Epidemiology of Aneurysmal Subarachnoid Hemorrhage

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Subarachnoid hemorrhage (SAH) is a devastating stroke subtype, which frequently occurs as the result of a ruptured intracranial aneurysm. Although it accounts for a small percentage of strokes overall, the resultant morbidity and mortality is substantial. This article serves to provide an up-to-date review of the epidemiology of aneurysmal SAH (aSAH), providing a framework for future clinical studies aimed at ameliorating the burden of this neurologic disease.

INCIDENCE

Spontaneous (nontraumatic) SAH most commonly is the result of aneurysmal rupture. Ruptured intracranial aneurysms account for approximately 75% to 80% of spontaneous SAH.[1] Overall, its incidence is between 6 and 8 per 100,000 persons per annum in most Western civilizations.[2,3] There is estimated to be between 16,000 and 30,000 new cases of aSAH in the United States annually.[4,5] Wide variations in aSAH incidence are observed between study populations, with rates reported to be as low as 2.2 per 100,000 persons per annum in China[6] and as high as 33 to 37 per 100,000 persons per annum in Finland[7,8] While the incidence of aSAH has remained relatively constant for the past 4 decades,[3,9] some studies have suggested that the actual incidence of aSAH is significantly higher secondary to misdiagnosis, death before hospital admission, or lack of autopsy in the general population.[10–16] Although developing countries have traditionally had a low burden of disease from aSAH, trends now indicate an increasing prevalence in these countries and a switch from medical problems dominated by infectious diseases to vascular and age-related diseases typically associated with western countries.[17] Overall, however, the epidemiology of aSAH seems to be similar in both developed and developing countries.[17]

PRESENTATION

Sudden onset of worst headache of life often signals a catastrophic event and is associated with high suspicion for aSAH. However, only 25% of individuals with severe, acute, paroxysmal headache actually have aSAH.[18] Other possibilities include benign thunderclap headaches and benign orgasmic cephalgia, both of which do not have subarachnoid blood on computed tomographic (CT) imaging or lumbar puncture. Benign thunderclap headaches may present similarly to SAH, with emesis in approximately 50% of patients, as well as occasional transient focal

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deficits.[19] Benign orgasmic cephalgia is a severe headache with onset just before or at the time of orgasm,[1] and has a strong association with a family history of migraines.[20] Less severe headaches may also mimic major intracranial aneurysm rupture. Sentinel headaches, which are similar in character to the classic aSAH headache, precede 30% to 60% of aSAH and usually resolve within 24 hours. Sentinel headaches might reflect a minor hemorrhage, aneurysmal enlargement, or a hemorrhage confined to the aneurysm wall.[21] Additional signs and symptoms are myriad and may include emesis, syncope, meningismus, and photophobia. The first presentation of such a severe headache should, and often does, prompt a workup for aSAH as this diagnosis carries substantial morbidity and mortality and must be ruled out.

The 2 most frequently used clinical aSAH grading scales by which patients are initially evaluated are the Hunt and Hess[22] and the World Federation of Neurologic Surgeons (WFNS) grading scales, the latter largely using the Glasgow Coma Scale (GCS).[23] Both scales are designed to aid in the prognosis of aSAH patients based on the initial clinical presentation. A study of 235 aneurysmal SAH patients using the Hunt-Hess grading scale found that approximately half of the patients enrolled (105 of 235, 44.7%) presented with less severe grades (I–II).[24] In a study of SAH in neurosurgical units in the United Kingdom and Ireland, the majority of the patients (59.0%) presented with the least severe WFNS grade, Grade I.[25] The next most frequent grade was Grade II. This distribution was confirmed during the International Subarachnoid Aneurysm Trial (ISAT), though this reflected aneurysms that were deemed appropriate for either neurosurgical or endovascular treatment.[26]

RISK FACTORS

Modifiable and nonmodifiable risk factors play an important role in aneurysmal subarachnoid hemorrhage epidemiology. The prevalence of risk factors for aSAH and the ability to address those risk factors may contribute to the wide variation in disease burden of aSAH between regions.[17,27]

Nonmodifiable Risk Factors

Age

The incidence of aSAH increases with age to a peak in the fifth and sixth decades of life.[6] Thereafter, the incidence has been shown to plateau or even decrease slightly with further aging.[6]

