Age and outcome after aneurysmal subarachnoid hemorrhage: why do older patients fare worse?

GIUSEPPE LANZINO, M.D., NEAL F. KASSELL, M.D., TERESA P. GERMANSON, PH.D., GAIL L. KONGABLE, M.S., LAURA L. TRUSKOWSKI, M.S., JAMES C. TORNER, PH.D., JOHN A. JANE, M.D., PH.D., AND THE PARTICIPANTS

Department of Neurological Surgery, Neuroclinical Trials Center, University of Virginia Health Sciences Center, Charlottesville, Virginia; and Department of Preventive Medicine and Environmental Health, University of Iowa, Iowa City, Iowa

Advanced age is a recognized prognostic indicator of poor outcome after subarachnoid hemorrhage (SAH). The relationship of age to other prognostic factors and outcome was evaluated using data from the multicenter randomized trial of nicardipine in SAH conducted in 21 neurosurgical centers in North America. Among the 906 patients who were studied, five different age groups were considered: 40 years or less, 41 to 50, 51 to 60, 61 to 70, and more than 71 years. Twenty-three percent of the individuals enrolled were more than 60 years of age. Women outnumbered men in all age groups.

Level of consciousness (p = 0.0002) and World Federation of Neurological Surgeons grade (p = 0.0001) at admission worsened with advancing age. Age was also related to the presence of a thick subarachnoid clot (p = 0.0001), intraventricular hemorrhage (p = 0.0003), and hydrocephalus (p = 0.0001) on an admission computerized tomography scan. The rebleeding rate increased from 4.5% in the youngest age group to 16.4% in patients more than 70 years of age (p = 0.002). As expected, preexisting medical conditions, such as diabetes (p = 0.028), hypertension (p = 0.0001), and pulmonary (p = 0.0084), myocardial (p = 0.0001), and cerebrovascular diseases (p = 0.0001), were positively associated with age. There were no age-related differences in the day of admission following SAH, timing of the surgery and/or location, and size (small vs. large) of the ruptured aneurysm.

During the treatment period, the incidence of severe complications (that is, those complications considered life threatening by the reporting investigator) increased with advancing age, occurring in 28%, 33%, 36%, 40%, and 46% of the patients in each advancing age group, respectively (p = 0.0002). No differences were observed in the reported frequency of surgical complications. No age-related differences were found in the overall incidence of angiographic vasospasm; however, symptomatic vasospasm was more frequently reported in the older age groups (p = 0.01). Overall outcome, assessed using the Glasgow Outcome Scale at 3 months post-SAH, was poorer with advancing age (p < 0.001). Multivariate analysis of overall outcome, adjusting for the different prognostic factors, did not remove the age effect, which suggests that the aging brain has a less optimal response to the initial bleeding. Age as a risk factor is a continuum; however, there seems to be a significant increased risk of poor outcome after the age of 60 years.

KEY WORDS • subarachnoid hemorrhage • intracranial aneurysm • cerebral vasospasm • age • prognosis

AGE is a recognized risk factor for poor outcome in patients who suffer aneurysmal subarachnoid hemorrhage (SAH), and wide differences in recovery rates exist in relation to patient age. In the International Cooperative Study of the Timing of Aneurysm Surgery, there was a linear correlation between age and outcome. The rate of good recovery progressively decreased from 86% in the 18 to 29 years age group to 26% in the oldest age group (70–87 years). Although several authors have considered age and outcome after SAH, no studies have systematically analyzed the relationships between age and clinical characteristics at admission, associated preexisting medical conditions, and outcome; therefore, it is not clear whether age per se has a direct impact on outcome or whether a poorer outcome is simply due to the presence of associated conditions that are prevalent in the elderly.

