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Roos, Y.B.W.E.M.; Beenen, L.F.M.; Groen, R.J.M.; Albrecht, K.W.; Vermeulen, M.

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Timing of surgery in patients with aneurysmal subarachnoid haemorrhage: rebleeding is still the major cause of poor outcome in neurosurgical units that aim at early surgery

Y B W E M Roos, L F M Beenen, R J M Groen, K W Albrecht, M Vermeulen

Abstract

Objective—To investigate prospectively the proportion of patients actually operated on early in units that aim at surgery in the acute phase of aneurysmal subarachnoid haemorrhage (SAH) and what is the main current determinant of poor outcome.

Methods—A prospective analysis of all SAH patients admitted during a one year period at three neurosurgical units that aim at early surgery. The following clinical details were recorded: age, sex, date of SAH, date of admission to the neurological centre, whether a patient was referred by a regional hospital or a general practitioner, Glasgow coma scale and grade of SAH (World Federation of Neurological Surgeons (WFNS) score) on admission at the neurological unit, results of CT and CSF examination, the presence of an aneurysm on angiography, details of treatment with nimodipine or antifibrinolytic agents, and the date of surgery to clip the aneurysm. At follow up at three months, the patients’ clinical outcome was determined with the Glasgow outcome scale and in cases of poor outcome the cause for this was recorded.

Results—The proportion of patients that were operated on early—that is, within three days after SAH—was 55%. Thirty seven of all 102 admitted patients had a poor outcome. Rebleeding and the initial bleeding were the main causes of this in 35% and 32% respectively of all patients with poor outcome.

Conclusions—In neurosurgical units with what has been termed “modern management” including early surgery, about half of the patients are operated on early. Rebleeding is still the major cause of poor outcome.

Keywords: aneurysmal subarachnoid haemorrhage; timing of surgery; rebleeding

Rebleeding in the first three weeks after aneurysmal subarachnoid haemorrhage (SAH) is a very frequent and severe complication. Without operative intervention and without antifibrinolytic treatment about 30% of the patients have a rebleed within one month of the initial SAH. In a series of patients with a rebleed established by CT about 50% progressively deteriorated and died from the rebleed and 30% died from other complications. Only 20% of the patients with a rebleed survived at three months and most had severe brain damage. The occurrence of rebleeds can be reduced not only by early surgery to clip the aneurysm (early surgery usually being defined as surgery within three days after SAH) but also by antifibrinolytic treatment in combination with delayed surgery. Antifibrinolytic treatment has been shown to reduce the occurrence of rebleeding by 60%. However, this reduced frequency of rebleeds was accompanied by an increase in the occurrence of cerebral ischaemia which offset the beneficial effects of antifibrinolytic drugs. During the 1980s, prevention and treatment of cerebral ischaemia after SAH have considerably improved. Therefore, the results of a study on the effectiveness of antifibrinolytic drugs might now be different. Whether or not this is true is—according to at least some neurosurgeons and neurologists—an irrelevant question as patients with aneurysmal haemorrhages should be operated on immediately to clip the aneurysm. A management protocol with early surgery would virtually eradicate the risk of rebleeding and early surgery can now be carried out with a similar mortality and morbidity as delayed surgery. Therefore the main cause of mortality and morbidity from SAH is currently considered to be cerebral ischaemia, not rebleeding.

In the neurosurgical units in Amsterdam there is consensus that patients should be operated on in the acute phase and that therefore the question of whether antifibrinolytic treatment is beneficial is clinically of no importance as surgery is delayed in very few patients.

The aim of this study was to investigate prospectively what is the proportion of patients operated on early in units that aim at surgery in the acute phase of aneurysmal SAH and what is currently the main determinant of poor outcome.

Patients and methods

The three centres of this study in Amsterdam are all teaching hospitals. Each centre has at least three neurosurgeons who operate on cerebral aneurysms. Patients are referred to
these neurosurgical units by 12 regional hospitals, all situated less than 85 km (50 miles) from the closest centre.

Before the study started it was verified that all three participating neurosurgical units adhered to what has been termed “modern management in SAH”. This treatment is based on the calcium antagonist nimodipine (2 mg/h intravenously or 6 x 60 mg orally), hypervolemic and hypertensive treatment to prevent delayed cerebral ischaemia, and early surgery to prevent rebleeding.12–14

All patients with the diagnosis “aneurysmal SAH” admitted during a one year period starting 1 January 1995 were prospectively studied. The diagnosis was based on clinical signs and symptoms with confirmation of an aneurysmal bleeding pattern on the initial CT.15 If the initial CT was negative and subsequent CSF examination positive (xanthochromia confirmed by spectrophotometry) an aneurysm had to be confirmed on angiography before the patient could be included.16 Patients with a perimesencephalic bleeding pattern or other non-aneurysmal SAHs on CT were excluded.17

The following clinical details were recorded: age, sex, date of SAH, date of admission to neurological centre, whether a patient was referred by a regional hospital or a general practitioner, Glasgow coma scale, and grade of SAH (World Federation of Neurological Surgeons (WFNS) score) on admission at the neurosurgical unit.18–20 Results of CT and CSF examination, the presence of an aneurysm on angiography, details on treatment with nimodipine or antifibrinolytic agents, and the date of surgery to clip the aneurysm.