Gender

Differences in the incidence of aSAH between genders have also been consistently noted, with aSAH disproportionally affecting women.[28] In a prospective study of aSAH in Texas between 2000 and 2006, women were found to have an age-adjusted risk ratio of 1.74 compared with men.[29] A review of international studies between 1950 and 2005 reported an aSAH incidence in women 1.24 times greater than that observed in men and demonstrated that this difference in incidence began at age 55 and increased thereafter.[30] Studies have also suggested that a relationship exists between hormonal status and development of aSAH. A Japanese study of 124 women, age 30 to 79 years with first occurrence of spontaneous aSAH, found that several factors, including earlier age of menarche (adjusted odds ratio [OR] 3.24), and nulliparity (adjusted OR 4.23), were associated with an increased risk of aSAH. These effects appeared to be additive, and women with both early menarche and null gravidity, had correspondingly increased risk (adjusted OR 6.37).[31]

Ethnicity

Disparities in the incidence of aSAH between ethnic groups has also been recognized in several studies.[32–34] It has been suggested that African Americans in the United States are more likely to suffer from SAH than Caucasians.[35,36] In addition, a study of 27,334 persons presenting with SAH in the United States between 1995 and 1998 found that all minorities had increased risk of aSAH compared with the Caucasian population.[35] These differences were observed in both men and women, with the highest incidence of SAH occurring in Asian/Pacific Islander males. Furthermore, the impact of several other risk factors has been shown to be heterogeneous across different ethnicities.[37]

Family history

In many study populations, across all geographic regions, family history of aSAH has consistently been shown to be one of the strongest predictors of aSAH.[6] Only recently have the genetic underpinnings of this association been explored on a genome-wide basis.[38–41] A review of 10 genome-wide linkage studies of intracranial aneurysms found that only 4 of the identified loci were replicated in different populations[42] In a recent study of a large Caucasian family (n = 35) in the U.S. with familial aggregation of intracranial aneurysms, 250,000 single nucleotide polymorphisms (SNPs) were screened and a possible susceptibility locus was located on chromosome 13q. A similar approach in a large Dutch family with

a high prevalence of intracranial aneurysms found 2 potential susceptibility loci at 1p36 and Xp22.[39] These studies have identified possible target mutations; however, most associations to date have been found in noncoding regions of DNA. More specific loci have also been identified in recent genetic studies, including a SNP in exon 7 of the endothelial nitric oxide synthase gene, G894T, which may be a risk factor for intracranial aneurysm rupture.[38]

Aneurysm location

In a series of 245 consecutive aSAH patients Forget and colleagues[43] demonstrated that the most frequent site of aneurysm rupture was the anterior communicating artery (ACoA, 29.0%). The next most common locations of aneurysm rupture were the posterior communicating artery (PCoA, 19.6%), the basilar artery (14.7%), and the middle cerebral artery (MCA, 11.8%). ISAT provides the largest multicenter series of aSAH patients (n = 2143).[26] Although not a random sample, one can appreciate general trends from this trial. As in the study by Forget and colleagues,[43] the aneurysm location with the highest frequency of rupture was the ACoA. About half of ruptured ACoA aneurysms were midline with the remainder evenly distributed between origins on the right or left side of the ACoA. In addition, ISAT confirmed the high prevalence of ruptured PCoA and MCA aneurysms, but due to the trial's exclusion criteria, there was also a much smaller proportion of posterior circulation aneurysms represented in ISAT than found in natural history studies. Of note, ISAT data also demonstrated differences in laterality of rupture based on aneurysm location.[26] Overall, the ratio of right- to left-sided ruptured anterior circulation aneurysms was 1.24. For MCA and PCoA aneurysms this ratio was 1.40 and 1.55, respectively, whereas for internal carotid artery (ICA) bifurcation aneurysms the laterality was reversed with a ratio of 0.76.

