Subarachnoid hemorrhage of unknown origin: prognosis and prognostic factors

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The cases of 127 consecutive patients with subarachnoid hemorrhage (SAH), in whom cerebral pan-angiography revealed no cause for the bleeding nor any sign of an intraparenchymatous hemorrhage, were reviewed in a study of the long-term prognosis and the possible prognostic factors in this condition. Data for all 127 patients in the study were obtained, with an average follow-up period of 5.4 years. After the 1st week post-SA H, only three rebleeds had occurred. In all, 80% of the patients had returned to full activity, 91% to at least part-time work; if the patients with hypertension were excluded, these figures rose to 86% and 95%, respectively. Decreased wakefulness on admission related to a slightly poorer prognosis, whereas age and red blood cell count in the cerebrospinal fluid had no prognostic significance.

Of those patients who, at the end of the 2nd week following the SAH, were fully awake and had not developed any symptoms of delayed cerebral ischemia (87% of all patients admitted), 88% returned to full activity, 97% to at least part-time work. The survival rate for this group, as well as causes of death, seem to be within the range for normal individuals. It should thus be possible to inform these patients (at least the normotensive ones) of the benignity of their condition, directly after normal angiography. Even among the patients who were able to return to full activity, symptoms attributable to the SAH were common: 22% experienced problems such as frequent headaches, vertigo, irritability, and increased fatigability.

**KEY WORDS** • subarachnoid hemorrhage • unknown etiology • prognosis • prognostic factor

In a significant percentage of patients with subarachnoid hemorrhage (SAH), no cause of the bleeding is found in spite of a complete angiographic evaluation. Computerized tomography (CT) in such patients sometimes demonstrates intracerebral hemorrhages too small to be observed on angiography. In spite of CT, however, in some 20% to 30% of patients with SAH no origin is found. It has long been known that the prognosis for these patients is more favorable than for those with a demonstrable bleeding source. Information concerning the long-term prognosis for a consecutive series of patients in more detailed terms than “mortality” or “risk of rebleeding” is, however, still scanty.

Subarachnoid hemorrhage is a frightening experience for patients. If no bleeding source has been identified and treated, the risk of rebleeding may for a long period of time be experienced as a sword of Damocles, especially if certain restrictions (avoiding strain or sexual activity) have been put on the patient. It is a reasonable assumption that such stress may sometimes explain different symptoms of a possibly psychosomatic nature (frequent headaches, vertigo, increased fatigability, irritability) that are often experienced following an SAH.

It would be of great value to be able to identify as early as possible patients prone to develop complications, so that the others can be reassured of the benignity of their disease and returned to a normal life at an early stage. This would also lead to considerable economic savings. The present study was designed to evaluate the long-term prognosis in a consecutive series of patients with SAH of unknown etiology and to try to establish criteria for early identification of those with a less favorable prognosis.

**Clinical Material and Methods**

The Department of Neurosurgery of the University Hospital in Lund is the sole neurosurgical facility for a region with 1.46 million inhabitants. Patients with a clinically suspected or verified SAH who are possible candidates for surgery are referred to Lund for further evaluation. An angiographic work-up is occasionally performed at the local hospital, but during the period covered by this study, an increasingly large majority of
patients have been evaluated at the Section for Neuroradiology in Lund.

The records for the years 1968 to 1978 were scrutinized to retrieve all patients with an SAH, who were subjected to a pan-angiographic evaluation (bilateral carotid angiography and unilateral or bilateral vertebral angiography) without any cause for the bleeding or any mass being identified. The clinical charts for these patients were reviewed and patients in whom the verification of an SAH by cerebrospinal fluid (CSF) analysis was doubtful or the angiography technically defective were excluded. The 127 patients who remained constituted the study group. For the eight patients who had died after hospital discharge, the cause of death was evaluated from the death certificate. The survivors were contacted either in person or through a questionnaire (formulated with special consideration to the avoidance of leading questions). The patient was asked whether he was working full-time or not, and if he had any problems or symptoms and signs. The age and sex distribution of the patients appears in Table 1, and the year of SAH in Table 2.

