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AHA Medical/Scientific Statement

Special Report

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association

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Subarachnoid hemorrhage (SAH) is a common and often devastating occurrence; each year approximately 30 000 Americans have nontraumatic SAH.[1] Despite considerable advances in diagnostic techniques, surgical, and anesthetic techniques and perioperative management, the outcome for patients with SAH remains poor, with overall mortality rates of 25% and significant morbidity among approximately 50% of survivors.[2]

The evolution of treatment protocols for patients with subarachnoid hemorrhage has been influenced considerably by large, multicenter prospective cohort analyses and, more recently, multicenter prospective, randomized trials. Nevertheless, several accepted treatment modalities have not been substantiated by rigorous clinical scientific assessment. In many cases specific treatments for SAH are not amenable to testing by randomized, prospective trials because of practical or ethical considerations.

To address these issues, the Stroke Council of the American Heart Association formed a task force to develop practice guidelines for the management of aneurysmal subarachnoid hemorrhage. A consensus committee reviewed existing data in this field and prepared recommendations. The database for this review was the existing literature regarding SAH assembled by the committee; a formal literature review was not conducted. The reports reviewed were selected on the basis of study design, sample size, and relevance to the issue involved. Each report was graded according to existing criteria of scientific merit,[3] and a grading scale derived from these data (Table 1). Recommendations were made by group consensus based on the grading scale and current practice standards according to four categories: strongly recommended, recommended, not recommended, or insufficient data. Recommendations for diagnostic modalities are not based on scientific merit, because of the absence of clinical trial data regarding the usefulness of these tests.

The management guidelines proposed by this committee relate to subarachnoid hemorrhage secondary to ruptured cerebral arterial aneurysms. These protocols are not necessarily applicable to treatment of SAH resulting from other causes (eg, trauma, arteriovenous malformation, bleeding disorders, etc). By nature of the consensus process, the recommendations in this report represent an overview of existing treatment protocols, which vary considerably. In addition, circumstances unique to specific clinical situations may appropriately mitigate treatment strategies that differ from those proposed; ie, these recommendations may not apply to all situations. Rather, these guidelines are intended to serve as the scientific framework for developing treatments for individual patients and as a basis for future research regarding management of SAH.

Epidemiology of Aneurysmal Subarachnoid Hemorrhage

Incidence and Prevalence

Using data collected from nonfederal hospitals, the National Hospital Discharge Survey of 1990[1] reported that 25 000 patients in the United States had had a subarachnoid hemorrhage during the previous year. Data from Rochester, Minn, for 1975 through 1984 suggest that an additional 12% of persons with SAH do not receive prompt medical attention[2] and that many cases of SAH are misdiagnosed.[4] Thus, the annual prevalence of aneurysmal SAH in the United States probably exceeds 30 000 persons. Population-based incidence rates for SAH vary from 6 to 16 per 100 000,[5,6] with the highest rates reported in Finland and Japan.[7,8] Unlike other types of stroke, the incidence of SAH has not declined over time.[9] It is likely, however, that these

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TABLE 1. Levels of Evidence and Grading of Recommendations for Treatment of Patients With Subarachnoid Hemorrhage

Levels of Evidence
Level I: Data from randomized trials with low false-positive (alpha) and low false-negative (beta) errors
Level II: Data from randomized trials with high false-positive (alpha) and high false-negative (beta) errors
Level III: Data from nonrandomized concurrent cohort studies
Level IV: Data from nonrandomized cohort studies using historical controls.
Level V: Data from anecdotal case series
Strength of Cumulative Data
Grade A Supported by level I evidence
Grade B Supported by level II evidence
Grade C Supported by level III, IV, or V evidence

comparative rates are influenced by the increased use of computed tomography in the diagnosis of stroke events during any particular epoch. The incidence of SAH increases with age (mean age of approximately 50 years) and is higher in women than in men.[9] Recent data also suggest that African-Americans are at higher risk than white Americans.[10]

Population-based mortality rates for SAH have progressively declined since 1970.[2,9] The survival rate after SAH has improved during this time, but differences between community rates and hospital rates are apparent, with a difference of approximately 20% in mortality at 1 year after SAH.[11]

Risk Factors

Risk factors for subarachnoid hemorrhage have been studied in cross-sectional and cohort studies; age, gender, and race have been described as putative risk factors.[10,12,13] Smoking is a consistent and strong risk factor for SAH,[14-20] although it is not known whether tobacco use is a long- or short-term risk factor. Longstreth et al[14] observed that risk of SAH among smokers was greatest 3 hours after smoking a cigarette. Use of alcohol or binge drinking may also be a risk factor for SAH.[14,21,22] Cohort studies suggest that hypertension may be a risk factor, although case-control studies do not demonstrate this relationship. Studies in the 1960s noted increased risk of SAH associated with the use of oral contraceptives.[12,13,23] Recent case-control studies have not supported this association, although the estrogen composition of these drugs has changed over time. Case reports of drug abuse in relation to SAH have been published,[24] and stimulants may also be a short-term risk factor. A cohort study by Knekt et al[18] has reported an inverse relationship between SAH and body mass index. Diabetes does not appear to be a risk factor for SAH.[25] Because surgical repair is the treatment of choice for most aneurysms, secondary prevention through modification of risk factors is less pertinent in SAH than in other cerebrovascular disorders.