The present study was conducted to define more clearly the relationships among age, baseline admission factors, and outcome in patients after aneurysmal SAH. Using a statistical model, we also tried to define the age limit after which rates of morbidity and mortality from SAH show a significant increase. For the purpose of this analysis, we used data that had been prospectively collected during a cooperative study (see Appendix) conducted between 1989 and 1991. The study, therefore, reflects the current management of SAH across different age groups in North American centers.
Age and aneurysmal subarachnoid hemorrhage

Clinical Material and Methods

Patient Selection

The 906 patients enrolled in this study were recruited from all patients with SAH admitted to 21 neurosurgical centers in the United States and Canada. All individuals were 18 years or older on admission, with SAH diagnosed on the basis of their medical history and confirmed by computerized tomography (CT) scan or lumbar puncture. The presence of a saccular aneurysm was confirmed by cerebral angiography. Patients were excluded if fusiform, traumatic, or mycotic aneurysms were the cause of the SAH. Other exclusion criteria included associated severe medical illness, prior use of calcium antagonist drugs at the time of hemorrhage, history of another neurological or psychiatric illness, allergy to calcium antagonist drugs, pregnancy or the suspicion of pregnancy, and inability to obtain informed consent. To be included the patient must have started therapy within the first 7 days of the most recent hemorrhage; all clinical Grades I to V based on the World Federation of Neurological Surgeons (WFNS) scale were allowed. Decisions on the timing of aneurysm surgery; the use of antifibrinolytic agents, steroids, induced hypertension, and hypervolemia; and other adjunctive therapies for treatment of ruptured aneurysm and vasospasm were determined by participating investigators.

Baseline prognostic factors, for admission neurological grade, and preexisting medical conditions (such as diabetes, hypertension, cardiac disease, pulmonary, renal, and hepatic diseases) were noted. The clot thickness measured on the admission CT scan and the location of the aneurysm were recorded. Trained investigators collected the following information in the first 14 days post-SAH: findings from daily neurological examinations, medical and surgical complications including vasospasm, and the treatment provided. Medical complications emerging during the 14-day treatment period (treatment emergent) were described as mild, moderate, or severe, depending on the amount of clinical intervention required. Mild complications were defined as those that did not alter the general medical condition, moderate complications as those that decreased the patient’s overall medical condition and required treatment, and severe complications as those that were life threatening. Neurological outcome was assessed by an evaluator blinded to the variables at 3 months post-SAH using the Glasgow Outcome Scale (GOS). According to this scale, outcome is divided into five categories: good recovery, moderate disability, severe disability, persistent vegetative state, and death.

All 906 patients were included in the study because there were no detectable drug-related influences on their clinical course and outcome except in the incidence of symptomatic vasospasm. Using a log linear model, we demonstrated that there were no second-order interactive effects of age and treatment on outcome. Age groups were categorized by advancing decades as 40 years or younger, 41 to 50, 51 to 60, 61 to 70, and more than 70 years.

Statistical Analysis

Several statistical procedures (the chi-square test, t-test, analysis of variance, Cochran-Mantel-Haenszel test, and binary and ordinal logistic regression) were used to determine the association of age with various outcome measures and other prognostic factors. Age was modeled as a continuous factor, a classification by decade, and a dichotomy. Multivariate prediction models of favorable outcome were determined in a step-down procedure, using binary logistic regression.

Results

Demographic Characteristics

Nine hundred six patients with a mean age of 50 years were enrolled in the study. Twenty-three percent of the patients were more than 60 years old. Women outnumbered men in all age groups considered (Fig. 1). The female/male ratio increased from 1.5:1 among patients younger than 40 years to 4.6:1 in the oldest age group.

Age-Related Clinical Characteristics at Admission

The baseline characteristics of the patient population by age group are summarized in Table 1. There were no age-related differences in the interval from SAH to hospital admission. A strong association between age and level of consciousness at admission (p = 0.0002) was noted. The percentage of patients who were stuporous or comatose increased from 12% in patients younger than 40 years old to 27% in the oldest age group.

Findings on admission CT scan are summarized in Table 2. Older patients were more likely to have a thick subarachnoid clot than younger patients (p = 0.0001). The incidence of both intraventricular hemorrhage (p = 0.0003) and hydrocephalus (p = 0.0001) increased with advancing age. No significant association was noted between age and either the location of the ruptured aneurysm or its size (small vs. large).

