Subarachnoid hemorrhage of unknown etiology: early prognostic factors for long-term functional capacity

Walter Oder, M.D., Harald Kollegger, M.D., Karl Zeiler, M.D., Peter Dal-Bianco, M.D., Peter Wesely, M.D., and Lüder Deecke, M.D.

Neurological Clinic, University of Vienna, Vienna, Austria

Forty-one patients suffering subarachnoid hemorrhage (SAH) of unknown etiology were re-investigated at an average of 91 months after the bleed to determine functional capacity. Nineteen patients were performing at their previous level of work, five were employed part-time, and four could not work due to the SAH. Five patients showed a moderate disability in activities of daily living but were not dependent on help, one patient was severely disabled, and two had died. There was one rebleed. Early prognosis of an unfavorable outcome was possible on the basis of three clinical variables on admission: a history of hypertension, a Hunt and Hess grade of greater than II, and the presence of focal neurological deficits. In addition, the presence of an organic mental syndrome at discharge was identified as a predictive factor for reduced functional capacity later on. Other clinical variables in the acute stage, including sex, age, history of headache, interval between SAH and admission, impaired consciousness, and cognitive deficits, were not related to a limited functional level. Residual neurological deficits and the Glasgow Outcome Scale score on discharge were also not predictive of restrictions in global functions evaluated by means of the Karnofsky Performance Scale status at follow-up review.

KEY WORDS • subarachnoid hemorrhage • prognosis • functional capacity

In patients with subarachnoid hemorrhage (SAH) of unknown etiology, angiographic visualization of the carotid and vertebrobasilar system fails to reveal any structural abnormality. Medical causes for the bleeding cannot be found. Depending on the frequency of repeated panangiography, the reported incidence of proven SAH of unknown etiology ranges from 4% to 27%. Ruptured microaneurysms, thrombosed aneurysms, cryptic arteriovenous malformations (AVM's), or leakage from small ventriculoatrial and thalamoperforating vessels have been suspected to be the sources of this type of subarachnoid bleeding. 1,11

Subarachnoid hemorrhage of unknown etiology has received less attention than aneurysmal SAH; however, the early prognosis is known to be much better than in aneurysmal or angiomatous SAH, although the long-term outcome is considered less favorable than expected. 10,17 There are still questions concerning the management and prognosis of these patients, including the rate of late complications, such as rebleeding, hydrocephalus, or epilepsy. There is little information about the late morbidity and the functional level of survivors. Since specific treatment of SAH of unknown etiology is impossible, prognostic factors deserve more attention. It would be of great value to be able to identify as early as possible patients with a favorable prognosis so that they can be assured of the benign nature of their disease and return to a normal life at an early stage. On the other hand, criteria for early identification of those with a less favorable long-term prognosis would help to develop individual strategies for further social management and support. The aim of this retrospective study of patients with proven SAH of unknown etiology was to evaluate: 1) the initial clinical features, the natural course, and the long-term prognosis of this disorder, including mortality rate and risk of rebleeding; 2) the influence of SAH of unknown etiology on later quality of life as regards subjective complaints, functional capacity, working status, and effect on family and social life; and 3) clinical variables available in the acute stage and widely used grading scales concerning their predictive power for long-term functional disability.

Clinical Material and Methods

Study Population

The study is based on 72 patients suffering from spontaneous SAH who were consecutively admitted to the Neurological Clinic, University of Vienna, between 1976 and 1985. The population did not include patients who were very severely impaired at the onset of the
bleeding; those patients were admitted directly to the Department of Neurosurgery. The diagnosis was confirmed by computerized tomography, four-vessel angiography, and cerebrospinal fluid examination. If angiography failed to reveal the source of the bleeding, a second four-vessel study was performed in all cases after an interval of 4 to 6 weeks. All patients underwent medical examination. In no case was SAH caused by recent head injury, blood dyscrasias, intracranial neoplasms, arteritis, meningoencephalitis, or anticoagulant drugs. None of the patients had a history of neurosurgical intervention, tuberculosis, or any other systemic infectious disease. A bleeding source could be identified in 31 (44%) of the 72 patients, and these patients were excluded from the present study.