Risk Factor Modification and Prevention of Subarachnoid Hemorrhage

Blood Pressure Control

Hypertension is a common risk factor for hemorrhagic stroke. In a review by Collins et al,[26] over multiple trials an average reduction in diastolic blood pressure of 6 mm Hg by antihypertensive medication produced an aggregate 42% reduction in stroke incidence. However, there is little information on aneurysmal SAH in these studies because of limited sample size for SAH events. The evidence that antihypertensive medications have a beneficial effect on the incidence of SAH has been ecological. Nevertheless, although there has been a marked improvement in blood pressure control in the general population in the past decade, there has been little change in the incidence of SAH during that time.[27-30]

Smoking Cessation

The evidence that smoking cessation reduces risk for subarachnoid hemorrhage is indirect. In a case-control study,[14] former smokers had a lower relative risk than light or moderate smokers, and there was an inverse relationship between time since the last cigarette and risk of SAH. In a prospective study of 117 006 women, it was observed that former smokers also had a lower relative risk of SAH than current smokers and that duration since quitting was associated with a decreased risk.[31]

Management of Unruptured Aneurysms

The prevalence of unruptured aneurysms in the general population is probably between 0.5% and 1.0% or approximately 2 million individuals in the United States.[32,33] The annual risk of SAH for unruptured aneurysms has been estimated at between 1% and 2%.[32,34] In several prospective studies the size of the aneurysm appeared to be a risk factor for future rupture; aneurysms of less than 3 mm in diameter had little chance of hemorrhage, whereas aneurysms of more than 10 mm were at greatest risk of rupture, with risk increasing with size.[35-37] In a retrospective series of ruptured aneurysms, the critical size determining risk of rupture was between 5 and 7 mm,[38-41] although SAH is frequently observed in aneurysms apparently smaller than 5 mm. Patients with symptoms related to the aneurysm (eg, mass effect) may be at higher risk for SAH than patients with aneurysms discovered incidentally.[42]

Screening High-Risk Populations

Possible high-risk groups for screening are those with familial cases and heritable disorders such as polycystic kidneys, Marfan's syndrome, or Ehlers-Danlos syndrome. The low yield of screening, the small risk of subsequent aneurysm rupture, and the inherent risk of angiographic complications has led to the recommendation that angiographic screening of these cohorts not be done[43]; screening studies using noninvasive technologies have not been performed. In a review of familial intracranial aneurysms, terBerg et al[44] suggested that screening by digital subtraction angiography might be appropriate in families with two or more affected members whose age is between 35 and 65 years. The benefit of

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screening with magnetic resonance angiography (MRA) has not been determined.[45]

Modification of Risk Factors for Subarachnoid Hemorrhage: Summary and Recommendations

1. The relationship between hypertension and SAH is uncertain (level of evidence III to IV, grade C). Treatment of high blood pressure with antihypertensive medication is strongly recommended to prevent stroke of varying etiology (level of evidence II to III, grade B).
2. Cessation of smoking may reduce risk of SAH, although evidence for this association is indirect (level of evidence III to IV, grade C).
3. In patients with acceptable surgical risk, clipping of unruptured aneurysms larger than 5 to 7 mm is recommended (level of evidence III to IV, grade C). Further studies are recommended to address this issue.
4. Screening of certain high-risk populations for unruptured aneurysms is of uncertain value; advances in MRA may facilitate screening in the future (level of evidence III to V, grade C).

Natural History of Ruptured Aneurysms

Recurrent hemorrhage remains a serious consequence of aneurysmal SAH, with a case-fatality rate of approximately 70% for persons who rebleed. In recent years improved diagnosis of SAH and rapid referral to specialized centers have delineated a distinct pattern of rebleeding compared with older studies.[46,47] In the prospective Cooperative Aneurysm Study,[48] rebleeding was maximal (4%) on the first day after SAH and then constant at a rate of 1% to 2% per day over the subsequent 4 weeks. Several prospective follow-up cohorts[49-51] have demonstrated that the risk of rebleeding with conservative therapy is between 20% and 30% for the first month after hemorrhage and then stabilizes at a rate of approximately 3% per year.[52]

Several potential risk factors for acute rebleeding have been identified from prospective and retrospective studies. The interval from hemorrhage to admission and treatment, initial blood pressure, and neurological status on admission have been related to recurrent hemorrhage in the first 2 weeks after SAH. Other factors related to rebleeding include gender, age, prior medical conditions, shape and direction of the aneurysm, early interval to angiography, variation in blood pressure, hydrocephalus, intraventricular blood, and use of ventricular drains.[49-58] Rebleeding in the late phase after SAH (more than 1 month) has been related to aneurysm location and size and persistent elevated blood pressure.[53]

Natural History of Aneurysmal Subarachnoid Hemorrhage: Summary

1. Case review and prospective cohorts have shown that for untreated, ruptured aneurysms, there is a 3% to 4% risk of rebleeding in the first 24 hours, a 1% to 2% per day risk in the first month, and a long-term risk of 3% per year after 3 months. Urgent evaluation and treatment of patients with suspected SAH are strongly recommended (level of evidence III to IV; grade C).
2. Factors that may play a role in determining the risk of rebleeding include interval to admission, neurological grade, blood pressure, gender, aneurysm characteristics, hydrocephalus, early angiography, and ventricular drains (level of evidence IV to V; grade C). Further studies are recommended to delineate these parameters.

Clinical Manifestations

Presenting Symptoms

Subarachnoid hemorrhage is a medical emergency. It is imperative that physicians, nurses, and emergency medical personnel recognize the clinical manifestations of SAH and institute immediate appropriate diagnostic and therapeutic measures. Because of the specialized nature of contemporary treatment for SAH, rapid referral to centers with appropriate facilities is warranted.