These observations alone, however, are not sufficient to differentiate between whether intracranial aneurysms at specific locations are more prone to rupture or rather if the prevalence of aSAH relative to location reflects the tendency of specific locations in the intracranial circulation to have varying predilections for aneurysm formation. The International Study of Unruptured Intracranial Aneurysms II (ISUIA-II) has helped to shed light on this question. In this study, 4,600 patients with unruptured aneurysms were reported,[44] with ICA aneurysms (excluding the cavernous ICA and PCoA) being the most frequent (29.9%), followed closely by MCA aneurysms (29.1%). Locations that are most commonly represented amongst ruptured aneurysms, ACoA and PCoA, were third and fourth in incidence, respectively, with 12.3% and 8.5% of the total. Thus, it seems that there is a higher rate of rupture of ACoA and PCoA aneurysms compared with aneurysms of the ICA and MCA, which likely form more frequently. ISUIA also reported a higher rupture rate for a combined group of PCoA and posterior circulation aneurysms, compared with a group that combined ACA, ICA, and MCA aneurysms. It is important to keep in mind that based on the study design, ISUIA data is likely biased toward lower risk lesions, as subjects were those patients who were enrolled after the recommendation of conservative management. Similar results were reported by Juvela and colleagues,[45] in which 181 patients with unruptured aneurysms were prospectively followed in a time when the investigators exclusively recommended conservative management for unruptured aneurysms.

Aneurysm size

Aneurysm size is often felt to be the most significant factor for aneurysm rupture and is generally accepted that the likelihood of aneurysmal rupture increases linearly with the cross-sectional diameter of the aneurysm.[45] However, this does not mean that the natural history of small aneurysms is benign. The International Study of Unruptured Intracranial Aneurysms (ISUIA) reported that in patients with no prior history of SAH, aneurysms less than 10 mm in size carry a very low (0.05%) annual risk of rupture; however, this finding was greeted in the neurosurgical community with much criticism, particularly because the ISUIA inclusion criteria a priori placed patients in a low-risk category.[46] Conversely, Forget and colleagues, found that 210 of 245 (85.7%) consecutive aSAH patients presented with aneurysms smaller than 10 mm. The majority (50.6%) of ruptured aneurysms in their study were 6 to 10 mm in size, and accounted for the largest percentage of ruptured aneurysm in all intracranial locations, except for the superior cerebellar (SCA) and posterior inferior cerebellar (PICA) arteries, For these 2 locations, the majority of ruptured aneurysms were less than 5 mm in size. A study by Langham and colleagues[25] also confirmed that the majority of patients (67.3%) presenting with SAH had aneurysms that were less than 10 mm in size. Findings by Juvela and colleagues[45] further support the assertion that even small aneurysms may pose a significant risk for SAH, with a 1.1% and 2.3% yearly rupture risk for aneurysms 2 to 6 mm and 6 to 9 mm in size, respectively.

Modifiable Risk Factors

Hypertension

Chronically elevated systolic blood pressure (SBP) has been shown to be a strong predictor of intracranial aneurysm rupture. In a recent publication from the Nord-Trøndelag Health (HUNT) study, a large population-based study from in Norway, both mild (SBP 130–139 mm Hg) and severe (SBP >170 mm Hg) chronic elevations of systolic blood pressure were associated with an increased risk of aSAH in the 22-year follow-up period compared with those with SBP of less than 130 mm Hg (hazard ratios of 2.3 and 3.3, respectively).[47] In a Japanese multicenter case control study, a history of hypertension was found to be associated have an increased risk of aSAH, with an OR of 2.65 compared with controls.[48] In 1996, a review of 9 longitudinal and 11 case control studies identified preexisting hypertension as a significant risk factor for the development of SAH, with a relative risk of 2.8 (for longitudinal studies; 95% confidence interval [CI], 2.1–3.6) and an OR of 2.9 (for case control studies; 95% CI 2.4–3.7).[49] Diurnal variations in blood pressure have also been associated with risk of aSAH.[50]

Body mass index

Of note, lower body mass index (BMI) has been reported to be associated with a higher risk of aSAH. A large Finnish population study found a relative risk of 18.3 for lean, hypertensive, smokers compared with matched controls, whereas in the HUNT study, overweight (BMI 25–29.9) and obese (BMI $\geq$30.0) individuals had a lower risk of developing aSAH during the follow-up period, with hazard ratios of 0.6 and 0.7, respectively, compared with those with a BMI of 18.5 to 24.9.[47]