Associated Medical Conditions and Age

The incidence of preexisting medical conditions in the different groups considered is shown in Table 3. Increased rates of diabetes (p = 0.028), myocardial disease (p = 0.0001), arterial hypertension (p = 0.0001), cerebrovascular disease (p = 0.0001), and pulmonary disease (p = 0.0084) were associated with increasing age. Other conditions such as renal (p = 0.0548) or liver disease (p =...
The mean systolic pressure values at admission increased with advancing age (p = 0.0001) (Fig. 2). The diastolic values recorded at admission did not differ significantly among the age groups. The electrocardiogram at admission was more frequently reported to be abnormal in older than in younger patients.

**Age and Clinical Course**

The clinical course of the patient population during the study period is summarized in Table 4. There were no age-related differences in the timing of surgery. Fifty-seven individuals suffered rebleeding during the study period, with the rebleeding rate increasing from 4.5% in patients younger than 40 years of age to 16.4% in patients who were 70 years of age or older (p = 0.002). There were no age-related differences in the overall incidence of vaso-spasm; however, symptomatic vasospasm was more frequently recorded in older patients (p = 0.01). Severe complications during the study period occurred at a rate of 28%, 33%, 36%, 40%, and 46% in the advancing age groups, respectively (p = 0.0002); however, no age-related differences were observed in the incidence of surgical complications.

**Age and Outcome**

The outcome of the patient population by age is shown in Tables 5 and 6. Outcome assessed using the GOS at 3 months post-SAH was associated with increasing age (p < 0.001). Seventy-three percent of patients who were 40 years and younger made a good recovery. The percent of patients who made a good recovery then progressively decreased to 62%, 55%, 41%, and 25%, respectively, in the other advancing age groups considered. Mortality rates increased from 12% in the youngest age group to 35% in the oldest age group. The age-related differences in outcome were still present when the admission WFNS grade was also taken into account (p < 0.001, Cochran-Mantel-Haenszel test) (Table 6).

An exploratory analysis was conducted to determine the optimal age cutoff for discriminating low and high risk of a favorable outcome at 3 months post-SAH. The age dichotomy that produced the highest chi-square in a comparison of favorable outcome rates was selected as the optimal cutoff. Age above 60 years was chosen as the cutoff that best discriminated favorable outcome rates (p < 0.0001) (Table 7).

**Multivariate Analysis**

A multivariate analysis was conducted to determine whether age as a continuous factor contributed independently to the multivariate prediction of favorable outcome after adjustment for other prognostic factors. First, a multivariate logistic model in a step-down model with probability equivalent to 0.1 as the entry and exit criteria was produced from a candidate list of prognostic factors: age, WFNS grade, thickness of clot on CT, preexisting medical conditions (arterial hypertension, diabetes, lung disease, cerebrovascular and cardiac diseases). The factors remaining in the model were WFNS grade, thickness of clot, and history of cerebrovascular disease. The additional contribution of age to this model was highly significant (p < 0.0001). When the step-down procedure was repeated with age included in the candidate list, the final multivariate prediction model included only age and WFNS grade. The interaction of age and WFNS grade did not contribute significantly to this model. Similar multivariate results
were obtained when age was modeled as a dichotomy: less than 60 years of age versus 60 years of age or greater. Missing data were excluded from the calculation of percentages and from the statistical analysis.

**Discussion**

The age-specific incidence of SAH increases with advanced age.\(^3,25,40,42,44\) In the Framingham study,\(^42\) the annual incidence per 100,000 population increased from 15 in the 30- to 59-year-old group to 78 in the 70- to 88-year-old group. As a result, patients older than 60 years constitute a significant proportion of patients with SAH. It can be anticipated that with the aging of the general population, aneurysm rupture in the elderly will become an issue of greater importance.

