Prognostic Factors of Subarachnoid Hemorrhage Due to Ruptured Cerebral Aneurysm: A Retrospective Analysis of 231 Patients

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Abstract: The clinical outcome of aneurysmal subarachnoid hemorrhage (SAH) is influenced by many variables. The purpose of this study was to determine the prognostic factors of patients diagnosed as having cerebral aneurysmal SAH. Medical records of 231 patients (86 men and 145 women), diagnosed with aneurysmal SAH at some time during an 8-year period between January 1991 and December 1998, were investigated retrospectively. All patients were diagnosed with SAH by computed tomography (CT), and the presence of an aneurysm was diagnosed by conventional cerebral angiography. Sixteen of the 231 patients died prior to surgery. Surgical clipping or wrapping of the aneurysm was performed on 181 patients; 149 (82.3%) were 69 years of age or younger, and 32 (17.7%) were 70 years of age or older. In the total 231 patients, favorable outcome and mortality rate was 60.6% and 23.4%, respectively. In operated cases, favorable outcome and mortality rate was 70.2% and 15.5%, respectively. One hundred and sixty-six patients (91.7%) underwent early surgery (Day 0, 1, 2 or 3), and 15 (8.3%) underwent delayed surgery. During surgery, 86.5% patients classified as grade I-III showed favorable clinical outcomes, in contrast to 44.3% of patients classified as grade IV and V. A total of 42.6% of patients over 70 years old had favorable outcomes. In conclusion, risk factors of aneurysmal SAH identified by this retrospective analysis were: Age 70 years or older, a poor grade according to Hunt and Hess upon admission, rebleeding of the aneurysm and symptomatic vasospasm.

Key words: cerebral aneurysm, subarachnoid hemorrhage, prognostic factors

Introduction

The clinical outcome of aneurysmal subarachnoid hemorrhage (SAH) is known to be influenced by many variables including patient age, clinical grade, rebleeding prior to surgery, surgical and management techniques and vasospasm after SAH or surgery\textsuperscript{1-4). During the last decade several advances in the management of SAH, such as early surgery, transcranial Doppler, hypervolemic therapy, calcium channel blockers, invasive monitoring and aggressive intensive care, have provided opportunities to improve the overall clinical
However, despite the dramatic improvement observed in patients diagnosed with ruptured intracranial aneurysms, the overall unsatisfactory outcomes remain due to a variety of serious problems that occur in the acute stage after SAH, particularly in elderly patients and in those having a high grade. In an era of increasing limitations on medical resources, accurately predicted outcomes will become increasingly important to avoid deleterious factors during treatment.

In the present study we investigated the prognostic factors of four main clinical parameters: 1) patient age, 2) grade assigned upon admission according to the scale of Hunt and Hess, 3) rebleeding and 4) symptomatic vasospasm.

Methods

Patients

During an 8-year period between January 1991 and December 1998, 231 patients (86 men, 145 women; average age 46.0±12.6, age range 16 to 89 years old) were admitted to Showa University Hospital due to SAH. The inclusion criteria used for patients in the present study, based upon a retrospective evaluation of patient’s medical records, were: 1) confirmed diagnosis of SAH by computerized tomography (CT), 2) the presence of an aneurysm diagnosed by conventional cerebral angiography and 3) the assignment of a grade according to the scale of Hunt and Hess determining the clinical condition of patients, which assigned grade V to patients whose condition subsequently deteriorated, and who died on admission or prior to surgery. Of the total 231 patients, 181 underwent surgical intervention (clipping or wrapping). Fifty patients were treated by conservative methods because of poor grade upon admission, complications such as pneumonia and heart diseases, and rejection of operation. One hundred and sixty-six (91.7%) patients underwent early surgery (Day 0, 1, 2 or 3) and 15 (8.3%) patients underwent delayed surgery. Sixteen of the 231 patients died prior to surgery. Information was obtained from patient’s medical records, operative reports and clinical follow-up.

Evaluation of Clinical Outcome

Clinical outcome was assessed upon discharge or 3 months after the SAH using the Glasgow Outcome Scale (GOS): good recovery (GR), moderate disability (MD), severe disability (SD), vegetative state (VS) and death (D). GR and MD are determined as favorable outcomes, whereas SD and VS and D are determined as unfavorable outcomes.

Statistical Analysis

The chi-squared test, unpaired t-test and Mann-Whitney U test were used to determine statistical significance. Statistical significance was established at the p<0.05 level.