The typical clinical presentation of aneurysmal SAH is one of the most distinctive in medicine. The history of the abrupt onset of a (usually) severe headache of atypical quality is characteristic of this disorder.[59] The onset of the headache may or may not be associated with a brief loss of consciousness, nausea and/or vomiting, focal neurological deficits (including cranial nerve palsies), or stiff neck. Despite the characteristic history, misdiagnosis of SAH is common.[4,60] A high index of suspicion must be maintained, as diagnosis of the "warning leak" before a catastrophic rupture may be life saving.[61]

Diagnosis

The cornerstone of SAH diagnosis is the noncontrast CT scan.[62] If the scan is performed within 24 hours of the ictus, high-density clot in the subarachnoid space can be demonstrated in 92% of cases.[63] The diagnostic sensitivity of CT scanning progressively declines after the first day, however, and diagnostic lumbar puncture should be performed if the initial CT scan is negative. A normal CT scan and spinal fluid examination in most cases exclude a warning leak and predict a favorable prognosis in the setting of severe and/or sudden headache.[64,65] The usefulness of magnetic resonance imaging (MRI) in the diagnosis of SAH is controversial. Adequate blinded studies comparing MRI with CT scanning have not been performed,[66-68] and concerns remain about the relative insensitivity of MRI for detecting subarachnoid blood in the acute stage after SAH.[69]

Selective catheter cerebral angiography is currently the standard for diagnosing cerebral aneurysms as the cause of SAH. Approximately 20% to 25% of cerebral angiograms performed for SAH will not indicate a source of bleeding.[70] Repeat angiography after approximately 1 week will disclose a previously unrecognized aneurysm in an additional 1% to 2% of cases.[71] Whether the additional small yield is worth the cost and morbidity of the second angiogram is a source of controversy.[72] MRA[73,74] and contrast infusion CT[75] have also been used to diagnose aneurysms but do not yet provide sufficient detail or sensitivity for neurosurgical decision making,[76] except in the emergency setting.[77] Based on rapid advancement in MRA quality, low morbidity, and decreased cost, it is possible that in the future MRA will supplant conventional angiography as the primary diagnostic modality for aneurysms. Because of the risk of recurrent hemorrhage from incompletely clipped aneurysms, postoperative angiography is usually performed. A recent retrospective analysis identified improper clip placement in 8% of cases.[78] Intra-

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operative angiography may facilitate proper clip placement and enables immediate reapplication of the clip if necessary.[79]

Transcranial Doppler ultrasonography (TCD) is commonly used for noninvasive diagnosis and follow-up of cerebral vasospasm[80] (see below). Limitations of this technique include inability to assess narrowing in distal cerebral artery branches and lack of an adequate ultrasonic window in as many as 10% of patients. However, most reports claim good correlation with angiography, particularly in assessing the middle cerebral artery stem.[80-83] Nevertheless, the diagnosis of vasospasm by TCD should be predicated on sequential, reliable examinations by a trained operator. Whether the use of TCD to treat SAH patients improves overall outcome has not been adequately studied. Many clinicians continue to rely on cerebral angiography for the diagnosis of vasospasm, especially since the development of new interventional radiological treatments for vasospasm (see below).

A variety of techniques for measuring regional cerebral blood flow have been used with varying success in attempting to diagnose cerebral vasospasm.[84-86] Although these techniques are very sensitive for detecting regional perfusion deficits, the findings are frequently nonspecific and do not always correlate well with angiographically demonstrated vasospasm. As with TCD, the influence of cerebral blood flow measurement techniques on overall outcome in patients with SAH has not been adequately studied. The usefulness of electroencephalography (EEG) and evoked potential studies has not been systematically studied in patients with SAH. However, because of their lack of sensitivity and specificity for this disorder,[87] EEG and evoked potential studies are not recommended in the routine management of SAH.

Diagnosis of Subarachnoid Hemorrhage: Summary and Recommendations

1. Subarachnoid hemorrhage is a medical emergency. Because of the specialized nature of contemporary treatment for SAH, rapid referral to centers with appropriate facilities is warranted.
2. CT scanning for suspected SAH is strongly recommended; lumbar puncture for analysis of cerebrospinal fluid is strongly recommended when the CT scan is negative.
3. Selective cerebral angiography to document the presence and anatomic features of aneurysms is strongly recommended in patients with documented SAH. MRA or infusion CT is recommended when conventional angiography cannot be performed.
4. TCD is recommended for the diagnosis and monitoring of vasospasm, although cerebral angiography may be required for definitive diagnosis.
5. Monitoring of cerebral blood flow after SAH is of uncertain value. Further studies are recommended to substantiate the role of such studies in patients with SAH. EEG and evoked potential studies are not recommended.

Prevention of Rebleeding After Subarachnoid Hemorrhage

Bed Rest

Before 1980, 6 weeks of regulated bed rest was proposed as a management strategy to prevent rebleeding from ruptured cerebral aneurysms. In the Randomized Treatment Study of the Cooperative Aneurysm Study,[88] bed rest alone was inferior to intracranial surgery in preventing rebleeding in the overall analysis and inferior to drug-induced hypotension, intracranial surgery, and carotid ligation in the groups which completed treatment. Although bed rest remains a component of current treatment protocols, it should be combined with other definitive measures to prevent rebleeding.

Antihypertensive Medications

Preventing rebleeding with antihypertensive medications remains controversial. In a randomized trial of antihypertensive and antifibrinolytic agents, Nibbelink[89] found that rebleeding was higher in groups treated with antihypertensive agents, although rebleeding in these patients was likely related to the existence of hypertension rather than its treatment. In the Randomized Treatment Study no difference was noted between conservative bed rest and antihypertensive therapy.[88] In an observational study by Wijdicks et al,[58] a higher rate of rebleeding occurred in patients not receiving antihypertensive therapy despite lower blood pressures in this group compared with patients treated with antihypertensive agents. Rebleeding may be related to variations or changes in blood pressure rather than to absolute blood pressure.[90]

Carotid Ligation

Before 1970 carotid ligation was commonly used to treat recently ruptured intracranial aneurysms. A large retrospective study by Nishioka,[91] however, demonstrated a high number of intervention failures and a rebleed rate of 7.8% for patients who received carotid ligation. In the Cooperative Aneurysm Randomized Treatment Study,[88,92] carotid ligation did not lead to a significant improvement in mortality or rebleeding in the acute period (1 month after SAH) compared with regulated bed rest in the intent-to-treat analysis; however, only 67% of patients randomly selected to receive carotid ligation actually received it. In the treatment-accomplished subgroup, a significantly lower rate of mortality and rebleeding was evident as early as 1 month after carotid ligation; no rebleeds occurred in the group that received carotid ligation during follow-up in patients surviving 6 months. Long-term follow-up demonstrated a benefit for carotid ligation in reducing rebleeding at 3 years and mortality at 5 years. A recent review by Taylor et al[93] of pooled long-term follow-up results from several uncontrolled series (level of evidence IV) concluded that the risk of rebleeding was lower than expected after carotid ligation for untreated ruptured aneurysms. In summary, compared with conservative therapy, carotid ligation may produce a decrease in rebleeding; however, the rate of treatment failures (ie, rebleeding plus complications of therapy) likely exceeds that of direct surgical treatment of the aneurysm.