In order to evaluate possible prognostic factors, the clinical course was correlated to the age of the patient; possible arterial hypertension; the red blood cell (RBC) count in the CSF during the immediate posthemorrhagic period; and the neurological findings on admission. The RBC count in CSF during the 1st or 2nd day after the SAH was available in only 90 patients.

### Summary of Cases

**Findings on Admission**

In direct association with the bleeding episode, eight patients lost consciousness for periods of time varying from a few minutes to several days. Another three patients exhibited solitary epileptic attacks. Depending on the initial clinical features, as well as on geographic factors, some patients were referred directly to the neurosurgical clinic in Lund, while most of them were first admitted to their local hospital. The day of admittance to Lund and the state of wakefulness on admission appear in Table 3. Level of consciousness was graded according to Lundberg:

- **Grade 1** = wide awake
- **Grade 2** = somewhat drowsy or torpid but answers promptly
- **Grade 3** = drowsy, answers sluggishly
- **Grade 4** = reacts to speech but does not answer
- **Grade 5** = reacts only to pain
- **Grade 6** = no reaction to pain.

A combination of Grades 1 and 2 in this classification corresponds to Grades 1 and 2 in the classification of Hunt and Hess; Grades 3, 4, and 5 are similar in both systems.

Except for a short period directly associated with the SAH, only one patient had a lower level of consciousness prior to admission. That patient was in Grade 4 to 5 on Days 1 and 2 after SAH, then, on admission on...
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Day 4, in Grade 2; the patient is classified as Grade 5 in subsequent prognostic correlations. Focal neurological symptoms and signs were noted on admission in 10 patients (six admitted on Day 1, three on Day 2, and one on Day 3). Five presented with hemiparesis, two with a leg paresis, one with a Babinski sign, one with a facial palsy, and one with a sixth and seventh nerve paralysis.

The number of RBC's in the first recorded CSF samples is shown in Table 4. In several cases the RBC count was analyzed at the local hospital before the patients were referred; in other cases CSF was not sampled for quantitative analysis until after the patient's arrival in Lund.

Hospital Course

For the majority of patients the hospital course was uneventful. Ninety-two patients were fully conscious and without focal symptoms and signs on admission, and remained so during the entire period at the hospital. Another 16 patients, although not fully conscious on arrival (nine in Grade 2, two in Grade 3, one in Grade 4, and four in Grade 5), soon became fully alert. Three patients decreased in consciousness during the first few days of hospitalization; two soon became fully conscious, and one deteriorated further. Three patients in all died during the initial period of hospitalization. Two patients, previously fully awake, died on the 5th day after the original SAH with the clinical picture of a progressive ischemic cerebral lesion and increased intracranial pressure.

In 12 additional patients neurological function was impaired during the 2nd week after SAH, indicating the presence of arterial spasm, which was angiographically verified in only one patient. Ten patients had a progressive decrease in consciousness; six of them also exhibited focal neurological signs. In two other patients the onset of focal neurological signs was the only finding. Of these 12 patients, seven were free of symptoms and signs at discharge (mean 22 days, range 11 to 32 days, after SAH), three were fully conscious but had remaining focal signs at discharge (on Days 30, 33, and 71), and two patients were still unconscious at transfer to another institution on Days 22 and 38. Seven (54%) of the 13 patients who developed delayed ischemic symptoms were hypertensive as compared to 24 (19%) of the total 127 patients. No patient developed delayed ischemic deficits later than the 2nd week post-SAH.

Course After Hospital Discharge

The average follow-up time for the remaining 124 patients was 5.4 years (1 to 12 years). Eight patients died after the immediate post-SAH period (Table 5). One died 2 years after the SAH without having regained consciousness, one died from “intracranial hemorrhage” 7 years after the initial SAH, and six died from an intercurrent disease. Two patients experienced a second SAH 2 and 5 years, respectively, after the first. In both of these patients, repeat angiography demonstrated a saccular arterial aneurysm that was successfully operated on. A third patient bled after 1 month: a second cerebral pan-angiographic study was normal, and recovery was complete.