Results

Relationship between grade and clinical outcome

The relationship between the grade and overall outcome is shown in Table 1. One hundred and forty of the 231 patients experienced a GR or MD favorable outcome, 37 experienced a SD or VS unfavorable outcome and 54 died. Neurological status upon admission, determined by the Hunt and Hess grade, strongly correlated with the eventual outcome (p<0.05). Furthermore, mortality rates increased as neurological grade worsened:
Table 1. Summary of clinical outcomes determined by grade upon admission in all 231 patients

<table>
<thead>
<tr>
<th>Grade upon admission</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR</td>
<td>33</td>
<td>21</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>79</td>
</tr>
<tr>
<td>MD</td>
<td>13</td>
<td>16</td>
<td>11</td>
<td>14</td>
<td>7</td>
<td>61</td>
</tr>
<tr>
<td>SD</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>VS</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>11</td>
<td>29</td>
<td>54</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>49</td>
<td>31</td>
<td>35</td>
<td>63</td>
<td>231</td>
</tr>
</tbody>
</table>

GR = good recovery, MD = moderate disability, SD = severe disability, VS = vegetative state, D = death

Favorable outcomes (GR + MD) were observed in 74.2% of grade III patients, 57.1% of grade IV patients, and 22.2% of grade V patients. Twenty-eight (56%) of non-surgically treated patients were poor condition such as grade IV and V upon admission. The ultimate clinical outcome in non-surgically treated patients, regardless of age, was extremely poor; 28 (56%) patients died. A significant difference was also found between grade and surgical outcome (P < 0.05) (Table 2).

Table 2. Summary of clinical outcomes determined by the grade during surgery in all 181 surgical patients

<table>
<thead>
<tr>
<th>Grade at surgery</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR</td>
<td>32</td>
<td>18</td>
<td>10</td>
<td>6</td>
<td>6</td>
<td>72</td>
</tr>
<tr>
<td>MD</td>
<td>13</td>
<td>16</td>
<td>7</td>
<td>14</td>
<td>5</td>
<td>55</td>
</tr>
<tr>
<td>SD</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td>VS</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>15</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>42</td>
<td>22</td>
<td>29</td>
<td>41</td>
<td>181</td>
</tr>
</tbody>
</table>

GR = good recovery, MD = moderate disability, SD = severe disability, VS = vegetative state, D = death

grade III admissions 16.1%, grade IV admissions 31.4% and grade V admissions 46.0%. Favorable outcomes (GR + MD) were observed in 74.2% of grade III patients, 57.1% of grade IV patients, and 22.2% of grade V patients. Twenty-eight (56%) of non-surgically treated patients were poor condition such as grade IV and V upon admission. The ultimate clinical outcome in non-surgically treated patients, regardless of age, was extremely poor; 28 (56%) patients died. A significant difference was also found between grade and surgical outcome (P < 0.05) (Table 2).

Relationship between age and clinical outcome

The relationship between age and overall outcome is shown in Table 3. Outcomes assessed using the GOS upon discharge correlated with age (p < 0.05). Young patients tended to have better outcomes and thus lower mortality rates. One hundred and seventeen of 177 patients (66.1%) who were under 70 years of age were classified as having a GR or MD outcome. However, in patients who were 70 years old or older, 23 of 54 patients (42.6%) experienced a GR or MD outcome. The mortality rate of patients under 70 years
of age and 70 years of age or older was 20.3% and 33.3%, respectively.

Rebleeding and clinical outcome

During hospitalization, 44 of the 231 patients (19.1%) suffered rebleeding, as confirmed by a CT scan. Patients who rebled had high mortality rates (63.6%) and 25% were determined to have a poor neurological prognosis. Of the 44 patients who experienced rebleeding, 16 died prior to surgery and 12 died post-operatively (Fig. 1). The final outcome differed significantly between patients who experienced rebleeding and those who did not (p<0.05).
Vasospasm and clinical outcome

A total of 50 patients experienced vasospasm (21.6%), as confirmed by cerebral angiography, CT scan or clinical observation. The mortality rate was 38% (n = 19, Fig. 2). The majority of cases of vasospasm were detected between postoperative days 3 and day 8. Hypertensive or hypervolemic therapy was implemented immediately upon detection of any clinical deterioration. The outcome differed significantly between patients experiencing vasospasm and those who did not (p < 0.001).

Discussion

The present retrospective report included all patients diagnosed with SAH due to a ruptured aneurysm who were admitted to our hospital at some point during an 8-year period. A standardized management policy, including early surgical intervention, and aggressive vasospasm management and intensive care treatment was provided to all patients.