At three month follow up, the patients’ clinical outcome was determined with the Glasgow outcome scale.21 Death, persistent vegetative state and severe disability on the Glasgow outcome scale were combined as “poor outcome” whereas moderate disability and good recovery were recorded in the study forms as “good outcome”. In patients with poor outcome, the physician or surgeon in charge of the patient was asked to fill in the cause for this poor outcome: initial bleed, rebleeding, cerebral ischaemia, operative complications, or other complications, which had to be specified. In cases of poor outcome caused by rebleeding or cerebral ischaemia, confirmation was sought on CT or at necropsy. In patients with poor outcome caused by rebleeding the actual timing of this rebleeding, suspected clinically or established on CT or at necropsy, was also recorded.

Results

CLINICAL CHARACTERISTICS AND TIMING OF TRANSFER OR ADMISSION

During the year starting 1 January 1995, 102 patients with a diagnosis of aneurysmal SAH were admitted to the three neurosurgical centres. Table 1 shows the characteristics of the patients and the timing of admission to a neurosurgical centre. Two thirds of all patients were referred by regional hospitals; the others were directly referred by general practitioners. Of the 102 patients 57 were admitted at the neurosurgical unit the day of the initial SAH (day 0), 18 on the day after (day 1), 10 on day 2, one on day 3, one on day 4, seven between days 5 and 9, and eight patients 10 days or more after the SAH. Of the 67 patients who were first referred to a regional hospital 28 (42%) were transferred the same day as the initial SAH to a neurosurgical unit (day 0), 16 patients (24%) were admitted at the neurosurgical unit the day after the SAH (day 1), nine (13%) were admitted on day 2, no patient was admitted on day 3, one (1%) on day 4, five patients (7%) were admitted between days 5 and 9 and eight (12%) were admitted 10 days or later after the SAH.

INVESTIGATIONS

Ninety three patients had an aneurysmal bleeding pattern on the initial CT. A positive lumbar puncture with proof of an aneurysm on subsequent angiography confirmed the diagnosis in all but two of the remaining patients. One patient died shortly after admission but was nevertheless included in the study because at postmortem examination an aneurysmal SAH was established. Another patient with a positive lumbar puncture but without angiography who died, was also included because she had a rebleed established by CT, with a bleeding pattern compatible with an aneurysmal bleeding, before the planned angiography.

Of the 93 patients with an aneurysmal bleeding pattern on CT, 84 patients underwent angiography that showed an aneurysm as the cause of bleeding in 76 patients.

In one of the nine patients with an aneurysmal CT pattern but without angiography, an aneurysm was found at postmortem examination. All of the remaining eight patients without angiography had a poor outcome, five because of the initial bleed (Glasgow coma scale 3 at admission in four patients, one patient with Glasgow coma scale 8), two because of rebleeds (Glasgow coma scale ≥ 13 at admission), and one who was in a nursing home before the SAH.

MEDICAL AND SURGICAL MANAGEMENT

Ninety five patients received treatment with the calcium antagonist nimodipine. The remaining patients had not had this treatment because death had seemed imminent on admission. Eight patients were treated with antifibrinolytic drugs.

Aneurysm surgery was performed in 74 of all 102 patients. In 11 of the remaining 28 patients...
Table 2  Timing of surgery in all patients and in patients who were admitted within three days after SAH

<table>
<thead>
<tr>
<th>Delay in days after SAH</th>
<th>Timing of surgery in all patients</th>
<th>Timing of surgery in patients who were admitted within three days after SAH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients (n(%))</td>
<td>Cumulative (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>10 (14)</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>17 (23)</td>
<td>38</td>
</tr>
<tr>
<td>3</td>
<td>13 (18)</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>8 (11)</td>
<td>66</td>
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<tr>
<td>5</td>
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<tr>
<td>6</td>
<td>2 (3)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>7-14</td>
<td>6 (8)</td>
<td>77</td>
</tr>
<tr>
<td>15-21</td>
<td>11 (15)</td>
<td>92</td>
</tr>
<tr>
<td>&gt; 21</td>
<td>6 (8)</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>74 (100)</td>
<td>61 (100)</td>
</tr>
</tbody>
</table>

Table 3  Outcome and causes of poor outcome

<table>
<thead>
<tr>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor outcome:</td>
</tr>
<tr>
<td>Cause of poor outcome:</td>
</tr>
<tr>
<td>Initial bleeding:</td>
</tr>
<tr>
<td>Rebleeding:</td>
</tr>
<tr>
<td>Cerebral ischaemia:</td>
</tr>
<tr>
<td>Surgical complications:</td>
</tr>
<tr>
<td>Other:</td>
</tr>
</tbody>
</table>
Timing of surgery in aneurysmal subarachnoid haemorrhage

still a major cause of poor outcome was also a finding of two recently published population based studies, in King County and in greater Cincinnati. In these studies rebleeding was also more important than cerebral ischaemia as a cause of poor outcome although the timing of surgery was early.

We did not prospectively study the factors that caused delay in surgery because we did not expect to find a considerable proportion of patients with delayed surgery. In some patients surgery was delayed because of the clinical condition on admission. The question is whether in these patients early surgery is beneficial or that other measures should be taken to prevent rebleeding, such as antifibrinolytic treatment or endovascular occlusion of the aneurysm. In other patients surgery was delayed for no obvious reason. It might be that logistic factors played a part.

In review articles on the management of SAH the impression is given that currently cerebral ischaemia and vasospasm are the main causes of morbidity and mortality after SAH. These reviews urge us to direct all efforts at prevention of vasospasm. This study shows that in neurosurgical units, with what has been termed “modern management”, including early surgery, rebleeding still is a far more important cause of poor outcome than cerebral ischaemia. Therefore the management of patients with aneurysmal SAH should be directed at the prevention of rebleeds. Further studies are needed to investigate whether this can be achieved by surgery alone or whether other measures such as antifibrinolytic treatment or endovascular techniques will be necessary as well.