In five of the eight patients who died after hospital discharge, information was too scanty to permit a valid classification of the quality of life following the SAH. In none of these patients was information obtained that gave any indication of persistent symptoms and signs; all were fully conscious and without any symptoms and signs on discharge and all had had an uneventful hospital course. One of these patients was somewhat drowsy (Grade 2) on admission, but was soon alert; the other four were wide awake even on admission.

The remaining 119 patients who survived the immediate posthemorrhagic period were classified according to final outcome as follows:

### TABLE 4

| Red blood cell (RBC) count in the first recorded cerebrospinal fluid (CSF) samples |
|-----------------------------|-----|-----|-----|-----|-----|-----|-----|
| RBC Count (x10^6/mm³) | 1   | 2   | 3   | 4   | 5   | 6   | 7   |
| ≤ 10,000         | 4   | 4   | 1   | 1   | 1   | 1   | 1   |
| 10,000-50,000   | 11  | 2   | 5   | 3   | 1   | 1   | 0   |
| 50,001-100,000 | 4   | 6   | 1   | 0   | 0   | 0   | 0   |
| 100,001-500,000| 19  | 8   | 0   | 1   | 0   | 1   | 0   |
| > 500,000       | 12  | 3   | 2   | 0   | 0   | 1   | 0   |
| "bloody," "red" CSF | 14  | 5   | 2   | 2   | 0   | 2   | 0   |
| total           | 64  | 28  | 11  | 7   | 2   | 8   | 2   |

Follow-Up Period | Cause of Death | Outcome Group
---|---|---
1 yr | suicide (strangulation) | —
1 yr 8 mos | stomach carcinoma & metastasis | —
2 yrs 3 mos | institutionalized, unconscious since SAH | IV
3 yrs | pulmonary carcinoma | II
3 yrs | stomach carcinoma | —
3 yrs 10 mos | myocardial infarct & diabetes | —
6 yrs | institutionalized, oriented, hemiparetic, renal failure | IV
7 yrs | intracerebral hemorrhage | —

* Includes only patients surviving the immediate period after subarachnoid hemorrhage (SAH).
† For outcome classification see text. — = not classified due to lack of data.
Prognosis related to age and blood pressure

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Outcome Group*</th>
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<tr>
<td></td>
<td>Total Factors</td>
<td>Ia No. Percent</td>
<td>I No. Percent</td>
<td>II No. Percent</td>
<td>III No. Percent</td>
<td>IV No. Percent</td>
<td>Dead Percent</td>
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<tr>
<td>&lt; 60 yrs</td>
<td>97</td>
<td>58 60</td>
<td>76 78</td>
<td>13 13</td>
<td>3 3</td>
<td>2 2</td>
<td>3 3</td>
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<tr>
<td>≥ 60 yrs</td>
<td>25</td>
<td>18 72</td>
<td>22 88</td>
<td>1 4</td>
<td>4 1</td>
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<td>blood pressure</td>
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<tr>
<td>normotensive</td>
<td>100</td>
<td>69 69</td>
<td>86 86</td>
<td>9 9</td>
<td>9 2</td>
<td>2 2</td>
<td>1 1</td>
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<tr>
<td>hypertensive</td>
<td>22</td>
<td>7 32</td>
<td>12 55</td>
<td>5 5</td>
<td>2 2</td>
<td>1 5</td>
<td>2 9</td>
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<tr>
<td>total cases</td>
<td>122</td>
<td>76 62</td>
<td>98 80</td>
<td>14 11</td>
<td>3 3</td>
<td>3 2</td>
<td>2 3</td>
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</table>

* For outcome classification see text.

The patient's age does not affect the prognosis, but arterial hypertension is an important prognostic factor (Table 6). Of the patients who were normotensive on admission, 86% returned to full activity, 95% to at least part-time work; for those with arterial hypertension the corresponding figures were 55% and 77%. It is thus possible to define a low-risk group at the time of admission merely by excluding those with hypertension. For further analysis, the series was therefore separated into two groups: normotensive patients and patients with arterial hypertension.