In our study, 23% of the patients were older than 60 years of age. Because of the characteristics of our patient population (subjects enrolled into a clinical trial) and the inclusion criteria of the study, a selection bias may have occurred, with only elderly patients in good clinical condition enrolled and available for analysis. However, other authors have reported similar age distributions of patients with SAH, suggesting that such a selection did not play a significant role. Our data, in fact, are consistent with the Cooperative Study on the Timing of Aneurysm Surgery\(^22\) in which 908 (26%) of the 3521 patients studied were 60 years or older. Similar percentages have also been reported in population-based studies\(^41\) and in autopsy studies.\(^14,29\)

The observation that population-based and autopsy studies match the percentage of patients over the age of 60 years observed in our study indicates that, in North America, older patients are appropriately referred to neurosurgical centers after aneurysmal rupture.

**Age and Baseline Clinical Characteristics**

There is an inverse association between age and neurological status at admission.\(^8,18,19,41\) The percentage of patients who are Grade I at admission progressively decreases from 66% in patients 40 years of age or younger to 30% in the oldest age group (> 70 years). Several factors responsible for the poorer neurological status in older patients are observed: the subarachnoid clot visualized on an admission CT scan is thicker in elderly patients,\(^19,43\) partially because of the parenchymal atrophy that allows for a larger quantity of blood to collect after aneurysm rupture. In addition, the likelihood of a history of hypertension in patients with aneurysmal SAH increases with advancing age,\(^22\) and elevated blood pressure is closely connected to the severity of SAH.\(^11\) Intraventricular hemorrhage and hydrocephalus at admission are also more frequently encountered in older patients (JP Elliot, et al., unpublished data).

Controversy exists concerning whether the location of ruptured aneurysms differs with age.\(^19,43\) Sakaki and co-workers,\(^43\) in comparing two groups of patients (< 65 years vs. > 65 years), found that aneurysms in older patients occur more frequently in the vertebral, basilar, and anterior communicating arteries and less often in the internal carotid artery. We, along with others,\(^19\) did not detect either an age-related difference in the location of the ruptured aneurysm or an association between age and

<table>
<thead>
<tr>
<th>TABLE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Findings on CT scans at admission in 797 patients with aneurysmal SAH by age</strong>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Characteristics on CT Scan</th>
<th>&lt;40</th>
<th>41–50</th>
<th>51–60</th>
<th>61–70</th>
<th>&gt;70</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAH (797 patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thin</td>
<td>117 (56)</td>
<td>92 (44)</td>
<td>73 (38)</td>
<td>57 (44)</td>
<td>11 (20)</td>
<td></td>
</tr>
<tr>
<td>thick</td>
<td>93 (44)</td>
<td>116 (56)</td>
<td>120 (62)</td>
<td>74 (56)</td>
<td>44 (80)</td>
<td>0.0001</td>
</tr>
<tr>
<td>IVH</td>
<td>44 (21)</td>
<td>55 (26)</td>
<td>53 (27)</td>
<td>45 (34)</td>
<td>24 (44)</td>
<td>0.0003</td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>65 (31)</td>
<td>60 (29)</td>
<td>82 (42)</td>
<td>53 (40)</td>
<td>36 (65)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

* CT = computerized tomography; IVH = intraventricular hemorrhage; SAH = subarachnoid hemorrhage.