Forty-one patients (24 men and 17 women) suffered from SAH of unknown etiology (that is, they had normal arteriograms in both four-vessel studies); therefore, the incidence of SAH of unknown etiology was 56% in this study. The cause of this remarkably high incidence is a selection bias due to the above-cited referral policy to this institution. The mean age at admission (± standard deviation) of the patients with SAH of unknown etiology was 47.3 ± 13.6 years (range 16 to 72 years). The clinical grade on admission was based on the Hunt and Hess system. Routine management included absolute bed rest, administration of analgesics, sedation, and control of blood pressure. Antihypertensive treatment was given when necessary. No antifibrinolytic agents, steroids, or calcium channel blockers were administered.

The follow-up examination was conducted at an average of 90.9 ± 36.0 months (range 25 to 143 months) after the onset of SAH in 39 patients. Two patients had died during the observation period.

### TABLE 1

Clinical parameters in the acute stage*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Factor</th>
<th>No. of Cases</th>
<th>Karnofsky Performance Scale Score</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>no</td>
<td>25</td>
<td>15 6 4</td>
<td>7.530 &lt; 0.05</td>
</tr>
<tr>
<td>(history)</td>
<td>yes</td>
<td>16</td>
<td>3 10 3</td>
<td>NS</td>
</tr>
<tr>
<td>Interval SAH</td>
<td>&lt; 72 hrs</td>
<td>11</td>
<td>3 5 3</td>
<td>3.350 NS</td>
</tr>
<tr>
<td>Admission</td>
<td>4-14 days</td>
<td>17</td>
<td>7 7 3</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>&gt; 14 days</td>
<td>13</td>
<td>8 4 1</td>
<td>NS</td>
</tr>
<tr>
<td>Impaired cons-</td>
<td>no</td>
<td>17</td>
<td>8 7 2</td>
<td>0.580 NS</td>
</tr>
<tr>
<td>Sciousness</td>
<td>yes</td>
<td>24</td>
<td>10 9 5</td>
<td>NS</td>
</tr>
<tr>
<td>Organic mental</td>
<td>no</td>
<td>12</td>
<td>8 4</td>
<td>5.040 NS</td>
</tr>
<tr>
<td>Syndrome</td>
<td>yes</td>
<td>29</td>
<td>10 12 7</td>
<td>NS</td>
</tr>
<tr>
<td>Neurological</td>
<td>no</td>
<td>18</td>
<td>9 9</td>
<td>6.740 &lt; 0.05</td>
</tr>
<tr>
<td>Signs</td>
<td>yes</td>
<td>23</td>
<td>9 7</td>
<td>NS</td>
</tr>
<tr>
<td>Hunt &amp; Hess</td>
<td>I &amp; II</td>
<td>28</td>
<td>14 12 2</td>
<td>6.181 &lt; 0.05</td>
</tr>
<tr>
<td>Grade</td>
<td>III &amp; IV</td>
<td>13</td>
<td>4 4 5</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Clinical parameters in the acute stage and clinical condition at the end of the observation period (41 survivors of subarachnoid hemorrhage (SAH) of unknown etiology). NS = not significant.

† Including two patients who died during the observation period.

### TABLE 2

Clinical parameters at the time of discharge*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Factor</th>
<th>No. of Cases</th>
<th>Karnofsky Performance Scale Score</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic mental</td>
<td>no</td>
<td>18</td>
<td>11 7</td>
<td>7.643 &lt; 0.05</td>
</tr>
<tr>
<td>Syndrome</td>
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<td>23</td>
<td>7 9 7</td>
<td>NS</td>
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<tr>
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<td>30</td>
<td>13 14 3</td>
<td>4.958 NS</td>
</tr>
<tr>
<td>Signs</td>
<td>yes</td>
<td>11</td>
<td>5 2 4</td>
<td>NS</td>
</tr>
<tr>
<td>Glasgow Outcome</td>
<td>V</td>
<td>29</td>
<td>14 12 3</td>
<td>3.200 NS</td>
</tr>
<tr>
<td>Score</td>
<td>&lt; V</td>
<td>12</td>
<td>4 4</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Clinical parameters in the acute stage and clinical condition at the end of the observation period (41 survivors of subarachnoid hemorrhage of unknown etiology). NS = not significant.

† Including two patients who died during the observation period.

