Age-related multifactorial causes of neurological deterioration after early surgery for aneurysmal subarachnoid hemorrhage

YUHEI YOSHIMOTO, M.D., AND SUYONG KWAK, M.D.

Neurosurgical Institute of Higashi Yokohama Hospital, Yokohama, Kanagawa, Japan

Although by no means universally accepted, early surgery for aneurysmal subarachnoid hemorrhage (SAH) seems to provide favorable management. Improvements in microneurosurgical and neuroanesthesiological techniques have resulted in an increasing number of operations for aneurysm clipping in the acute stage even in elderly patients. Early surgery may reduce mortality and morbidity due to rebleeding, thus allowing postoperative management protocols to focus on the prevention and treatment of delayed ischemic phenomena. The induction of hypervolemic therapy seems to have decreased the incidence of ischemic symptoms. However, the clinical picture after surgery is still complex; appearance of the clinical syndrome of chronic vasospasm is often accelerated or precipitated by a reduction in blood pressure, a decrease in intravascular volume, or metabolic disturbance, as well as the effects of surgical manipulation. Although several studies have examined the ratio of delayed ischemic neurological deficits in relation to age, quantitative studies of the effect of age on angiographic vasospasm in humans have been rare. The present study was designed to investigate the relationship between the age of patients with SAH and the severity of quantified angiographic vasospasm and the additional pathophysiological changes underlying the development of delayed ischemic deficits after SAH.

Clinical Material and Methods

One hundred seventy-eight consecutive patients with ruptured intracranial aneurysms were treated surgically between 1988 and 1993. Eleven of these patients were excluded from the present study because they underwent surgery later than Day 4 postrupture. Twenty-five patients who showed a prolonged decrease in the level of consciousness after surgery (due mainly to primary brain damage by SAH, but also to the effect of surgery in a few instances) were also excluded, because the diagnosis of neurological deterioration in such cases is often difficult. The remaining 142 patients were classified by age into three groups: 49 years of age or younger (Group A), 50 to 64 years old (Group B), and 65 years of age or older (Group C). Among these, 40 patients (28%) overall showed neurological deterioration; these cases were analyzed in detail. Although the highest incidence of deterioration was noted in patients in Group C (42%), angiographic vasospasm, quantified by measuring the change in the ratio of the diameters of the intracranial arteries to the extracranial internal carotid artery, was negatively correlated with age. In elderly patients, the severity of angiographic vasospasm was not related to the reversibility of symptoms or the outcome. At the time of aggravation, associated systemic complications such as cardiac decompensation, hypoxia, and electrolyte imbalance were noted in two (18%) of 11 patients in Group A, five (38%) of 13 in Group B, and eight (50%) of 16 in Group C, and these complications were significantly correlated with poor outcome in Group C. Although arterial narrowing is a leading cause of neurological deterioration after early aneurysmal surgery, the etiology is often multifactorial, especially in elderly patients, suggesting that hypervolemic therapy, which might provoke various complications, should be performed carefully under intensive monitoring.
Age as risk factor for vasospasm

was verified in all patients by admission computerized tomography (CT) scanning, and the amount of subarachnoid blood was categorized according to the scale of Fisher, et al. Cerebral angiography was performed as early as possible after admission and repeated between Days 5 and 10 after SAH. Twenty-five patients underwent surgery on Day 0, 12 on Day 1, two on Day 2, and one on Day 3. Postoperative management principles varied somewhat from patient to patient. Most patients underwent hypervolemic therapy, which was provided by intravenous drip infusion of albuminates, fresh-frozen plasma, and low-molecular-weight dextran, as necessary, to maintain central venous pressure (CVP) at approximately 5 to 8 cm H2O. Hematocrit was kept in the 30% to 35% range. Dopamine or dobutamine was used for inotropic support to enhance cardiac output and to increase the mean arterial pressure during periods of vasospasm.