Antifibrinolytic Drugs

The role of antifibrinolytic therapy in prevention of rebleeding has been investigated since 1967. Among 30 publications, only half of the reports were randomized studies with concurrent controls; 11 studies used accept-

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able randomization. Adams et al[94] reviewed the antifibrinolytic experience from three studies (two randomized studies and one prospective phase IV study), which consistently showed a significant reduction in rebleeding among treated patients compared with nonantifibrinolytic control subjects. However, nearly one third of treated patients in these trials were worse at 14 days compared with time of admission. In 1984 a multicenter, randomized, double-blind, placebo-controlled study using tranexamic acid showed that rebleeding was reduced by more than 60% in the treatment group, but an increased rate of cerebral infarction in these patients offset any improvement in overall outcome.[54] A nonrandomized, controlled study[95] demonstrated similar findings; a 40% reduction in rebleeding in patients receiving antifibrinolytic therapy was offset by a 43% increase in focal ischemic deficits. In a double-blind, placebo-controlled trial of tranexamic acid,[96] there was no difference in rebleeding between groups and an increase in cerebral ischemia for treated patients, although the sample size was not sufficient to demonstrate significance. Retrospective studies[97,98] showed similar results, regardless of the duration of antifibrinolytic therapy with either epsilon aminocaproic acid (36 g/d) or tranexamic acid (6 to 12 g/d).

Intraluminal Coils

In the past 5 years platinum coils have been used to achieve intraluminal thrombosis of ruptured and unruptured aneurysms. Several clinical series[99-101] of varying sample size have shown efficacy in promoting short-term occlusion of the aneurysm. Casasco et al[100] reported a total occlusion rate of 85% using intraluminal coils at a mean follow-up of 13 months; aneurysm size was related to occlusion rate. A larger multicenter study of 120 patients using the Guglielmi detachable coil[101] included patients who were poor surgical candidates or surgical failures; 57% had SAH. Complete occlusion was reported in 81% of small-necked aneurysms and 19% of wide-necked aneurysms. These preliminary reports suggest that coils can promote aneurysmal thrombosis in a majority of cases, although long-term occlusion remains indeterminate. In addition, the risk of rebleeding after treatment with detachable coils may be similar to that for incompletely clipped aneurysms (see below).

Detachable Balloons

Several clinical series with differential selection criteria have been reported for balloon embolization of aneurysms.[102,103] The variability of timing for treatment and nature of the aneurysms treated significantly limit the evaluation of efficacy for prevention of recurrent hemorrhage. Higashida et al[104] reported an occlusion rate of 77% using detachable balloons, with early rebleeding in 7% and late rebleeding in 5%. Similar uncontrolled reports have described aneurysm thrombosis with polymers.[105] Long-term follow-up (particularly of partially occluded aneurysms) and control of selection criteria are needed to compare balloon embolization with other treatment modalities for preventing rebleeding after SAH.

Measures to Prevent Rebleeding After Subarachnoid Hemorrhage: Summary and Recommendations

1. Regulated bed rest or antihypertensive therapy alone is not recommended to prevent rebleeding after SAH, although both are frequently included in the overall treatment of patients with SAH (level of evidence I to III, grade B).

2. Antifibrinolytic therapy to prevent rebleeding is recommended in certain clinical situations, eg, patients with a low risk of vasospasm and/or a beneficial effect of delaying surgery (level of evidence I to V, grade A). However, antifibrinolytic therapy has been associated with a higher rate of cerebral ischemia, resulting in no benefit in terms of overall outcome. Future studies are recommended to determine whether a combination of antifibrinolytic therapy with other treatments to reduce vasospasm will be beneficial.

3. Carotid ligation is of indeterminate value in preventing rebleeding (level of evidence I to III, grade A).

4. The use of intraluminal coils and balloons is experimental. Further studies are recommended (level of evidence IV to V, grade C).

Direct Surgical Treatment of Ruptured Aneurysms

Clinical series concerning surgical repair of cerebral aneurysms have not directly addressed the efficacy of the procedure to reduce rebleeding. The Cooperative Study[106] evaluated 979 patients who underwent intracranial surgery only. Nine of 453 patients (2%) rebled after surgery; four of these hemorrhages occurred in patients with multiple aneurysms. In the Randomized Treatment Study,[53,107] surgery (either clipping or wrapping of the aneurysm) performed within the first 3 months after SAH significantly lowered rebleeding during this interval compared with bed rest, hypotension, or carotid ligation. Long-term rebleeding was significantly reduced by either intracranial surgery or completed carotid ligation. In the large retrospective series reported by Sundt et al,[108] 11.1% of grade 1 and 2 patients (Table 2) rebled before surgery, 80 of 644 total patients (12.4%) had intraoperative bleeding, and 8 of 644 patients (1.2%) had postoperative bleeds. These results are comparable to those in other large contemporary series.[109,110]

TABLE 2. Grading Scales for Subarachnoid Hemorrhage

Hunt and Hess Scale [192]	
Grade	Neurological status
1	Asymptomatic
2	Severe headache or meningismus; no neurological deficit (except cranial nerve palsy)
3	Drowsy; minimal neurological deficit
4	Stuporous; moderate to severe hemiparesis
5	Deep coma; decerebrate posturing
Glasgow Coma Outcome Scale[193]	
Category	Outcome
1	Good recovery; independent lifestyle
2	Moderate disability; independent lifestyle
3	Severe disability; conscious but not independent
4	Vegetative state
5	Death