Tobacco use

Current smoking and a previous history of smoking have both been shown to be important independent risk factors for aSAH.[5,51–56] In the HUNT study, compared with those who had never smoked, former smokers had a hazard ratio of 2.7 (95% CI 1.4–5.1) and current smokers had a hazard ratio of 6.1 (95% CI 3.6–10.4) for development of aSAH.[47] In addition, recent evidence from a study involving 17 hospitals in Cincinnati suggests a gene-environment interaction with smoking. Compared with nonsmokers with no family history of aSAH, current smokers both with and without a positive family history had an increased risk of aSAH (OR 6.4, 95% CI 2.2–4.4; and OR 3.1, 95% CI 3.1–13.2, respectively).[57] Furthermore, differences in susceptibility to the harmful effects of smoking have been noted between ethnicities. Therefore the differences in incidence of aSAH between ethnic groups may in part be due to the differential effects of smoking.[37] In a study of 120 consecutive SAH patients in Sweden, the relative risk for SAH was approximately 2.5 times greater in smokers compared with the general population, but not elevated in patients who used smokeless tobacco, indicating that nicotine is unlikely to represent the main agent leading to increased SAH risk from tobacco use.[58]

Other risk factors

Recreational cocaine use in within the previous 3 days has been shown to confer an increased risk of SAH (OR 24.97, 95% CI 3.95–∞) in young patients (age 18–49 years).[59] It is possible, however, that undiagnosed, pre-existing vascular malformations may contribute to the increased risk in this population. High daily coffee consumption (>5 cups per day) was also found to be associated with an increased risk of SAH in the Tromso study (OR 3.86, 95% CI 1.01–14.73).[54]

DIAGNOSIS

The evaluation of the patient with symptoms suggestive of SAH begins with confirmation of the presence of subarachnoid blood. This confirmation is primarily accomplished with a noncontrast CT scan, which in the first 12 hours after SAH has a 98% to 100% sensitivity for SAH. This number drops to 93% at 24 hours after SAH, and[60–64] after 6 days decreases further to 57% to 85%.[65,66] In the setting of suggestive symptomatology a negative CT scan should be followed up with a lumbar puncture and analysis of the cerebrospinal fluid for xanthochromia.[67]

The gold standard for evaluation of cerebral aneurysms remains digital subtraction angiography, which demonstrates the source of SAH in approximately 85% of patients. Two less invasive modalities are increasingly being used, magnetic resonance angiography (MRA) and CT angiography. Three-dimensional time of flight MRA has a sensitivity to detect cerebral aneurysms is between 55% and 93%.[68–71] Dichotomizing by size, the sensitivity is 85% to 100% for aneurysms 5 mm or greater, but only 56% for those less than 5 mm in size.[68,70,72,73] CT angiography, however, is the more frequently used noninvasive modality, as it is faster and more readily available. In addition, it has a sensitivity for aneurysms between 77% and 100% and a specificity between 79% and 100%.[74–80]

Nontraumatic Nonaneurysmal Subarachnoid Hemorrhage

One can broadly classify SAH into traumatic and nontraumatic etiologies. Trauma is the most

common cause of SAH.[81,82] SAH has been cited as occurring in up to 60% of traumatic brain injury patients,[83] a population with an incidence of approximately 540 per 100,000 in the United States.[84] The pattern of hemorrhage, associated injuries, and clinical history often make this diagnosis readily apparent.

Nontraumatic SAH may also occur in patients not harboring intracranial aneurysms. Perimesencephalic SAH is defined by a relatively distinct radiographic pattern, with hemorrhage centered anterior to the midbrain or pons, with or without extension of blood around the brainstem, into the suprasellar cistern, or into the proximal Sylvian fissures.[85] A negative 4-vessel cerebral angiogram confirms the diagnosis. Nontraumatic SAH has an incidence rate of 0.5 persons per 100,000 in adults.[86] These patients tend to less likely be female, hypertensive, or of older age than aSAH patients.[86] Diffuse, angiographic negative SAH that does not fit the perimesencephalic distribution of blood is thought to be a distinct entity with an incidence rate approximately twice as high as perimesencephalic SAH, and a higher incidence of complications such as hydrocephalus and vasospasm as well as the need for cerebrospinal fluid shunting and frequency of poor outcomes.[87]

Additional possibilities include arteriovenous malformations, vasculitis, tumor, cerebral artery dissection, rupture of a small superficial artery, coagulation disorder, sickle cell disease, rupture of an infundibulum, and pituitary apoplexy.[1] However, no cause can be determined in 14% to 22% of nontraumatic SAH.[1]