<table>
<thead>
<tr>
<th>TABLE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preexisting medical conditions in 906 patients with aneurysmal subarachnoid hemorrhage by age</strong>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preexisting Medical Condition</th>
<th>&lt;40</th>
<th>41–50</th>
<th>51–60</th>
<th>61–70</th>
<th>&gt;70</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>arterial hypertension</td>
<td>58 (23.8)</td>
<td>90 (40)</td>
<td>102 (49)</td>
<td>66 (47)</td>
<td>41 (65)</td>
<td>0.0001</td>
</tr>
<tr>
<td>cardiac disease</td>
<td>5 (2.0)</td>
<td>14 (6)</td>
<td>29 (13.9)</td>
<td>19 (13.4)</td>
<td>16 (25.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>cerebrovascular diseases</td>
<td>7 (2.9)</td>
<td>6 (2.6)</td>
<td>13 (6.3)</td>
<td>14 (9.8)</td>
<td>12 (19.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>pulmonary diseases</td>
<td>13 (5.3)</td>
<td>14 (6)</td>
<td>18 (8.7)</td>
<td>14 (9.8)</td>
<td>8 (12.7)</td>
<td>0.0084</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>2 (0.8)</td>
<td>4 (1.7)</td>
<td>9 (4.3)</td>
<td>5 (3.6)</td>
<td>2 (3.1)</td>
<td>0.028</td>
</tr>
<tr>
<td>renal diseases</td>
<td>8 (3.3)</td>
<td>10 (4.3)</td>
<td>7 (3.4)</td>
<td>6 (4.2)</td>
<td>7 (11.3)</td>
<td>0.0548</td>
</tr>
<tr>
<td>hepatic disease</td>
<td>6 (2.5)</td>
<td>6 (2.6)</td>
<td>5 (2.4)</td>
<td>5 (3.6)</td>
<td>1 (1.6)</td>
<td>0.6493</td>
</tr>
</tbody>
</table>

J. Neurosurg. / Volume 85 / September, 1996
multiplicity. Because aneurysms are considered acquired lesions whose incidence increases with age, one would expect older patients to harbor larger aneurysms; however, this is not the case. No differences were found in the size of aneurysms in the different age groups, a finding reported by other investigators.

Age and Cerebral Vasospasm

After aneurysmal SAH, the amount of blood visualized on the admission CT scan is closely related to the subsequent development of vasospasm. In elderly patients, despite a thicker clot on CT, the incidence of angiographic vasospasm is lower than expected; this is especially true in older hypertensive patients. These observations suggest that the cerebral vessels become more rigid with advancing age, especially in the presence of chronic elevated blood pressure, and are less responsive to spasmogenic factors, preventing these vessels from developing vasospasm.

Even though vascular narrowing is relatively less severe in the elderly patients, the incidence of symptomatic vasospasm is either similar to that observed in younger patients or, as shown in our series, increases with advancing age (HE Benalcazar, et al., unpublished data). In a study of cerebral blood flow after SAH in two groups (<50 years vs. >50 years), Benalcazar, et al. (unpublished data) reached similar conclusions after observing that more younger patients suffer vasospasm. Older patients, however, were more likely to die or sustain a permanent neurological deficit from vasospasm. It is well known that cerebral blood flow (CBF) decreases with advancing age and older patients have a decreased cerebrovascular reserve. In addition, SAH is also associated with impairment of the cerebrovascular reactivity (autoregulation) that normally prevents CBF from falling when cerebral perfusion pressure is reduced. In such circumstances older individuals are more vulnerable because their CBF would have less far to fall before reaching the ischemic threshold.

Management of SAH in the Elderly

The observation that elderly patients fare worse after aneurysmal SAH has generated an animated debate on the best therapeutic strategy to adopt in such cases. Operative results in the past have been less favorable in older than in younger patients; in 1960 McKissock, et al., reported an operative mortality rate of 44% for patients between 60 and 70 years old, and the authors of a provocative article, published as recently as 1978, suggested that no patients older than 60 years should undergo operation. There are indications, however, that surgical results in the older age groups and, as a consequence, overall management results have significantly improved in the past two decades, making surgical repair of a ruptured aneurysm or surgical treatment of giant aneurysms a valid option even in the eighth and ninth decades. The operative mortality in patients older than 60 years has decreased from 51% in the Cooperative Study published in 1966 to 20% in the Cooperative Study on Timing of Aneurysm Surgery conducted between 1980 and 1983.

