et al<sup>60</sup> found a low permanent complication rate (3.7%) but a high rate of incomplete obliteration (46%). Recent data from the neurosurgical literature indicate a significantly higher rate of aneurysm recurrence in incompletely treated lesions.<sup>50</sup> It is not clear how incomplete coil embolization affects the bleeding rate of UIAs.<sup>93</sup>

Coil embolization is a treatment option for UIAs. Although its primary use in North America has been for patients whose aneurysms are considered to have a high surgical risk, for patients considered to be medically unsuitable for surgery, or for patients who refuse open surgery,<sup>87,92,96,97</sup> the technique appears to be used with increasing frequency. It is not known how many patients with UIAs have been treated, and no large-scale studies devoted to the endovascular treatment of UIAs have been reported. Consequently, it is premature to judge the effectiveness or efficacy of endovascular treatment for UIAs. A case-controlled, randomized prospective trial

will be required to adequately compare this technique with direct clipping.

## Management Considerations

Aneurysmal SAH is a devastating condition for which prevention has been advocated as the most effective strategy aimed at lowering mortality rates.<sup>6</sup> However, all current treatments carry risks, and recommendations for treatment versus observation are often difficult and controversial. Treatment complications generally occur at or around the time of the procedure but could potentially improve during the patient's remaining lifetime. In contrast, the risk of rupture of an untreated aneurysm is cumulative but may provide a period of unimpaired life. Nonlethal complications in both settings can potentially improve over time.

Deliberations must take into account important characteristics of the aneurysm and the patient in whom it exists. Of the former, particular consideration must be given to aneurysm size, form, and location and its symptomatic versus incidental status. As a general rule, exclusively extradural, intracavernous (internal carotid artery) aneurysms, even if symptomatic with pain or ophthalmoparesis, do not carry a major risk for intracranial hemorrhage, and thus management decisions are primarily aimed at symptom relief more than at hemorrhage prevention.<sup>87,98</sup>

Among patient factors, patient age, general medical condition, and family history of aneurysmal SAH are prime considerations in the treatment analysis. Symptoms due to UIAs should be discriminated relative to those developing rapidly and related to smaller aneurysms, presumably due to acute aneurysmal expansion. Although minimal data regarding this subgroup are available, studies from Locksley,<sup>9</sup> Eskesen et al,<sup>99</sup> and Juvela et al<sup>16</sup> show a high rate of rupture within several months of symptom onset. More commonly, symptomatic aneurysms are larger, occasionally giant in size, and sometimes partially thrombosed, producing subacute symptoms due to adjacent cranial nerve or brain compression. Such lesions carry a major risk for both progressive neurological deficit and aneurysm rupture.<sup>14,16,99</sup>

As found in the recent ISUIA, UIAs must be considered in the context of the patient's previous history of aneurysmal SAH or lack thereof due to a difference in rupture rates in these 2 populations. In addition, it should be recalled that in 2 studies in which UIAs later ruptured, the majority of UIAs showed enlargement, although the temporal course of this change remains undefined.<sup>12,16</sup> Finally, recommendations regarding the treatment of UIAs should be influenced by characteristics such as aneurysm morphology, extensive calcification, thrombosis, and more rarely encountered clinical features such as previous confirmation of the aneurysm and stability of size.

## Recommendations

The existing body of knowledge supports the following recommendations (options) regarding the treatment of UIAs:

1. The treatment of small incidental intracavernous ICA aneurysms is not generally indicated. For large symptomatic intracavernous aneurysms, treatment decisions should be individualized on the basis of patient age,

severity and progression of symptoms, and treatment alternatives. The higher risk of treatment and shorter life expectancy in older individuals must be considered in all patients and favors observation in older patients with asymptomatic aneurysms.

2. Symptomatic intradural aneurysms of all sizes should be considered for treatment, with relative urgency for the treatment of acutely symptomatic aneurysms. Symptomatic large or giant aneurysms carry higher surgical risks that require a careful analysis of individualized patient and aneurysmal risks and surgeon and center expertise.
3. Coexisting or remaining aneurysms of all sizes in patients with SAH due to another treated aneurysm carry a higher risk for future hemorrhage than do similar sized aneurysms without a prior SAH history and warrant consideration for treatment. Aneurysms located at the basilar apex carry a relatively high risk of rupture. Treatment decisions must take into account the patient's age, existing medical and neurological condition, and relative risks of repair. If a decision is made for observation, reevaluation on a periodic basis with CT/MRA or selective contrast angiography should be considered, with changes in aneurysmal size sought, although careful attention to technical factors will be required to optimize the reliability of these measures.
4. In consideration of the apparent low risk of hemorrhage from incidental small (<10 mm) aneurysms in patients without previous SAH, treatment rather than observation cannot be generally advocated. However, special consideration for treatment should be given to young patients in this group. Likewise, small aneurysms approaching the 10-mm diameter size, those with daughter sac formation and other unique hemodynamic features, and patients with a positive family history for aneurysms or aneurysmal SAH deserve special consideration for treatment. In those managed conservatively, periodic follow-up imaging evaluation should be considered and is necessary if a specific symptom should arise. If changes in aneurysmal size or configuration are observed, this should lead to special consideration for treatment.
5. Asymptomatic aneurysms of  $\geq 10$  mm in diameter warrant strong consideration for treatment, taking into account patient age, existing medical and neurological conditions, and relative risks for treatment.

### Synthesis and Conclusions

The current literature contains level IV and level V evidence and can support grade C recommendations. Patients' experiences, biases, and personal preferences influence the decision to treat and should also be considered.<sup>23</sup>

Factors that favor surgery include a young patient with a long life expectancy, previously ruptured aneurysms, a family history of aneurysm rupture, large aneurysms, symptomatic aneurysms, observed aneurysm growth, and established low treatment risks.

Factors that favor conservative management include older patient age, decreased life expectancy, comorbid medical conditions, and asymptomatic small aneurysms.

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KEY WORDS: AHA Scientific Statement ■ aneurysm ■ surgery ■ natural history ■ outcome ■ epidemiology ■ risk factors ■ diagnosis