TREATMENT

Treatment of SAH requires a multifaceted, collaborative team approach. In addition to acute neurologic concerns aSAH patients are medically ill and require intensive management. Following medical stabilization the primary concern is rebleeding of the ruptured aneurysm, a fact that has resulted in a shift toward early definitive management by either surgical or endovascular means. Of the aforementioned methods of treatment, clipping has long been the mainstay of neurosurgical treatment of aneurysms since it was first performed in 1937. Coiling, on the other hand, is a relatively new development with the Gugliemi detachable coil becoming approved by the Food and Drug Administration in 1995. Since that time, coiling has been gaining popularity, particularly after the publication of the ISAT trial, which revealed a potential benefit of endovascular coiling over clipping for specific ruptured aneurysms.[88]

A longitudinal study by Andaluz and Zuccarello documented these treatment trends using the National Inpatient Sample between 1993 and 2003.[89] These investigators found that while the number of discharges for surgical clip placement has stayed relatively constant over these 10 years, the number of discharges for endovascular treatment has steadily increased. In 1993 both treatments had approximately 12,000 discharges, whereas in 2003 the number of discharges with endovascular treatment (24,638) was approximately double that of surgical clip placement (12,626). The fraction of patients receiving endovascular treatment, however, varies widely between centers. Regardless of center preference, endovascular techniques tend to be the preferred approach for posterior circulation aneurysms, which can be difficult to treat surgically.

There also exists a population of patients with SAH who do not undergo any definitive treatment to secure their aneurysm. An analysis of patients in the United Kingdom and Ireland found that 199 (8.3%) of 2397 patients admitted with SAH over a year did not undergo surgical repair.[25] These patients tended to be older, be of a higher WFNS Grade, have more blood on their CT scans, have larger aneurysms, have more aneurysms in the posterior circulation, have more concurrent medical conditions on admission, and have more frequent prerepair deterioration.

OUTCOME

General Trends and Grading

Over the past 2 decades, mortality following SAH has decreased dramatically.[90] Previous death rates consistently occurred in a range around 50%,[2,8] whereas more recently they have been found in the 10%[91] to 24% range.[89] These reductions likely stem from advances in multiple aspects of SAH management, including improved diagnostic capabilities, aggressive neurocritical care management, and use of modern microsurgical and endovascular instruments and techniques.[26]

The 3 SAH-specific scales most widely used for classifying clinical presentation of SAH patients are the Hunt and Hess (H&H) Scale, the WFNS Scale, and the Fisher Scale.[92] The H&H Scale was designed to gauge surgical risk of admitted SAH patients by evaluating intensity of meningeal inflammatory reaction, severity of neurologic deficit, and level of arousal. Gradation of the scale is 1 to 5, with 1 representing a nearly asymptomatic state and 5 denoting a deep moribund coma.[22] There is evidence that differences between each H&H grade may not correlate with a unique outcome,[93,94] but dichotomizing the

scale has demonstrated that a good H&H grade (1 to 3) predicts a better outcome than a high H&H grade (4 and 5). In a series of 230 patients, 19% of good grade H&H patients had an unfavorable outcome compared with 90% of poor grade patients.[95] A later study showed that H&H grades of 4 and 5 had 4.87 times greater odds of unfavorable outcome compared with grades 1 to 3 (95% CI 2.57–9.21; $P<.001$).[96]

The WFNS Scale, developed in 1988, is also a 5-grade system, but is based on the GCS and is designed to acknowledge the significance of a focal neurologic deficit. Higher grades on the WFNS Scale indicate worse clinical presentation of SAH.[97] The predictive value of this scale has been repeatedly called into question because widely varying outcomes have been observed in patients presenting with the same grade.[98] Some investigations have even failed to predict any difference in outcome among adjacent WFNS grades when assessing patients with Glasgow Outcome Scale (GOS) at 1 month after discharge.[99] In contrast to this, a large study of approximately 3500 SAH cases evaluated patients with the GOS at 3 months following SAH and found that the likelihood ratio of a poor outcome varied linearly with increasing WFNS: WFNS grade 1 = 0.36, WFNS grade 2 = 0.61, WFNS grade 3 = 1.78, WFNS grade 4 = 2.47, and WFNS grade 5 = 5.22.[100]