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Timing of Surgery

Timing of aneurysm surgery has been addressed in several nonrandomized clinical series.[111-113] Kassell et al[112] observed no preoperative rebleeds in 27 patients with early (less than 3 days after SAH) surgery compared with 7 of 24 patients (29%) with late surgery. At surgery, both groups had the same intraoperative hemorrhage rate (26%). Chyatte et al[113] found 4.7% preoperative rebleeds with acute (0 to 3 days) surgery, 6.0% with intermediate (4 to 7 days) surgery, and 16% with late (more than 7 days) surgery. The International Cooperative Study on the Timing of Aneurysm Surgery[114,115] analyzed management comparison in 3521 patients, of whom 83% underwent surgical repair of the ruptured aneurysm. Timing of surgery after SAH was significantly related to the likelihood of preoperative rebleeding (0 to 3 days, 5.7%; 4 to 6 days, 9.4%; 7 to 10 days, 12.7%; 11 to 14 days, 13.9%; and 15 to 32 days, 21.5%). Postoperative rebleeding did not differ among time intervals (1.6% overall). Nevertheless, there was no significant difference in overall outcome in this study related to timing of surgery. In the randomized trial of nimodipine conducted by Ohman and Heiskanen,[116] patients who underwent early surgery had a significantly lower preoperative rebleed rate than those who underwent later surgery (3% versus 11%). The complexity of the aneurysm, the difficulty of the surgical approach, and the clinical grade of the patient clearly influence the timing of surgery. In recent years there has been a trend toward early surgery for ruptured aneurysms, especially in good- and moderate-grade patients. In addition, early surgery facilitates the aggressive therapy of vasospasm (see below). Regardless of surgical timing, early referral to centers with facilities for intensive care of patients with SAH is essential, since many therapies need to be initiated in the acute period (see below).

Incompletely Clipped Aneurysms

Few studies have been conducted to determine the natural history of incompletely clipped aneurysms. Feuerberg et al[117] retrospectively examined 715 patients operated on between 1970 and 1980. Twenty-seven patients (3.8%) showed incomplete obliteration on follow-up angiography; only one patient rebled during 266 person-years of follow-up. However, in another case series reported by Lin et al,[118] 19 patients with incompletely clipped aneurysms were readmitted for regrowth of the aneurysm; 17 had a recurrent hemorrhage.

Wrapping or Coating

Anecdotal clinical series have reported a reduction of rebleeding after external wrapping or coating of intracranial aneurysms.[119-121] In a recent long-term follow-up study,[122] the rebleeding rate was 11.7% (upper confidence limit, 19.8%) at 6 months and 17.8% (upper confidence limit of 28.9%) at 6 months to 10 years. Based on the sample size, this was not significantly different from the rate of rebleeding for conservatively treated aneurysms. Another small series with a mean follow-up of 11.2 years[123] demonstrated an overall risk of rebleeding of 33%. The available data suggest that wrapping or coating of intracranial aneurysms does not prevent rebleeding and that studies are of insufficient size to conclude a consistently lower rate of rebleeding than that for conservative management.

Surgical Treatment of Ruptured Aneurysms: Summary and Recommendations

1. Surgical clipping is strongly recommended to reduce the rate of rebleeding after aneurysmal SAH (level of evidence III to V, grade B).

2. Although early surgery reduces the risk of rebleeding after SAH, older studies showed that overall outcome is not different than that for delayed surgery (level of evidence II to V, grade B). Early surgery is recommended for the good-grade patient with an uncomplicated aneurysm. For other clinical situations, either early or delayed surgery is recommended, depending on the specific clinical situation. Early referral to specialized centers is strongly recommended.

3. Wrapped or coated aneurysms or incompletely clipped aneurysms probably have an increased risk of rehemorrhage (level of evidence IV to V, grade C). Complete surgical obliteration of the aneurysm is recommended whenever possible.

Anesthetic Management During Aneurysm Surgery

Induced hypotension has been used to prevent intraoperative aneurysm rupture, although the efficacy of this technique has not been studied. Cerebral blood flow was decreased during induced hypotension in patients with impaired autoregulation, but there was no increase in postoperative neurological deficits.[124] In a larger retrospective study (n=112), increased risk of early and delayed neurological deficits was associated with a systolic arterial blood pressure of less than 60 mm Hg and with longer periods of hypotension.[125] In summary, existing data suggest potential harm from induced hypotension without any evidence regarding benefit. Temporary vascular occlusion has been used during aneurysm surgery to prevent intraoperative rupture of large or difficult-to-approach aneurysms. In a retrospective review of 185 operations with uniform anesthetic management, outcome did not differ with or without vascular occlusion.[126] The use of thiopental-[127] and etomidate-[128]induced EEG burst suppression was not associated with any adverse hemodynamic effects. Induced hypertension is used to improve cerebral blood flow in settings such as vasospasm and carotid endarterectomy but has not been studied during vessel occlusion in aneurysm surgery. In selected patients with giant aneurysms, particularly of the basilar artery, deep hypothermia with circulatory arrest under cardiopulmonary extracorporeal circulation is an acceptable technique at selected centers with significant experience.[129,130]

Anesthetic Management: Summary and Recommendations

1. It is recommended that the degree and duration of intraoperative hypotension during aneurysm surgery be minimized (level of evidence IV to V, grade C).

2. There are insufficient data on neuroprotective agents and induced hypertension during temporary vessel occlusion (level of evidence IV to V, grade C). Further studies are recommended.