This trend has been confirmed by reports from single institutions and, comparing the treatment of SAH in the elderly in two periods (1980–1985 and 1986–1990), observed improvement in the overall management outcome, especially in patients aged 70 to 79 years, a factor contributing to improvement of surgical outcome in this age group. In a recent retrospective analysis of 98 patients 70 years or older who were treated in Sweden between 1988 and 1993, satisfactory results were obtained in 74% of individuals in good clinical condition.
Age and aneurysmal subarachnoid hemorrhage

(Grades I and II) at admission; this figure approaches the results of aneurysm treatment in younger age groups. However, in elderly patients amenable to treatment but for whom surgery is deferred solely because of age, the late outcome is catastrophic. In conservatively managed elderly subjects, in fact, the mortality and morbidity rate exceeds 75% 1 year after the bleeding, with more than 50% of the patients dying within 3 months.

In North American centers, advanced age does not seem to influence the timing of surgery; in our series early surgery was performed in 60% of patients aged 61 to 70 and in 67% of patients aged over 70 years. There are several theoretical reasons that support early surgery in elderly patients; the rebleeding rate increases with advancing age; elderly people are more likely to experience intraventricular hemorrhage and acute hydrocephalus (both treatable with treatment with early intervention); and, as previously discussed, elderly people are at high risk for symptomatic vasospasm. When vasospasm occurs, it can be more aggressively treated with hyperdynamic therapy if the aneurysm has been secured. Although caution has to be exercised with patients over 70 years of age, there is convincing evidence that early surgery can be performed in elderly patients as safely as in younger subjects.

In the International Cooperative Study on the Timing of Aneurysm Surgery, it was clearly shown that patients older than 65 years who had surgery planned for Days 0 to 3 did not have an especially unfavorable outcome. In medically unstable patients or in the presence of serious associated risk factors, endovascular therapy represents a valid alternative to surgical exclusion of the aneurysm.

Age and Outcome

Overall outcome as assessed by the patient’s GOS score 3 months post-SAH was significantly worse in the older age groups. The percentage of patients who made a good recovery decreased from 73% in patients of age 40 years or less, to 41% in the age group 61 to 70 years and to 25% in patients older than 70 years. The overall poor outcome observed with advancing age is only partially explained by other factors such as poor clinical condition at admission, increased amount of blood on the CT scan, and pre-existing medical diseases that are associated with increasing age. In our study, adjustment for these factors did not remove the age effect. Age itself, therefore, has an independent negative influence on outcome after SAH, suggesting that the aging brain has a less than optimum response to the initial bleeding; a similar phenomenon has been observed in traumatic brain injury.

The upper age limit after which there is a significant increased risk of poor outcome is unclear. Some authors have used 50 years as the limit, whereas others have considered 60, or 65 years (JB Stachniak, et al., unpublished data). In our study and in the Cooperative Study on the Timing of Aneurysm Surgery, the negative relationship between age and outcome was a linear one. However, when we conducted an exploratory analysis it became evident that the percentage of patients who experienced a poor outcome was significantly higher when an age cutoff of 60 years was considered. A similar conclusion was reached when we tried to develop a computer-generated mathematical model to predict outcome after SAH based on a series of risk factors present at admission. In this model, age greater than 60 years was the most important predictor of outcome after level of consciousness. On the basis of these observations, we suggest that the age cutoff of 60 years should be used when the risk factor age is considered in patients with SAH.

Vulnerability of the Aged Brain to SAH

The basic mechanisms responsible for the vulnerability of the aged brain to SAH and to any injury in general are not completely understood. Comprehension of these mechanisms would open a fascinating window on the molecular processes underlying neuronal aging. Based on current knowledge, several speculations can be made and different factors can be hypothesized: 1) in the brain as well as in every organ, tissue, and many cells, a time-dependent loss of structure, function, and chemistry proceeds slowly as the consequence of small, but cumulative, microinsults; 2) the accuracy of translation, which depends on the cell’s ability to decode the triple codons in messenger RNA molecules, is impaired with aging (codon restriction theory of cellular aging); 3) the number of neuronal mitochondria are reduced with aging and metabolically active, nondividing neuronal cells become highly susceptible targets of oxidative and excitatory amino acid damage (it is well known that these conditions occur after SAH); and 4) the “reactive synaptogenesis” or axonal sprouting that represents a compensatory reaction to neuronal loss or damage and is characterized by an
increase in the number of synaptic contacts provided by the adjacent neurons, although not entirely lost, is slowed with aging. As a result of all these factors, the brain is limited in its ability to repair the lost function/structure after any type of damage.