Several authors have attempted to predict the final clinical outcome after SAH from baseline factors present upon admission\(^8\)\(^,\)\(^9\). These attempts have resulted in the identification of multiple prognostic factors including the clinical condition upon admission using the Hunt and Hess scale, localization of the ruptured aneurysm, pre-existing hypertension, hyperglycemia, clot thickness determined by computed tomography and age. Furthermore, Taylor et al\(^10\) reported that a poor prognosis after SAH due to an aneurysm is associated with multiple factors including poor neurological grade upon admission, proximity to bleeding (time interval between SAH and the start of treatment), increasing age, hypertension, occurrence of rebleeding, poor medical condition and preoperative herniations.

In a retrospective study, Saveland et al\(^11\) reported that 81% of the 145 patients diagnosed as having supratentorial aneurysms, pre-operatively assigned Hunt and Hess grades I to III and treated within 72 hours made a good recovery. However, 5.5% of patients had an unfavorable outcome because of delayed ischaemia. Miyaoka et al\(^12\) reported that the
relationship between the timing of surgery and surgical outcome in cases of a ruptured aneurysm correlates with the Hunt and Hess grade assigned to patients. Grade V patients experienced considerably lower mortality rates when surgical management was delayed.

An increasing number of recent studies have investigated the age factor. A favorable clinical outcome appears to be inversely related to patient age. Several have examined the link between clinical outcome and the prognostic factors of aneurysmal SAH\(^1,2,9,13\). In the study of Lanzino et al\(^1\) using GOS 3 months post-SA\(H\) reported a poor final clinical outcome as age increased \((p<0.001)\). The percentage of patients who were classified as grade I upon admission progressively decreased from 66% in patients of 40 years of age or younger to 39% in the oldest age group \((\geq 70\) years). Age has an independent negative influence on the clinical outcome after SAH. Lanzino et al\(^1\) proposed that this phenomenon may be due to the vulnerability of the aged brain to SAH. The aging brain has a less than optimum response to initial bleeding and is more limited in its ability to repair lost function/structure after SAH than in young patients. Inagawa\(^13\) studied the management outcomes in elderly patients following SAH, approximately 80% undergoing surgery by day 3. No real age-related difference was found in patients aged 69 years or less and classified as pre-operative grades I - III. However, patients aged 70 to 79 years of age showed a significantly worse outcome than patients aged 69 years or less. Hernesniemi et al\(^14\) also reported a strong correlation between age and outcome. Mortality rates and numbers of severely disabled patients are increasing steadily over time.

An ischaemic deficit due to vasospasm is also a critical prognostic factor in patients presenting with SAH. Numerous studies have suggested that surgery performed after aneurysmal rupture results in a high incidence of symptomatic vasospasm and poor clinical outcome\(^11,15,16\). This increase is attributed to an aggravation of preoperative vasospasm. Possible explanations for cases of worsening vasospasm include operative manipulation of cerebral blood vessels, compromise of cerebral perfusion by both interaction with and compression of the brain, and intraoperative cardiovascular fluctuations. Shimoda et al\(^16\) reported a 35% unfavorable outcome rate in cases of delayed ischaemic deficit following early surgical intervention for the aneurysm. Shimoda's result is similar to the 38% unfavorable outcome rate in the present study. Awad et al\(^17\) reported 16.7% \((7/42)\) mortality due to delayed ischaemia secondary to vasospasm. The mortality rate reported in the present study was slightly higher at 38%, partly due to the inclusion of patients who were found to have a poor grade prior to surgery.

The use of transluminal angioplasty or intra-arterial infusion of papaverine in patients who developed a delayed ischaemic deficit following SAH has been previously reported\(^18\). However, because the previously damaged brain may easily sustain an irreversible ischaemic lesion due to the decrease in cerebral blood flow resulting from vasospasm, the effectiveness of these techniques remains unclear. In the present retrospective study, all patients presenting with vasospasm underwent effective hypervolemic therapy.

As previously mentioned, the clinical outcome after aneurysmal SAH is associated with multiple factors, however, the results of the present study indicate that a poor prognosis is clearly associated with patients of 70 years of age or older, poor grade upon admission and symptomatic vasospasm. Furthermore, outcomes of surgically treated patients worsen due to preoperative bleeding of the aneurysm and severe swelling of the brain during surgery. Patients determined to have more than 2 factors showed worse outcomes than those having
only one factor. However, the authors advise caution in the interpretation of the prognostic significance of initial clinical features. Decision making must rely upon a multiparametric approach, giving consideration to the temporal changes in clinical signs. The results of the present study suggest that a combination of prognostic factors can predict clinical outcomes after SAH more accurately than any single factor. Recently, we have implemented the new approaches such as endovascular surgery for elderly patients and hypothermia for severe SAH patients. Further investigation of these new methods will be important to improve overall outcome of aneurysmal SAH.

References


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