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Cerebral Vasospasm After Subarachnoid Hemorrhage

Clinical Features and Incidence

Cerebral vasospasm is the delayed narrowing of large capacitance arteries at the base of the brain after SAH, often associated with radiographic or cerebral blood flow evidence of diminished perfusion in the distal territory of the affected artery. Angiographic vasospasm has a typical temporal course, with onset 3 to 5 days after the hemorrhage, maximal narrowing at 5 to 14 days, and gradual resolution over 2 to 4 weeks.[131] In about one half of cases, vasospasm is manifested by the occurrence of a delayed neurological ischemic deficit, which may resolve or progress to cerebral infarction. In contemporary series, 15% to 20% of such patients suffer stroke or die from vasospasm despite maximal therapy.[132,133] The delayed ischemic neurological deficit associated with symptomatic vasospasm usually appears shortly after the onset of angiographic vasospasm with the acute or subacute development of focal or generalized symptoms and signs.[131,134] Progression to cerebral infarction occurs in approximately 50% of symptomatic cases; recovery without deficit in the remaining individuals may occur despite the persistence of angiographic vasospasm.[108,131]

Analysis of the incidence of cerebral vasospasm is complicated by the lack of consistent diagnostic criteria among reported studies. In 1987 the Cooperative Aneurysm Study reported an incidence of angiographic vasospasm of more than 50%, with symptomatic vasospasm in 32% of patients.[135] These values have remained consistent with contemporary retrospective reviews.[136,137]

Treatment of Vasospasm

Hypertension/Hypervolemia/Hemodilution

Several reports from uncontrolled studies described resolution of deficits from vasospasm following elevation of blood pressure, volume expansion, and/or hemodilution,[137-140] with improved outcome relative to vasospasm compared with historical controls. However, the efficacy of hypertension/hypervolemia/hemodilution (H/H/H) has not been demonstrated in controlled trials, and studies of cerebral blood flow after initiation of therapy have been equivocal. In addition, studies have not been performed to determine which component of this therapy (hemodilution versus hypervolemia versus hypertension) is most important. Only a proportion of patients with vasospasm respond to H/H/H therapy, with stroke and death rates from vasospasm approaching 15% in the series with the best outcome.[137,140] Initiation of H/H/H therapy is associated with significant risk, including cardiac failure, electrolyte abnormalities, cerebral edema, bleeding abnormalities, and rupture of an unsecured aneurysm.[139] Patients receiving this treatment are usually monitored in an intensive care setting with a Swan-Ganz catheter, arterial lines, and frequent serum electrolyte determinations. In many protocols measurements of left ventricular end-diastolic pressure and cardiac output are used to optimize hemodynamics according to the Starling curve.[139] An uncontrolled series suggested that therapy may be more effective if initiated prophylactically before the onset of symptoms (preferably after clipping of the aneurysm).[141] Treatment is usually continued beyond the period of risk for vasospasm or until abatement of vasospasm by clinical and TCD parameters.

Calcium-Channel Antagonists

A number of prospective, randomized trials for the oral agent nimodipine were initiated in the past decade.[142-146] The characteristics of these trials can be summarized as follows: (1) oral nimodipine consistently reduced poor outcome due to vasospasm in all grades of patients; (2) with the exception of one trial, the incidence of symptomatic vasospasm was not affected by nimodipine treatment; (3) vessel caliber by angiography was not affected by nimodipine therapy; and (4) complications and side effects of the drug were minimal.

Several prospective nonrandomized trials[136,147,148] have reported a lower incidence of permanent deficit or death from vasospasm after intravenous administration of calcium-channel antagonists, with rates ranging from 1% to 10%. In a prospective, randomized trial for intravenous nicardipine[149,150] there was a significant reduction in symptomatic and angiographic vasospasm in treated patients. However, no difference in overall outcome was noted between groups at 3 months. AT877, which sequesters intracellular calcium and inhibits protein kinase C, significantly reduced symptomatic and angiographic vasospasm and improved outcome at 3 months in a prospective, randomized trial.[151]

Clot Removal and Agents Affecting Fibrinolysis

Considerable clinical and experimental evidence has related the severity of cerebral vasospasm to the volume and duration of perivascular thrombus in the subarachnoid space. This concept led to the practice of aggressive clot removal at surgery.[152] However, no controlled studies have demonstrated the effectiveness of this technique in reducing vasospasm. Lysis of subarachnoid thrombus by intracisternal recombinant tissue-type plasminogen activator is under investigation in a prospective, randomized trial.[153]

Transluminal Angioplasty

There have been numerous reports from uncontrolled studies[154-157] describing profound neurological improvement following transluminal angioplasty for patients with vasospasm refractory to other modes of therapy. The effects of transluminal angioplasty can be summarized as (1) significant improvement in 60% to 80% of patients, often within hours after dilatation; (2) normal angiographic caliber in nearly all cases, without recurrent vasospasm; (3) evidence of improved cerebral blood flow by TCD or single-photon emission CT correlated with clinical improvement; and (4) complications (rupture of vessels or unsecured aneurysm) in approximately 5% of cases. Although controlled trials have not been done, the generally good outcome observed in these reports is notable due to the ominous natural history of vasospasm in this cohort of patients with symptomatic vasospasm refractory to other therapies. Similar encouraging results have been reported for intra-arterial administration of papavarine,[158] although controlled trials are also lacking for this treatment.

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Antioxidant and Anti-inflammatory Agents

In a prospective, nonrandomized study, Chyatte et al[159] showed a reduction in cerebral vasospasm compared with historical controls in patients treated with high-dose methylprednisolone. Preliminary data from ongoing prospective, randomized trials have demonstrated improved outcome and decreased vasospasm for patients treated with Tirilizad, a nonglucocorticoid 21-aminosteroid with antioxidant and iron-chelating properties.[160]

Vasospasm: Summary and Recommendations

1. Oral nimodipine is strongly recommended to reduce poor outcome related to vasospasm (level of evidence I to II, grade A). Other calcium antagonists administered orally or intravenously are of uncertain value (level of evidence I to V, grade B).
2. Hypertension/hypervolemia/hemodilution are recommended for prevention and treatment of ischemic complications from vasospasm (level of evidence III to V, grade C). The aneurysm should be clipped when possible, and patients receiving this therapy should be closely monitored in an intensive care setting for hemodynamic function. Clinical trials are recommended to further document the efficacy of this therapy.
3. Intracisternal fibrinolysis and antioxidant and anti-inflammatory agents are of uncertain value (level of evidence III to V, grade C). Studies to determine their efficacy are recommended.
4. Transluminal angioplasty is recommended for treatment of vasospasm in patients for whom conventional therapy has failed (level of evidence IV to V, grade C). Further studies are recommended.