The severity of the SAH was estimated both from the state of consciousness on admission and from the RBC count in the CSF during the immediate post-SAH period. The RBC count did not affect the prognosis (Table 7); however, there is a correlation between the state of consciousness on arrival and the final outcome (Table 8). Of the 84 normotensive patients who were fully awake (Grade 1) and without focal neurological signs on admission, 74 (88%) went back to their previous activities and 81 (96%) were able to do at least part-time work.

Of the 106 patients (hypertensive patients included) who passed the 2nd week post-SAH without developing delayed ischemic symptoms, and who were then fully awake, 103 (97%) returned at least to part-time work, and 93 (88%) to full activity.

Discussion

The diagnosis of "SAH of unknown cause" may be defined in different ways. Locksley, et al., chose to include SAH secondary to intracerebral hemorrhage in this category "because of the clinical difficulty of distinguishing hypertensive-arteriosclerotic parenchymal hemorrhages from those due to aneurysm, AVM [arteriovenous malformation], and others." Refinement of the angiographic technique and, above all, CT have now changed these premises. Intraparenchymatous hemorrhages can now be easily identified, and it is well known that they carry a worse prognosis than an SAH of unknown cause. In order to obtain a homogeneous prognostic group, we therefore chose to try to eliminate cases with an intraparenchymatous hemorrhage from this study.

In order to achieve as long an observation time as possible, this study only includes cases examined before the CT era. We have thus been limited to angiographic criteria for the exclusion of parenchymatous hemorrhages. It is therefore possible that the SAH in a few cases in our series was caused by a minor primary parenchymatous brain hemorrhage. Personal experience of the routine use of CT as the primary examination in the evaluation of SAH, however, indicates a low incidence of intracerebral hemorrhages, too small to be detected by angiography, as the cause of an SAH.
Subarachnoid hemorrhage of unknown origin

<table>
<thead>
<tr>
<th>Neurological Findings</th>
<th>Ia</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>Dead</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percent</td>
<td>No.</td>
<td>Percent</td>
<td>No.</td>
<td>Percent</td>
<td></td>
</tr>
<tr>
<td>normotensive group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>wide awake (Grade 1), no focal signs</td>
<td>63</td>
<td>75</td>
<td>74</td>
<td>88</td>
<td>7</td>
<td>8</td>
<td>1</td>
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<tr>
<td>somewhat drowsy (Grade 2), no focal signs</td>
<td>2</td>
<td>25</td>
<td>7</td>
<td>88</td>
<td>0</td>
<td></td>
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<tr>
<td>confused, stuporous, or comatose (Grade 3 to 5), or focal signs</td>
<td>4</td>
<td>50</td>
<td>5</td>
<td>63</td>
<td>2</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>hypertensive group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>wide awake (Grade 1), no focal signs</td>
<td>5</td>
<td>38</td>
<td>8</td>
<td>62</td>
<td>4</td>
<td>31</td>
<td>0</td>
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<tr>
<td>somewhat drowsy (Grade 2), no focal signs</td>
<td>1</td>
<td>20</td>
<td>2</td>
<td>40</td>
<td>1</td>
<td>20</td>
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<td>confused, stuporous, or comatose (Grade 3 to 5), or focal signs</td>
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<td>17</td>
<td>2</td>
<td>33</td>
<td>0</td>
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</tbody>
</table>

* For grade of consciousness and outcome classification see text.

Furthermore, both the age distribution of the patients (Table 1) and the comparatively low frequency of arterial hypertension (19%) indicate that the number of such hemorrhages in the series was small.

A normal pan-angiographic evaluation with routine use of different oblique views to clearly demonstrate all bifurcations, as used in all patients in this series, almost excludes the possibility of a common berry aneurysm or an arteriovenous malformation. Neither a thrombotic lesion nor a microaneurysm can be excluded by angiography. Theoretically, spasm could cause nonfilling of an aneurysm; this, however, seems to be exceedingly rare if no spasm is observed at the angiographic evaluation (as was the case in our patients). Nevertheless, two patients in the present series eventually rebled because of aneurysms. This low figure, however, hardly justifies repeated angiographic investigations in cases of technically complete primary angiography.