The Fisher Scale is a radiographically defined score primarily concerned with predicting cerebral vasospasm after SAH. A grade of 1 to 4 is assigned depending on the amount of blood visible on CT imaging and presence of intracerebral or intraventricular clot.[101] Fisher grade 3 is associated with the highest incidence of clinical vasospasm. Although the scale has been used to predict outcome (for scores of 3 or 4, relative risk of poor outcome >4),[102] it is not considered to be comprehensive enough to be used as a primary grading system for SAH.[92]

Several other diagnostic factors on admission have been shown to correlate with outcome following SAH. Specific portions of the GCS can be strong predictors of outcome. In poor grade SAH patients (H&H Grades 4 and 5), an additional point on the GCS motor examination at admission predicted a 1.8-fold increase in the odds of achieving a favorable long-term outcome as defined by a mRS score of 3 or less (95% CI 1.4–2.3). At discharge, an additional point in the eye examination was associated with a 3.1-fold increase in favorable outcome (95% CI 1.8–5.4).[103] In another study, pupillary reactivity at admission predicted a 6.44 increase in the odds of favorable outcome at 12 months ($P = .008$) in a population of 204 poor grade patients.[104]

The modified Rankin scale (mRS) is an instrument frequently used for outcome assessment following SAH, and the scale is often dichotomized such that scores of 0 to 3 represent a favorable outcome with functional independence, whereas scores of 4 to 6 report a poor outcome with loss of a patient's functional independence.[105] The GOS is a second important measure of outcome composed of 5 points that reflect the following states: death, persistent vegetative state, severe disability, moderate disability, and good recovery.[106]

Rebleeding, Timing of Intervention, and Vasospasm

Rebleeding is the major cause of death in patients who survive the initial hemorrhage but do not undergo surgical intervention.[2,107,108] In untreated SAH, the greatest risk of rebleeding occurs on the first day (4%), with a daily frequency of 1.5% until 13 days. By 2 weeks, the rebleed rate is 15% to 20%, and up to 50% by 6 months.[108] The goal of surgical and endovascular treatment is to prevent this occurrence, and since the 1980s there has been a shift toward early intervention.[90]

Although the timing of intervention is still a source of debate,[109] there are substantial efforts being made to carry out early management protocols[90] on account of broad-based support for their implementation garnered through favorable outcome data.[109–112] In the pursuit of early intervention, there is a widely recognized trade-off between early surgical risk of operative mortality and the benefits it confers in terms of rebleeding prevention. No outcome difference has previously been found between intervention at 0 to 3 days after the original bleed versus 11 to 14 days, but outcomes were definitively worse in the 7- to 10-day interval.[111] Subsequent studies and meta-analyses have argued that the benefits derived from reduction of rebleeding seem to outweigh the risks of early intervention.[109,110,112]

In the current context, the rate of rebleeding is near 7% when pre-hospital events are excluded,[113] although several studies refer to a 10% to 20% incidence of ''ultra-early'' rebleeds by taking into account events that occur before patients receive neurosurgical attention.[114–117] Overall, rebleed events in the first day are associated with a drastically reduced chance of survival with functional independence at 3 months (mRS score, ≤ 4; OR 0.08; 95% CI 0.02–0.34).[113]

Ischemic neurologic deterioration secondary to cerebral vasospasm represents another major cause of morbidity after SAH.[118,119] On average, symptomatic vasospasm occurs in 20% to 30%

of patients, but vasospasm can be identified by arteriogram in 30% to 70% of patients with SAH, resulting in observed infarction in 10% to 45% of patients.[119–124] For compounds that attempt to mitigate the effects of vasospasm, class I evidence has been obtained only in demonstrating the beneficial effects of the calcium channel blocker nimodipine. Although this medication does not alter radiographic vasospasm,[125] it does improve the odds of favorable outcome to 1.86:1 ($P<.005$).[126]

Age, Gender, and Race

Patient age is strongly associated with worse outcome following SAH. In a study of 409 patients undergoing craniotomy for SAH, the investigators found that increased age correlated with significantly worse outcome such that a patient older than 63 years was at a 30-times greater risk for a poor outcome (GOS scores 1–3) than a patient aged 43 to 52 years.[102] Less drastically, a study of 98 patients treated for SAH demonstrated that those who were 65 years or older fared significantly worse than younger patients on mRS outcome measures (hazard ratio 6.6; 95% CI 1.8–24.1; $P<.001$).[127] Despite a higher mortality rate for elderly SAH patients, Stachniak and colleagues[128] determined that quality of life (QOL) scores appeared acceptable for elderly survivors of SAH, suggesting that surgery need not be ruled out as an option for this population.