Other Complications Associated With Subarachnoid Hemorrhage

Hydrocephalus

Ventriculomegaly frequently occurs concomitant with SAH, although the clinical significance of this finding on CT scanning is uncertain. In several retrospective series,[161-164] acute hydrocephalus (ventricular enlargement within 72 hours) was noted in 20% to 27% of patients surviving the ictus of SAH. The etiology of acute ventriculomegaly after SAH is usually obstructive hydrocephalus caused by intraventricular blood[161,162]; the incidence of acute hydrocephalus in SAH parallels clinical grade with a greater frequency among poor-grade patients. Chronic ventriculomegaly occurred in more than 60% of patients by 30 days after SAH in a retrospective analysis,[165] although others have reported rates in the range of 14%[35] to 23%.[166] The significance of chronic ventriculomegaly after SAH is uncertain since the diagnosis depends on the radiographic criteria,[165] many patients are apparently asymptomatic,[162] and shunting produced clinical improvement in only a moderate proportion of cases. There is an apparent association between ventriculomegaly and the development of vasospasm.[165]

The management of acute hydrocephalus after SAH is controversial, and current data are derived exclusively from single-institution retrospective reviews. Ventriculostomy has been generally recommended for patients with acute hydrocephalus and diminished level of consciousness after SAH; approximately 50% to 80% of these individuals will show some degree of improvement after the procedure.[161-164] However, this subgroup of patients has a higher mortality rate than untreated patients with hydrocephalus or patients with SAH overall.[164] Ventriculostomy has been associated with an increased rate of rebleeding after SAH,[161,167] although this has not been documented in controlled studies. Ventriculostomy after SAH can also be complicated by meningitis/ventriculitis, with reported infection rates of 5% to 10%.[161,167]

Management of chronic ventriculomegaly after SAH (presumably due to communicating hydrocephalus) is similarly controversial and not substantiated by controlled trials. Ventriculoatrial, ventriculoperitoneal, or lumboperitoneal shunts may improve clinical status in this group of patients.[165,168] Alternatively, sequential lumbar punctures or lumbar drain may be effective in controlling hydrocephalus in the subacute period after SAH.

Hydrocephalus: Summary and Recommendations

1. Acute (obstructive) hydrocephalus after SAH complicates approximately 20% of cases. Ventriculostomy is recommended, although it may be associated with increased rebleeding and infection (level of evidence IV to V, grade C).
2. Chronic (communicating) hydrocephalus is a frequent occurrence after SAH. Temporary or permanent cerebrospinal fluid diversion is recommended in symptomatic patients (level of evidence IV to V, grade C).

Hyponatremia/Volume Contraction

The reported incidence of hyponatremia following SAH ranges from 10% to 34%. It usually develops several days after the hemorrhage and often parallels the time course of vasospasm. Hyponatremia is more common in patients with poor clinical grade and hydrocephalus and may be an independent risk factor for poor outcome.[169] Recent uncontrolled prospective studies suggest a relationship of hyponatremia to excessive natriuresis and volume contraction.[170-173]

Fluid restriction for the treatment of hyponatremia was associated with increased incidence of delayed ischemic deficits,[174] and volume contraction was linked to symptomatic vasospasm.[175] In several uncontrolled studies, the development of volume contraction was ameliorated by the administration of large amounts of fluids (hypervolemic therapy).[173,176] In a randomized, controlled trial, Hasan et al[176] found that fludrocortisone helped to correct the negative sodium balance but did not significantly prevent volume contraction or hyponatremia. Although the incidence of hyponatremia has not been altered by administration of large volumes of fluid or the administration of fludrocortisone,[177] the hyponatremia is usually too mild to produce symptoms. Therefore, aggressive measures to correct hyponatremia appear unwarranted, especially if they might lead to volume contraction.

Hyponatremia: Summary and Recommendations

1. It is strongly recommended that management of hyponatremia after SAH emphasize the avoidance of volume contraction; management should include intravascular administration of isotonic fluids (level of evidence III to IV, grade C).

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2. It is recommended that volume status in certain patients with recent SAH be assessed by monitoring central venous pressure, pulmonary capillary wedge pressure, fluid balance, and body weight, although these parameters have not been tested in clinical trials. Trends indicating volume contraction should be corrected by increasing the volume of fluids administered (level of evidence III to IV, grade C).

3. It is recommended that hypotonic fluids be avoided as they may contribute to hyponatremia; fluid restriction should not be instituted to treat hyponatremia (level of evidence IV to V, grade C).

Seizures

The risk and implications of seizures associated with SAH are not well defined, and the need and efficacy for routinely administered anticonvulsants following SAH are not well established. A large number of seizure-like episodes are associated with aneurysmal rupture[178,179] and have an incidence of about 25%, although seizure incidence as high as 90% has been reported.[179] However, it is unclear whether these episodes are truly epileptic in origin or reflect a release phenomenon associated with a sudden rise in intracranial pressure.[178,180] The routine use of prophylactic anticonvulsants during the perioperative period has been addressed in several studies, but none have clearly established their use as beneficial.[181-186] Nonrandomized studies of craniotomy patients indicate a benefit of prophylactic anticonvulsants[184-186]; however, the number of patients with SAH in these studies is too small to address this issue. Risk factors for seizures after SAH have been noted in several retrospective studies, including middle cerebral artery aneurysms,[187,188] intraparenchymal hematoma,[184,187,189] infarcts,[190,191] and a history of hypertension.[190] Although retrospective studies[178,181] have concluded that prophylactic anticonvulsants are of no benefit after SAH, the studies had small numbers of patients and anticonvulsant levels were not routinely monitored.