There is a high frequency of rebleeding in series of patients with unoperated aneurysms. Walsh12 reported that 50% of his patients rebled during the first 2 months; Winn, et al.,13 estimated the yearly risk for rebleeding, after 6 months had passed, as 3.5%. The frequency of rebleeding in our 127 cases amounted to 4.7% (six patients) during an average observation period of 5.4 years. If the two fatal rebleeds in the immediate post-hemorrhagic period are excluded, the incidence was 3.1% (four cases), or less than 0.6% a year.

In the Cooperative Study7 the prognosis for a 1-year survival dropped sharply in patients aged 60 years. This is in contrast to our results (Table 6). The percentage of patients returning at least to part-time work or corresponding activities was the same for patients of 60 years of age and more as for those less than 60 years old. The fact that a higher percentage of the older group was classified as returning to full activity may be due to a different interpretation of the words “full activity” for those patients.

For the 119 patients who survived the 2nd week post-SAH, the prognosis was excellent: 94% (112 patients) returned at least to part-time work, 82% (98 patients) returned to full activity. These figures correspond well with those of Hayward4 (95% and 68%, respectively) and also with those of Locksley, et al.,7 for the subgroup that survived 1 year (93% at least able to provide self-care, 77% capable of full activity). In this context, however, it must be noted that, whereas our data were obtained for all 127 patients and the mean observation time was 5.4 years, the comparable figures for the Cooperative Study7 were 95% retrieval and 1-year observation time, and for the study of Hayward4 were 80% retrieval and 3.5 months to 2.5 years follow-up period.

Ability to return to previous activity (usually to full-time work) has in most previous reports1,4,7 been used as the criterion for complete recovery. It is, however, well known that complaints of frequent headaches, vertigo, fatigability, and irritability are common among patients who have had an SAH. In this series only 76 (78%) of the 98 patients who returned to full previous activity (Group I) felt fully healthy (Group Ia). No difference was found between patients under 60 years old (76%) and those 60 years of age and older (82%). Of the patients who were fully awake (Grade 1) on admission, 83% had no complaints on follow-up review as compared to only eight (50%) of 16 patients classified as Grade 2 to 5 on admission. Even a slight drowsiness (Grade 2) impaired the prognosis for full subjective recovery: only three of the nine patients classified as Grade 2 on admission had no complaints. This difference in subjective outcome in Group I (full objective recovery) between those classified on admission as Grade 1 and Grade 2 (p < 0.05) suggests that the subjective symptoms experienced have a pathophysiological cause and are not merely psychosomatic.

Conclusions

When complete angiographic evaluation fails to demonstrate an aneurysm or mass in a patient with an SAH, the prognosis is good. If cases with arterial hypertension are excluded, 95% of patients will return at least to part-time work and 86% will be able to resume full
activity (for patients with arterial hypertension the corresponding figures are 78% and 55%, respectively). It should, therefore, be possible to reassure the normoten-
sive patients directly after angiography as to the benign-
ity of their disorder and thereby, hopefully, reduce the
risk for future psychosomatic problems. Symptoms
such as frequent headaches, vertigo, and increased fa-
tigability were often experienced in this series: 22% of
patients who returned to full activity had some problems.

After 2 weeks, the prognosis is excellent for all pa-
tients (those with arterial hypertension included) who
are fully awake and have not exhibited any symptoms
of delayed ischemia. Of these, 97% will return at least
to part-time work and 88% to full previous activity.
After the end of the 2nd week post-SAH, no new
complications developed in any of our patients, and the
mortality rate and causes of death were as in a normal
population. Three patients suffered a rebleed, two of
which proved to be due to undiscovered aneurysms. It
seems reasonable to discharge the patient after 2 to
3 weeks and let him resume his previous activities.
There seems to be no necessity to restrict the patient's
future life.

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