Although subarachnoid hemorrhage (SAH) comprises only 1% to 7% of all strokes,1 the loss of productive life years in the general population from SAH is comparable to that of cerebral infarction2 because of the relatively young age of onset and poor outcome in SAH.1,3,4 However, unlike other stroke subtypes, the incidence of SAH exhibits little geographical variation and did not significantly change over the last decades.1 In the most recent overview of 14 longitudinal and 23 case-control studies of risk factors for SAH published in English from 1966 through March 2005,5 it was concluded that smoking, hypertension, and excessive alcohol are the most important risk factors for SAH. Exposure to these risk factors individually and/or in combination promotes formation, growth, and rupture of intracranial aneurysm(s),6–8 a major cause of SAH. The consistency of the data across studies involving different designs and populations suggests that cigarette smoking and elevated blood pressure are causally related to SAH.9 There is also evidence that genetic factors play an important role in the pathogenesis of SAH.10 Accumulating evidence suggest a temporal (seasonal and diurnal) pattern in the occurrence of SAH,11,12 but reasons for these temporal patterns remain unclear. However, there is still lack of good quality population-based epidemiological studies on incidence, trends, and outcomes of SAH in different populations (especially from developing countries).

Diagnosis and Investigation
Misdiagnosis of SAH occurred in 12% of 482 SAH patients admitted to a large American tertiary care hospital and was associated with a smaller hemorrhage and normal mental status on first assessment as well as poorer 1-year outcome resulting from neurological complications before correct diagnosis (primarily rebleeding).13 All patients with suspected SAH, including those with mild symptoms after an otherwise typical thunderclap onset, should have an emergency computed tomography (CT) scan without contrast interpreted by an expert. Hyperdense blood located near common aneurysm locations in the basal cisterns is usually diagnostic, but parenchymal clot in the temporal or basal frontal lobes and intraventricular hemorrhage are also suggestive of an underlying aneurysm.14 If CT scanning is considered normal (uncommon in the first 24 hours after aneurysm rupture), lumbar puncture for cerebrospinal fluid analysis must be performed. It is often necessary to distinguish a true SAH from a traumatic spinal tap,15 and although no single method is fail-safe, the presence of visible xanthochromia after centrifugation of bloody cerebrospinal fluid strongly suggests SAH.

Since its introduction to the clinical management of SAH in the 1990’s16 the use of CT angiography for rapid aneurysm detection and treatment planning has become increasingly practical and popular, particularly since the introduction of rapid multislice CT scanners.17–22 Three-dimensional anatomical information provided by CT angiography or computer reconstruction of catheter angiography23 is useful when planning and performing aneurysm repair. The utility of magnetic resonance studies in the setting of acute SAH has received some interest but remains limited, especially in unstable patients.24

Medical Treatment
Medical treatment of patients with aneurysmal SAH is directed toward the prevention and management of neurological (eg, aneurysm rebleeding, hydrocephalus, cerebral vasospasm and ischemia and seizures) and systemic complications (eg, hyponatremia, cardiac arrhythmia and myocardial damage and neurogenic pulmonary edema).25,26

A recent randomized trial showed that immediate administration of antifibrinolytic agent tranexamic acid (1 g IV, followed by 1 g every 6 hours until aneurysm repair carried out as soon as possible) reduced the rate of often devastating early aneurysm rebleeding from 11% to 2.4%.27 Short-term antifibrinolytic treatment may protect from acute aneurysm rebleeding, but long-term antifibrinolytic treatment in patients in whom late aneurysm repair is planned does not improve overall outcome because the reduction in the rate of rebleeding before delayed surgery is offset by an increase in poor outcome secondary to cerebral ischemia.28 Pain management, sedation, and control of hypertension are also important in the prevention of aneurysm rebleeding, particularly in distressed, agitated patients seen soon after aneurysm rupture. In conscious patients without evidence of raised intracranial pressure, active hypertension treatment is indicated. Although the best antihypertensive agent and blood pressure in this situation is unsettled (although undoubtedly related to individual patient’s baseline blood pressures), intravenous labetolol and a target mean arterial pressure of <130 mm Hg are reasonable.25
Strict avoidance of hypovolemia, hypotension, and hyponatremia are important in preventing delayed cerebral ischemia (DCI) in patients with SAH. Hyperthermia and hyperglycemia are associated with DCI and should also be prevented using paracetamol, cooling blankets, and insulin when indicated. Routine use of the calcium blocking agent nimodipine (60 mg orally every 4 hours) provides a modest but significant improvement in outcome. There is no evidence that corticosteroids are of benefit. Antiplatelet agents in the prevention of DCI warrant further investigation. Neuroprotective strategies being investigated in SAH have recently been reviewed. Noteworthy new treatments under investigation include intravenous magnesium sulfate, which was associated with a trend toward improved outcome in 2 phase II randomized trials, and the statin agents pravastatin and simvastatin, which in separate phase II randomized trials reduced angiographic vasospasm and DCI when given for 14 days after aneurysmal SAH. Endothelin A is a powerful vasoconstrictive autacoid implicated in the pathogenesis of vasospasm. Clazosentan is an endothelin receptor antagonist, which has been shown to reduce vasospasm in a phase II study, and it is currently under investigation in a phase III trial.