### Prognostic Factors

The prognostic factors were arranged in three groups, as follows. The first group included demographic variables at the time of admission. These were gender, age at admission, headache prior to the SAH, and hypertension (Table 1). The second group comprised clinical variables at the time of admission: interval between SAH and admission and clinical criteria. Regarding the level of consciousness, focal neurological signs, and organic mental syndrome on admission, the patients were classified into two subgroups: patients with and without impairment. The presence of an organic mental syndrome (that is, memory deficits, reduced reasoning ability, mental slowing, and emotional changes) was assessed using the criteria proposed by Berner, ranging from 0 (none) to 3 (severe). In addition, patients were categorized according to the clinical grading of Hunt and Hess (Table 1). The third group included clinical variables at the time of discharge, such as presence or absence of residual focal neurological signs and of an organic mental syndrome and overall outcome assessed according to the Glasgow Outcome Scale (Table 2).

### Outcome Measures

On follow-up evaluation, a detailed neurological and psychiatric examination was carried out. A standardized clinical interview was performed to determine the patient's mental and emotional abilities influencing functional reintegration. Frequency of persisting headache was graded semiquantitatively (never, rare, or often). The neurological condition as well as cognitive functions were again categorized using the criteria mentioned above. Patients were grouped according to the Glasgow Outcome Scale. The Karnofsky Performance Scale was used to determine the level of global functions. Finally, note was taken of overall family and social coping capabilities and employment status at the end of the observation period by means of a semistructured interview. Statistical analysis was performed using the chi-square test.
Results

Clinical Condition on Admission

Thirty-one patients had a history of headache prior to the SAH and three reported previous seizures. Hypertension had been found before the SAH in 16 patients. Five patients reported regular heavy drinking. Heavy physical strain was associated with the bleeding in 16 patients, whereas SAH occurred during sleep in four. Four patients suffered cerebral seizures in direct association with the bleeding episode. In the acute stage, 40 of the 41 patients complained of headache. Thirty-seven patients had symptoms of nausea, dizziness, and vomiting. The interval between the onset of SAH and admission was extremely variable (Table 1).

On admission, impaired consciousness was recorded in 24 patients. Signs of an organic mental syndrome were found in 29 patients: mild in 19, moderate in five, and severe in five. Twenty-three patients presented with focal neurological deficits (motor signs in 15, cranial nerve signs in 13, speech disorders in eight, and visual field defects in three); these deficits were usually mild. The Hunt and Hess evaluation on admission showed six patients in Grade I, 22 in Grade II, 10 in Grade III, and three in Grade IV (Table 1).

Clinical Condition on Discharge

At the time of discharge, 11 patients demonstrated focal neurological deficits and 23 had an organic mental syndrome (Table 2). According to the Glasgow Outcome Scale, 29 patients were in Grade V, 10 in Grade IV, and two in Grade III. All 41 patients returned to their homes.

Long-Term Outcome

During the observation period, only one patient rebled, 20 months after the first SAH. A third angiographic study did not reveal a source of the bleeding. This 57-year-old man died due to a myocardial infarction 10 years after the first SAH. There was no fatal rebleed in our series. Another patient died 2 years after the SAH due to an anaphylactic shock.

At follow-up review, 29 of the 39 survivors of SAH of unknown cause complained of persisting headache. Five patients had seizures and were receiving antiepileptic treatment. None of these patients developed communicating hydrocephalus. Thirteen patients showed focal neurological deficits, mild in most cases. An organic mental syndrome was present in 22 patients (mild in 19, moderate in two, and severe in only one patient). Based on the Glasgow Outcome Scale, 33 patients were categorized at follow-up review in Grade V, five in Grade IV, and one in Grade III.

Seven patients reported persistent family tensions after the bleed and 11 patients experienced handicaps in social functioning. Among the 28 survivors of SAH of unknown cause who had not retired due to age, 19 reported employment at their previous level, five patients were working part-time, and four were incapable of work.

Factors on Admission Related to Long-Term Outcome

According to our results, a history of hypertension, focal neurological deficits, and a Hunt and Hess grade of greater than II on admission are reliable prognostic indicators of late functional disability. Other clinical variables available on admission, including gender, age, headache prior to SAH, or interval between SAH and admission, had no significant influence on the long-term functional capacity. Neither an impaired level of consciousness nor the presence of an organic mental syndrome affected the prognosis (Table 1).