Seizures: Summary and Recommendations

1. Because of the potential risk of rebleeding with a seizure, the administration of prophylactic anticonvulsants is recommended in the immediate posthemorrhage period (level of evidence IV to V, grade C).

2. The long-term use of anticonvulsants is not routinely recommended for patients with no seizure episodes and should be considered only for patients with risk factors such as prior seizure, hematoma, infarct, or middle cerebral artery aneurysms (level of evidence IV to V, grade C).

Treatment Protocols: Overview and Recommendations

Emergency Evaluation and Care

Subarachnoid hemorrhage is a medical emergency; diagnostic measures should be undertaken immediately. Once the diagnosis of SAH has been made by clinical, CT, and lumbar puncture (if necessary) findings, decisions about initial management will depend to a large extent on the patient's neurological condition. A number of grading scales have been described (Table 2), and overall prognosis appears to be predicted by the patient's neurological grade according to these scales.[192] Patients who are relatively alert (those with Hunt and Hess grades of 1 or 2) should be admitted to a setting where frequent neurological assessments can be made by trained personnel. Most protocols include strict bed rest, and prophylactic measures for deep vein thrombosis (eg, pneumatic compression devices) should be instituted. A central intravenous line may be desirable in the perioperative period for administration of fluids, medications, and blood products, if necessary. Monitoring of intracranial pressure may provide important information for differentiating neurological deterioration in the perioperative period. Oral nimodipine therapy should be initiated, and an angiogram designed to examine all of the common sites for the occurrence of cerebral aneurysms should be performed before surgery. The timing of the angiography depends on the interval between admission and planned surgery.

Patients with significant lethargy or neurological deficits (Hunt and Hess grades 3 to 5) should be admitted to the intensive care unit. Isotonic or hypertonic intravenous fluids should be administered, and a central intravenous access (with the ability to measure either the central venous pressure or pulmonary artery pressures) is desirable in most of these patients. If the patient is obtunded, an endotracheal intubation for airway protection should be performed if necessary. If the initial or subsequent CT scan shows significant hydrocephalus and the patient is lethargic or has a decreasing level of consciousness, a ventriculostomy should usually be performed. In the poor-grade patient or one with a technically complex aneurysm, endovascular obliteration of the aneurysm may occasionally precede later definitive surgical repair.

Patients with intracerebral hemorrhage may be considered for emergency evacuation of the intracerebral clot. Clipping of the aneurysm can often be accomplished during removal of the clot. Patients who are obtunded and/or have a significant lateralizing deficit but who are otherwise neurologically stable may undergo cerebral angiography before surgical removal of the blood clot. Selected patients with rapid neurological deterioration may be candidates for immediate removal of the clot and clipping of the aneurysm without a preoperative angiogram. Often, an infusion CT scan or intraoperative angiography may be helpful in such patients in locating the offending aneurysm.[77]

Overview of Surgical Techniques

The current standard of surgical practice calls for microsurgical dissection and clipping of the aneurysmal neck whenever possible.[108,194] Surgical morbidity is determined by numerous factors, including the location, size, and configuration of the aneurysm; the medical and neurological condition of the patient; and the coincidence of other complications of SAH. Decisions about the timing of surgery, the surgical approach, and specific technical adjuncts to surgery must be based on the individual clinical setting. Many neurosurgeons initiate preoperative therapy with corticosteroids, although this practice has not been substantiated by clinical trials.[195] The use of temporary clips in the afferent artery (or arteries) during the critical parts of the dissection and clipping, particularly with large and difficult aneurysms, has become frequent practice.[126,196]

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Some aneurysms, particularly fusiform and giant aneurysms, cannot be clipped, and other direct techniques such as aneurysmorrhaphy, trapping, coating, or excision with interposition vein grafts or other forms of arterial reconstruction can be used.[197-199] In some instances of giant or fusiform aneurysm, the neurosurgeon may use permanent proximal arterial occlusion to reduce intra-aneurysmal pressure. Depending on the capacity for collateral circulation, this procedure may be accompanied or preceded by an extracranial-to-intracranial bypass procedure.[198,200,201]

Postoperative Care

Most patients will require observation in the intensive care unit for variable periods after surgical repair of the ruptured aneurysm. Although the optimum period for postoperative ICU observation has not been studied, monitoring of intracranial pressure, hemodynamic parameters, intravascular volume, and pulmonary status, and TCD monitoring for vasospasm may necessitate prolonged ICU observation. Sequential CT scans may be necessary to differentiate neurological deterioration caused by vasospasm, hydrocephalus, or cerebral edema. A rehabilitation program is often recommended for patients recovering from SAH, because of the variety of motor, cognitive, communicative, and psychosocial deficits that may be present (see below). The value of rehabilitation in determining overall outcome after SAH has not been determined.

Outcome Assessment After Subarachnoid Hemorrhage

Results of management outcome in patients with SAH from a ruptured intracranial aneurysm have not been reported in a standardized manner.[108,202] Recent reports have described neurological outcome using the Glasgow Coma Scale outcome score (Table 2)[193]; however, it should be noted that this scale was designed to describe outcome after head injury and is not ideal for assessing outcome after SAH. In addition, patients who have no grossly evident neurological deficits after SAH frequently have subtle cognitive or neurobehavioral difficulties that impair their social adjustment and ability to return to their previous occupation.[203-207] At least one study suggests that these neurobehavioral deficits are not correlated with tissue loss as seen in a late MRI[208]; therefore, it is likely that they are due to a diffuse effect of SAH. At the present time there is no standardized method of measuring these deficits in patients with SAH, and a wide variety of standard neuropsychological tests have been used by a variety of investigators.[203-207] Perhaps the most meaningful and simple measure of the effect of these deficits is whether the patient is able to return to his or her previous occupation.[206]

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