Conclusions

This study confirms that age is an important predictor of poor outcome after SAH. Several factors that can independently affect outcome are associated with increased age. These include a poorer clinical status at admission, larger amount of subarachnoid blood, higher incidence of hydrocephalus and intraventricular hemorrhage on admission CT scan, associated preexisting medical conditions, and higher rebleeding rates. The incidence of asymptomatic vasospasm is lower in the elderly than in younger patients. However, symptomatic vasospasm is more frequently observed in the older age groups because of a reduced cerebrovascular reserve. Adjustment for these factors, however, does not remove the age effect, suggesting that age itself (and by implication the aging brain) has a negative effect on outcome independent of any other factors.

Operative morbidity rates do not significantly differ with advancing age and surgical results in the elderly have significantly improved in the past decades. Therapeutic nihilism would not appear to be justified in older age groups. The overall costs of hospitalization are higher for patients older than 65 years because these patients spend more time in the intensive care unit (JB Stachniak, et al., unpublished data); however, treatment of a ruptured aneurysm should not be refused to the elderly patient solely on the basis of advanced age.

Acknowledgments

The authors wish to express their gratitude to Elizabeth Fisher, Desiree J. Lanzino, and Sarah Hudson, who edited the manuscript, and to Carl Gaines and Katie Redick for their help in preparing the manuscript.

Dedication

This work is dedicated to the memory of Sergio Vitari who did not survive the rupture of his aneurysm.

Appendix

Participants in the Study

Barrow Neurological Institute, University of Arizona, Phoenix and Tucson, Arizona

Principal Investigator: Robert L. Campbell, M.D.
Clinical Coinvestigators: Scott Shapiro, M.D., and Martin Farlow, M.D.
Coordinator: Sandy Kay, R.N.

Indianapolis Neurosurgical Group, Indianapolis, Indiana

Principal Investigator: Terry Horner, M.D.
Clinical Coinvestigator: Thomas Leipzig, M.D.
Coordinator: Kathy Redelman, R.N.

Medical College of Virginia, Richmond, Virginia

Principal Investigator: J. Paul Muizelaar, M.D.
Clinical Coinvestigators: Robert Turner, M.D., Walid Kamsheh, M.D., and Gerrit Bouna, M.D.
Coordinator: J. Paul Muizelaar, M.D.

Montefiore Medical Center, New York, New York

Principal Investigator: Raúl De Los Reyes, M.D.
Clinical Coinvestigator: Daniel Rosenbaum, M.D.
Coordinator: Emilia Klonowski, R.N.

Notre-Dame Hospital, Montreal, Quebec, Canada

Principal Investigator: Gerard Mohr, M.D.
Clinical Coinvestigators: Michael Bojanowski, M.D., Giles Bernier, M.D., and Pierre Duquette, M.D.
Coordinator: Pauline LalPante, R.N.

St. Vincent’s Hospital, New York, New York

Principal Investigator: Raj Murali, M.D.
Clinical Coinvestigator: Christine Crisafulli, M.D.
Coordinator: Cindy Merkel, R.N.

University of Alabama, Birmingham, Alabama

Principal Investigator: Michael J. Rosner, M.D.
Clinical Coinvestigators: M. Stephen Mahaley, M.D., Patricia A. Aronin, M.D., and Richard B. Morawetz, M.D.
Coordinators: Sheila Rosner, R.N., and Rebecca Brock-Sillers, R.N.

University of California–San Diego, San Diego, California

Principal Investigator: Roderick G. Lamond, M.D.
Clinical Coinvestigators: Lawrence Marshall, M.D., and John Rothrock, M.D.
Coordinators: Beth Benedict, R.N., and Susan Moore, R.N.

University of Kentucky, Lexington, Kentucky

Principal Investigator: Byron Young, M.D.
Clinical Coinvestigators: Robert Dempsey, M.D., and Phillip Tibbs, M.D.
Coordinator: Renee Phillips, R.N.