Factors on Discharge Related to Long-Term Outcome

The presence or absence of focal neurological deficits and the Glasgow Outcome Scale on discharge were analyzed with respect to their prognostic relevance for the patients' later functional outcome. Neither of these two parameters was related to the amount of disability at follow-up review. However, the presence of an organic mental syndrome on discharge was an additional prognostic factor for reduced functional capacity at follow-up evaluation (Table 2).

Discussion

The study presents a retrospective analysis of 41 patients suffering from SAH of unknown etiology. It documents the natural course of the disease and reveals prognostic factors as related to long-term outcome.

Clinical Condition in the Acute Stage

Our own series as well as previous reports demonstrated that most of the patients with SAH of unknown origin are referred while in a relatively good condition. 4,6,9,11,17,24,26 Focal neurological signs on admission were reported in 5% to 33% of cases. 2,7,13,15,28 In our series, detailed neurological examination revealed focal neurological deficits in 56% of the patients. Mental deficits in survivors of SAH of unknown etiology have received scant attention in previous reports. However, about two-thirds of the patients in our series had mental deficits during the acute stage.

Long-Term Course

Generally, the course of the disease is benign; rebleeding and mortality rates are very low. In our own series, the incidence of rebleeding was only 2.5% (one of 41 patients) during a mean observation period of 90.9 months. In previous reports with follow-up periods ranging from 18 months to 22 years, the late rebleeding frequency was 3% to 10.4%. 3,8,0,13,15,22,24 Fatal rebleeds were extremely rare. 28 During the observation period, only two (5%) of our 41 patients died. The mortality rate ranged between 0% and 21.5% in earlier stud-
The rebleeding and mortality rates were found to be markedly lower as compared to the data in aneurysmal SAH. 12,22,27

**Follow-Up Results**

In previous reports mental deficits were present at follow-up review in 29% to 33% of cases, and residual lateralizing signs were seen in 15% to 23%. In our series, however, there was a marked late morbidity as regards headache and mental deficits. We found a high incidence of recurrent headache. Twenty-nine (74%) of the 39 patients surviving at follow-up suffered this complaint as compared to a range from 21% to 50% in previous reports. Similarly, Juul, et al., reported a total morbidity rate of 56%.

**Functional Outcome**

As regards working status, 86% of our patients were employed full-time or at least part-time. In previous reports, 37% to 94% returned to full activity. In contrast, only 44% of 112 “good-risk” patients with aneurysmal SAH (Hunt and Hess Grade I or II on arrival) were reported to have returned to their previous jobs or a comparable position. The results of the present study are in accordance with previous findings of a reduced daily functional capacity in 14% to 31% of patients with SAH of unknown origin. A dependence on help from other persons was noted in 0% to 9% of the patients. Thus, the long-term functional outcome after SAH of unknown etiology has to be considered relatively favorable.

**Early Prognostic Factors**

The role of arterial hypertension in causation and prognosis of SAH is well known. In previous studies, more than one-third of patients with SAH of unknown etiology had a history of hypertension. These figures correspond with the prevalence of 38% hypertensive patients in our series. Brismar and Sundbärg found decreased wakefulness on admission related to a slightly poorer prognosis. McKenna, et al., reported a good prognosis in patients without neurological deficits on discharge in a population of patients with SAH of mixed etiology.

Some limitations of the current study must be considered. First, it should be emphasized that this investigation deals with patients admitted consecutively to the Neurological Clinic at the University of Vienna and, thus, is not defined epidemiologically. Second, the incidence of SAH of unknown origin reported in other neurosurgical series ranges between 4% and 27% and is 56% in our series. This marked difference reflects a referral bias for our hospital. Therefore, our population represents a selection of patients with predominantly minor SAH showing an extremely high incidence of SAH of unknown etiology.

In conclusion, patients suffering spontaneous SAH without a demonstrable bleeding source have an excellent prognosis in regard to survival and only a minimal risk of a rebleed. Furthermore, the results of our study indicate that it is possible to define at an early stage an “extremely low-risk” group of patients within the population suffering SAH of unknown etiology: patients without history of hypertension, without focal neurological deficits, and with Hunt and Hess Grade I or II on admission. If an organic mental syndrome is not present at the time of discharge, these patients can be informed about the benign nature of their disease. We recommend that after repeated panangiography they should be encouraged to return to a normal lifestyle without any restrictions.

**References**


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