Vasospasm-associated systemic and intracranial complications were reviewed in the patients’ charts. All the systemic complications developed at the time, or before, evidence of new neurological symptoms became manifest. Hypoxia was diagnosed on the basis of a PaO2 level of less than 80 mm Hg despite adequate oxygen delivery. Cardiac decompensation was defined in this study as a value of CVP exceeding 15 cm H2O. Intracranial complications such as atherosclerotic stenosis of major cerebral arteries (50% reduction), postoperative subdural effusion, or contusional hematoma due to surgical manipulation were diagnosed from the radiographic findings. An outcome of “good” was applied for independence in activities of daily living at 3 months after onset; otherwise the outcome was considered to be “poor.”

Quantitation of Vasospasm

Cerebral angiography was performed at least twice: on admission (preoperatively, Day 0 or 1) and between Days 5 and 10. Of the 40 patients who showed neurological deterioration, both angiograms for the two periods were available in 36. Angiograms obtained on the side of the thicker SAH on CT scans were input into a personal computer system and magnified. Vasospasm was quantified by measuring arterial diameters on anteroposterior projections of internal carotid angiograms (Fig. 1). Arterial diameters were measured at four predetermined points using an image analyzer, and the ratio of the diameters of the intracranial arteries to the extracranial internal carotid artery were calculated. Thus, diameter ratio (DR) = (C1 + M1 + A1)/C5, where C1 (M1, A1, C5) = the arterial diameter at the center of each segment. The average of the ratios for preoperative (Day 0 or 1) angiograms (DRpre) was 1.52 (range 1.06–2.09). To offset the variability in the values for each of the 36 individuals, the degree of angiographic spasm was expressed as the relative alteration in the DR for the postoperative (Days 5–10) angiogram (DRpost) range 0.53–1.96, average = 1.11) to that for the preoperative ones: DRpost/DRpre range 0.41 to 1.02, average = 0.73.

Statistical Analysis

The data are expressed as mean ± standard deviation. For statistical comparison, chi-square test, Student’s unpaired t-test, and analysis of variance (ANOVA) were used as appropriate. In all cases, differences in p values of less than 0.05 were considered to be statistically significant. For evaluation of the correlation between age and angiographic narrowing in each patient, simple linear regression was used.

Results

Of the 142 patients, 40 (28%) subsequently suffered neurological deterioration. The incidence was 26% (11 of 42) in Group A, 21% (13 of 62) in Group B, and 42% (16 of 38) in Group C. Characteristics of patients with neurological deterioration in each age group are shown in Table 1 and did not differ significantly between any of the groups.

In Fig. 2, the degree of angiographic vasospasm is plotted against age for patients with reversible and fixed neurological deficits. Older patients showed less arterial narrowing than younger ones in both groups. As shown by the two regression lines, the degree of angiographic vasospasm in younger patients was more severe in those with fixed deficits than in those with reversible deficits; however, in elderly patients, the degree was almost identical between the two subgroups.

Systemic and/or intracranial complications were observed in many patients, and the incidence and the types of associated pathology in each group are shown in Tables 2 and 3.
Prognostic factors in each group were analyzed and are shown in Table 4. In Groups A and B, the patients with good outcome tended to have less severe angiographic vasospasm than those with poor outcome (DRpost /DRpre = 0.72 vs. 0.65, not significant). In patients in Group C, systemic complications were correlated with poor outcome (significant at p < 0.05), whereas angiographic vasospasm was almost identical between the patients with good outcome and those with poor outcome (0.83 vs. 0.82, not significant).

Discussion

Quantification of Angiographic Vasospasm

The correlation between angiographic vasospasm and the age of patients with SAH has been investigated with varying results. Some studies have suggested that the incidence of angiographic vasospasm is lower in the elderly, whereas some authors have maintained that there is no correlation between the two. The main reason for the controversy is the application of relatively subjective judgment or qualitative assessment as to the “presence” or “absence” of this phenomenon. Because of variations in the normal anatomy of the intracranial vessels, attempts to quantify vasospasm in a reliable manner have been frustrated. Our method provides a ratio between arterial diameter in the subarachnoid space and that of the extracranial carotid artery, overcoming any variation in measurement caused by differences in angiogram magnification. Variability in each individual was also offset by calculating the ratio of the diameter during the period of cerebral vasospasm (Days 5–10) to that on Day 0 or 1.