Although a great deal of anecdotal evidence has led to the routine use hyperventilation and induced hypotension to reverse symptomatic DCI in patients with delayed-onset vasospasm after SAH, there is little information on the efficacy of either blood volume expansion alone or in combination with hypertension and hemodilution (“triple-H therapy”) to either prevent or reverse cerebral ischemia. Endovascular vasospasm reversal, particularly with balloon angioplasty, has emerged as an important intervention for treating medically refractory DCI before irreversible infarction, although again it has not been validated in a randomized trial.

Aneurysm Ablation

Patients with ruptured aneurysms should be immediately transferred to an institution with a comprehensive neurosurgical service, and there is evidence linking high-volume hospitals staffed by experienced clinicians to better patient outcomes. Despite a lack of scientific proof that it is a superior strategy, aneurysm ablation timed as early as possible to maximally prevent aneurysm rebleeding is a uniform policy in most centers.

A multicenter randomized trial involving 1001 good-grade SAH patients found that mild intraoperative hypothermia (target temperature 33°C using surface cooling techniques) provided no benefit in terms of neurological outcome and was associated with a higher incidence of postoperative bacteraemia. Intraoperative and postoperative angiography helps ensure correct anatomical repair of aneurysms. SAH is associated with obstructive hydrocephalus, and several cohort studies have suggested that microsurgical opening (“fenestration”) of the third ventricle into the basal subarachnoid cisterns reduces the need for ventriculoperitoneal shunting. Extended “decompressive” craniectomies help relieve intracranial hypertension in patients (generally poor grade) with large intracerebral hemorrhages or generalized brain swelling, but the quality of life experienced by survivors is frequently poor.

It has been several years since publication of the International Subarachnoid Aneurysm Trial (ISAT) results. That study randomized 2143 primarily good-grade patients with ruptured aneurysms (mostly small and located in the anterior circulation) between aneurysm clipping and endovascular coiling. At 1 year there was no difference in fatality rates between the 2 treatment groups, but for combined death and dependent rates there was an absolute risk reduction of 7.4% associated with coiling, which was significant. Endovascular treatment has been accepted by most as the preferred treatment modality for basilar artery aneurysms, which are relatively uncommon and difficult to repair surgically, so the main impact of ISAT has been a steady increase in the use of endovascular coils in the management of anterior circulation aneurysms, depending on the availability of endovascular expertise at individual centers. Technical developments include introduction of the Neuroform stent to help treat wide-necked and complex cerebral aneurysms, and coils coated with polymeric materials to stimulate a more robust cellular reaction in the thrombosed aneurysm and theoretically reduce aneurysm reformation. Accumulating clinical experience confirms that early and midterm results after endovascular repair can be very good, although it does not appear to be cheaper or reduce resource utilization compared with surgery at the present time. The major limitation of endovascular coiling remains incomplete aneurysm obliteration (more common in large, complex and wide-necked aneurysms) associated with remnant growth or aneurysm recanalization, seen in up to one-third of treated aneurysms over just several years, and rebleeding. This risk mandates long-term follow-up angiography and in many patients retreatment with either more coiling or microsurgery along with the attendant risks of these interventions. The impact of coiling on the incidence and severity of vasospasm remains unclear, and shunt-dependent hydrocephalus was comparable between surgical and endovascular treatment groups in 1 study. Patients with large intracerebral hemorrhages whose aneurysms are coiled may require subsequent surgical clot evacuations. Longer term follow-up of patients with ruptured aneurysms treated with endovascular coils is required in order to establish what method of aneurysm repair is best suited for anterior circulation aneurysms.

Prognosis

Death or dependence (poor outcome) occurs in almost 70% of patients with aneurysmal SAH and is attributed to DCI in approximately one third of the patients. DCI typically develops 3 days after the hemorrhage with the maximal risk between 4 to 14 days. Previous research has shown that advanced patient age (>60 years), a large amount of subarachnoid blood on CT scan, and a depressed level of consciousness on admission are important predictors for the development of DCI in patients with aneurysmal SAH. There is evidence that cardiac dysfunction and pulmonary edema are commonly observed during SAH. A modified version of the Massachusetts General Hospital Scale for predicting outcome after SAH has recently been validated. Rebleeding occurs in 7% of SAH patients and is associated with the clinical severity of SAH and aneurysm size.

There is lack of population-based data on long-term outcomes in SAH. In a recent Australasian study, incomplete
recovery at 1 year after SAH was found in 46% of survivors, of which ongoing memory problems were recorded in 50%, mood abnormalities in 39%, and speech problems in 14%, whereas a substantial proportion of survivors had diminished level of health related quality of life. No predictors of complete recovery from SAH were determined in this study. In a large population-based Finnish stroke incidence study, low socio-economic status was shown to be associated with poorer outcomes in SAH.

References