University of Maryland, College Park, Maryland

Principal Investigator: Michael Salcman, M.D.
Clinical Coinvestigator: Daniele Rigamonti, M.D.
Coordinator: Susan Kulick, R.N.

University of North Carolina, Chapel Hill, North Carolina

Principal Investigator: Stephen Powers, M.D.
Coordinator: Mary Lee Baker, R.N.

University of Pennsylvania, Philadelphia, Pennsylvania

Principal Investigator: Eugene S. Flamm, M.D.
Clinical Coinvestigators: Martin Reivich, M.D., Michael Kushner, M.D., and Roger Farber, M.D.
Coordinator: Susan Parrott, R.N.

University of Texas–Galveston, Galveston, Texas

Principal Investigator: J. Marc Simard, M.D.
Clinical Coinvestigators: Howard M. Eisenberg, M.D., Barry Kapler, M.D., Thomas Kent, M.D., and Francois Aldrich, M.D.
Coordinator: Barbara Turner, R.N.

University of Texas–Houston, Houston, Texas

Principal Investigator: James Grotta, M.D.
Clinical Coinvestigators: Daniel Kopaniecy, M.D., Frank Yatsur, M.D., and Tom DelGrapa, M.D.
Coordinator: Patti Bratina, R.N.

University of Utah, Salt Lake City, Utah

Principal Investigator: H. Peter Heilbrun, M.D.
Clinical Coinvestigators: Gregory Call, M.D., Robert Hood, M.D., and Stuart Goodman, M.D.
Coordinator: Peter Sunderland, R.N.

University of Virginia, Charlottesville, Virginia

Principal Investigator: Neal F. Kassell, M.D.
Clinical Coinvestigator: E. Clarke Haley, M.D.
Coordinator: Karen Parks, R.N.
Age and aneurysmal subarachnoid hemorrhage

University of Washington, Seattle, Washington
Principal Investigator: H. Richard Winn, M.D.
Clinical Cointvestigators: Sean Grady, M.D., and Marc Mayberg, M.D.
Coordinator: Cathy Burnal, R.N.
Washington University, St. Louis, Missouri
Principal Investigator: Robert L. Grubb, Jr., M.D.
Clinical Cointvestigators: William Coxe, M.D., William Landou, M.D., Keith Rich, M.D., and Alan Levin, M.D.
Coordinator: Virginia Hobbs, R.N.

Other Participants:

Advisory Committee
Harold P. Adams, M.D., University of Iowa
Charles G. Drake, M.D., University of Western Ontario
Mark L. Dyken, M.D., Indiana University
Eugene S. Flamm, M.D., University of Pennsylvania
Ralph F. Frankowski, Ph.D., University of Texas (Houston)
John F. Kurtzke, M.D., Georgetown University
Bryce K. A. Weir, M.D., University of Chicago

Central Registry (University of Virginia)
Principal Investigator: Neal F. Kassell, M.D.
CoPrincpal Investigators: E. Clarke Haley, Jr., M.D., and James C. Torner, Ph.D.
Cointvestigator, Neuoradiology: Wayne S. Cail, M.D.
Biostatistics: Teresa P. Germanson, Ph.D., and Laura L. Truskowski
Data Manager: Angela L. Lightfoot, B.A.
Image Analysts: Jennifer A. Marron, B.A., and Angela S. Polin, B.S.

References

Manuscript received January 5, 1996. Accepted in final form March 27, 1996.
This study was supported by grants from the National Institute of Neurological Disorders and Stroke (NS24806), Dupont-Merck Pharmaceuticals, and Syntex Research.
This paper was presented in part at the 45th Annual Meeting of the Congress of Neurological Surgeons, San Francisco, California, October 14–19, 1995.
Address reprint requests to: Giuseppe Lanzino, M.D., Department of Neurological Surgery, University of Virginia Health Sciences Center, Box 212, Charlottesville, Virginia 22908.