Mortality rates for female SAH patients have been reported to be higher than those for males.[129–131] In an analysis of national death certificate data of SAH (n = 27,334) from 1995 to 1998, women had a higher death rate compared with men following SAH (4.9% versus 3.1%; Rate Ratio = 1.58; 95% CI 1.54–1.62).[129] Although there exists a significant difference in mortality among men and women, gender has not been found to predict severity of presentation, outcome, or survival following SAH.[132,133] In a trial for high-dose intravenous nicardipine, after adjustment for age, no difference was observed between women and men in terms of favorable outcomes at 3 months as measured by the GOS (69.7% for women versus 73.4% for men, $P = .243$; n = 565 women and 320 men).[133] Thus, some investigators conclude that higher death rates in women may simply be the result of higher SAH incidence among females.[134]

Although there exist variations in incidence and presentation of SAH among racial groups, the same cannot be concluded about differences in outcome, as several studies have shown no relation between outcome and race.[29,94,128,135–137] In a 1970 study of SAH patients (n = 319) selected from a 20% systematic sample of hospital veterans, there were no racial differences in terms of survival after SAH.[137] A retrospective case series from a single-center study of patients (1971–1976) similarly reports that race was not associated with adverse events in surgery.[136] Although these 2 studies were conducted before the establishment of current guidelines for early treatment of SAH, subsequent and more recent work corroborates their conclusions.

In an analysis of 107 patients prospectively identified from 2000 to 2006 in the Brain Attack Surveillance in Corpus Christi Project, no ethnic difference in outcome or discharge was found between whites and Mexican Americans.[29] Likewise, a prospective/retrospective case series of patients undergoing craniotomy for clipping of ruptured aneurysms (n = 219, recruited from 1989 to 1994), demonstrated no racial difference in QOL score after clipping for SAH.[128] Lastly, a retrospective study of prospectively collected data for a randomized-control trial of tirilazad in SAH patients (1991–1997) found no difference in 3-month outcome as measured by GOS.[94] A retrospective case series of cranial surgery among Medicare beneficiaries, however, demonstrated that black SAH patients had a longer length of hospital stay than the average SAH patient (12.2 days versus average 9.6 days, $P = .001$).[138] Interpretation of these results is inherently limited as only 5.7% of the study subjects were diagnosed with SAH (2526 SAH cases of 44,078 enrolled patients), while the stated results are for all cranial surgeries. The preponderance of studies that report a lack of association between race and outcome, coupled with the consistency of that observation before and after the shift to early treatment guidelines, would suggest that outcome following SAH is largely unaffected by race.

Other Prognostic Indicators

Hospitals with a high volume of SAH admissions generate better treatment outcomes for SAH than do low-volume hospitals.[89,139–144] In a large-sample study that examined 16,399 hospitalizations for SAH from 18 states in the US, patients who were treated in hospitals that see a low volume of SAH had 1.4 times the odds of dying in the hospital (95% CI 1.2–1.6) as patients admitted to high-volume hospitals.[142] Larger hospital size seems to be associated with lower mortality rates especially in patients who undergo aneurysm clipping ($P<.01$).[89] In New York state hospitals, those treatment centers that performed more than 30 craniotomies per year reported

a 43% (95% CI 29%–57%) lower mortality rate for SAH patients compared with hospitals performing less surgery.[144] Furthermore, country or continent has no bearing on outcome after SAH,[145] and outcome is unaffected by weekend versus weekday admission.[146]

SUMMARY

aSAH is a form of hemorrhagic stroke that affects up to 30,000 individuals per year in the United States. The incidence of aSAH has been shown to be associated with numerous nonmodifiable (age, gender, ethnicity, family history, aneurysm location and size) and modifiable (hypertension, BMI, tobacco and illicit drug use) risk factors. Although early repair of ruptured aneurysms and aggressive postoperative management has improved overall outcomes, it remains a devastating disease, with mortality approaching 50% and less than 60% of survivors returning to functional independence. As treatment modalities change and the percentage of minority and elderly populations increase it is critical to maintain an up-to-date understanding of subarachnoid hemorrhage epidemiology.

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