We found that older patients developed less severe angiographic vasospasm, probably due to atherosclerosis and increased stiffness of the arterial wall; other investigators have confirmed this finding using a similar method for quantitation of angiographic vasospasm. Rohde, et al., used transcranial Doppler, a promising alternative to angiography for demonstrating narrowing of the major cerebral arteries, and reported that increased flow velocity suggestive of cerebral vasospasm (mean blood flow velocities over 120 cm/sec) was detectable in 65% of patients aged 59 years or less and in 28% of those aged 60 years or more.

Prognostic factors in each group were analyzed and are shown in Table 4. In Groups A and B, the patients with good outcome tended to have less severe angiographic vasospasm than those with poor outcome (DRpost /DRpre = 0.72 vs. 0.65, not significant). In patients in Group C, systemic complications were correlated with poor outcome (significant at p < 0.05), whereas angiographic vasospasm was almost identical between the patients with good outcome and those with poor outcome (0.83 vs. 0.82, not significant).

Discussion

Quantification of Angiographic Vasospasm

The correlation between angiographic vasospasm and the age of patients with SAH has been investigated with varying results. Some studies have suggested that the incidence of angiographic vasospasm is lower in the elderly, whereas some authors have maintained that there is no correlation between the two. The main reason for the controversy is the application of relatively subjective judgment or qualitative assessment as to the “presence” or “absence” of this phenomenon. Because of variations in the normal anatomy of the intracranial vessels, attempts to quantify vasospasm in a reliable manner have been frustrated. Our method provides a ratio between arterial diameter in the subarachnoid space and that of the extracranial carotid artery, overcoming any variation in measurement caused by differences in angiogram magnification. Variability in each individual was also offset by calculating the ratio of the diameter during the period of cerebral vasospasm (Days 5–10) to that on Day 0 or 1.

We found that older patients developed less severe angiographic vasospasm, probably due to atherosclerosis and increased stiffness of the arterial wall; other investigators have confirmed this finding using a similar method for quantitation of angiographic vasospasm. Rohde, et al., used transcranial Doppler, a promising alternative to angiography for demonstrating narrowing of the major cerebral arteries, and reported that increased flow velocity suggestive of cerebral vasospasm (mean blood flow velocities over 120 cm/sec) was detectable in 65% of patients aged 59 years or less and in 28% of those aged 60 years or more.
Age as risk factor for vasospasm

Multifactorial Etiology of Neurological Deterioration

In this study, a higher incidence of neurological aggravation was found in elderly patients, whereas angiographic vasospasm was less severe in these patients. Several additional factors contributing to neurological worsening can be suggested. Preoperative angiograms obtained on Day 0 or 1 after SAH, when chronic vasospasm was absent,18,23 revealed moderate- to high-grade (> 50%) stenosis in major cerebral arteries more frequently (five of 16, 31%) in patients aged 65 years or more, which would cause inadequate collateral circulation to the ischemic lesion in the chronic vasospasm phase after SAH.9 Systemic complications such as cardiac decompensation resulting in decreased cardiac output, hypoxia, or electrolyte imbalance would contribute to neurological deterioration; these conditions were also observed more frequently in elderly patients.

As indicated by the difference between the two regression lines in Fig. 2, there was a trend in younger patients for reversible deficits to be associated with less severe angiographic vasospasm than fixed deficits. On the other hand, in elderly patients, the degree of angiographic vasospasm was almost identical to the two groups, suggesting that its severity was not a predictor of symptom reversibility. These findings reemphasize the complexity of the relationship between reduction of arterial caliber and the clinical syndrome of delayed cerebral ischemia. In fact, the existence of systemic complications was shown to be significantly related to poor prognosis in the elderly patients. The etiology of delayed neurological deficit is often multifactorial, with problems other than arterial narrowing that potentially contribute to the clinical picture or might predominantly determine the prognosis in elderly patients with SAH.

Hypervolemic Therapy

Hypervolemic hypertension therapy and/or hemodilution has been a mainstay for the prevention and treatment of cerebral vasospasm induced by SAH.8,10,13,21 The rationale underlying the treatment is to increase the cerebral perfusion pressure10 and cerebral blood flow to the ischemic areas or at least to correct hypovolemia to normovolemia. More important, dilutional hypervolemia is thought to improve ischemia by decreasing blood viscosity, thereby improving microcirculation.25 Solomon, et al.21 considered that volume status might be the key differential separating patients with asymptomatic angiographic vasospasm from those who develop signs of cerebral ischemia in association with vasospasm. Once a ruptured aneurysm has been corrected surgically, elevation of systemic arterial pressure in a state of cerebrovascular insufficiency resulting from vasospasm appears to be safe and beneficial.

However, several investigators consider that hypervolemic therapy is sometimes ineffective and could have harmful effects,14,20,26 including an increase of blood-brain barrier permeability, aggravation of cerebral edema, or a rise in intracranial pressure. Additionally, this therapy could result in a high incidence of congestive heart failure and/or pulmonary edema, which could be expected to occur predominantly in elderly patients, as shown in the present study. In a recent study, prophylactic hypervolemia for SAH patients was found to be associated with pulmonary edema in 12 (26%) of 47 patients due to volume expansion.14 Thus, the efficacy of hypervolemic therapy should be determined by the balance between these factors. Because patients suffering from SAH have been shown to have reduced intravascular volume,11,13,21 and the combination of vasospasm and hypovolemia has disastrous effects, maintenance of a normal or slightly increased intravascular volume does help to prevent any insidious drop in systemic arterial blood pressure and ischemic symptoms. However, it can be concluded from the present study, at least, that elderly patients, who would

### TABLE 3
Intracranial complications observed in 40 patients with neurological deterioration

<table>
<thead>
<tr>
<th>Factor</th>
<th>Group A (≤54 yrs old)</th>
<th>Group B (50–64 yrs old)</th>
<th>Group C (≥65 yrs old)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>preexisting stenosis (50% reduction)</td>
<td>0</td>
<td>2 (1)*</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>subdural effusion or hematoma</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>contusional hematoma in the frontal lobe</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>total patients</td>
<td>11</td>
<td>13</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>total with specific complications†</td>
<td>1 (9%)</td>
<td>2 (15%)</td>
<td>6 (38%)</td>
<td>9 (23%)</td>
</tr>
</tbody>
</table>

* Complete occlusion of the middle cerebral artery.
† Some patients had two or more different complications.

### TABLE 4
Correlation of various factors and outcomes in 40 patients with neurological deterioration

<table>
<thead>
<tr>
<th>Factor</th>
<th>Outcome</th>
<th>Group A &amp; B (≤564 yrs of age)</th>
<th>Group C (≥65 yrs of age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Good</td>
<td>Poor</td>
<td>Good</td>
</tr>
<tr>
<td>systemic complication</td>
<td>2 (29%)</td>
<td>5 (29%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>intracranial complication</td>
<td>1 (14%)</td>
<td>2 (12%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>angiographic vasospasm (DR_{post}/DR_{pre})†</td>
<td>7 (0.72 ± 0.15)</td>
<td>15 (0.65 ± 0.11)</td>
<td>6 (0.83 ± 0.08)</td>
</tr>
<tr>
<td>total</td>
<td>7</td>
<td>17</td>
<td>9</td>
</tr>
</tbody>
</table>

* Significant difference (p < 0.05).
† DR_{post}/DR_{pre} = relative alteration in the diameter ratio (DR) for postoperative (Days 5–10) to that for preoperative angiograms.
be expected to have less severe arterial narrowing and less tolerance for volume expansion, should not be managed in exactly the same manner as younger patients. Rheological or hemodynamic manipulations to prevent or reverse the ischemic consequences of vasospasm are effective, but sometimes complicated and hazardous. Therefore, meticulous attention should be paid not only to neurological and radiographical findings, but also to physiological, biochemical, and hematological parameters.

References


Manuscript received October 3, 1994. Accepted in final form May 25, 1995.

Address reprint requests to: Yuhei Yoshimoto, M.D., Department of Neurosurgery, Dokkyo University School of Medicine, 880 Kitakobayashi, Mibu, Shimotsuga, Tochigi 321-02, Japan.