

# Cost-Effective Outcome for Treating Poor-Grade Subarachnoid Hemorrhage

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**Background and Purpose**—The goal of this study was to prospectively assess outcome and cost for poor-grade subarachnoid hemorrhage patients presenting to a regional neurosurgical center (Addenbrooke's Hospital, Cambridge, UK) between 1994 and 2001. Outcome measures were clinical outcome at 6 months, number needed to treat (NNT) for favorable outcomes, and cost analysis.

**Methods**—Poor-grade patients (World Federation of Neurological Surgeons grades 4 and 5) were transferred to the neurocritical care unit after intubation and ventilation. After resuscitation and drainage of ventricular cerebrospinal fluid for 24 hours, sedation was stopped, and patients were assessed clinically. Patients with a Glasgow Motor Score (GMS)  $\geq 4$  underwent angiography and surgical treatment of culprit aneurysms. Patients with a subsequent GMS of 6 were not deemed poor grade and were discounted from the study.

**Results**—We deemed 166 ventilated patients genuinely poor grade (mean age, 53.4 years; 94 women [56.6%]). Of these, 88 patients ( $4 < \text{GMS} < 6$ ; 53%) progressed to angiography and possible definitive treatment. Seventy-five patients had an identifiable aneurysm, but only 64 survived for treatment. Operative mortality was 31.3%, and of the 44 survivors, 22 (34.4% of operated patients) achieved a favorable outcome. Favorable outcomes were more frequently seen in women than men (21.3% versus 6.9%) but were unrelated to patient age. The NNT for 1 favorable outcome was 7 (male NNT, 15; female NNT, 5) at a cost of £84 336 per favorable outcome (female, £60 240; male, £180 720).

**Conclusions**—Poor-grade aneurysmal subarachnoid hemorrhage is associated with a high mortality but a significant subset of patients can achieve favorable outcomes. (*Stroke*. 2003;34:2508-2511.)

**Key Words:** cost-effective analysis ■ outcome ■ subarachnoid hemorrhage

An aggressive approach to patients of a poor clinical grade after subarachnoid hemorrhage (SAH) is warranted because grading can improve dramatically after fluid resuscitation and drainage of cerebrospinal fluid.<sup>1</sup> Untreated, mortality associated with poor-grade aneurysmal SAH approaches 100%.<sup>2</sup> However, treatment is associated with significant morbidity.<sup>3-5</sup> A means of identifying subgroups of poor-grade SAH patients who attract a more favorable outcome is welcomed, whether based on physical or clinical parameters.<sup>1,6</sup>

Even with selection parameters in place, treatment for poor-grade SAH is potentially costly and demanding on intensive care facilities. The present study examines the proportion of patients achieving a favorable clinical outcome after treatment for poor-grade SAH based on clinical selection criteria. Influences such as age and sex are examined, and treatment costs based on number needed to treat (NNT) and cost per quality-adjusted life-year (QALY) are calculated.

## Subjects and Methods

Study data are derived from the prospective East Anglian Regional Neurosurgical Unit audit of patients with aneurysmal SAH.<sup>1,5</sup> Case notes were examined for relevant data, including inpatient activity, investigations, surgery, and use of consumables. Patients with SAH who presented between 1994 and 2001 in poor clinical grade were examined (World Federation of Neurological Surgeons grades 4 and 5).<sup>7</sup> All patients had CT-demonstrable subarachnoid blood of an aneurysmal distribution. All were ventilated before transfer from the referring hospital. Patients were excluded from analysis if they (1) required urgent evacuation of space-occupying clots, (2) were able to obey commands (GMS = 6) after resuscitation, and (3) were shown to have other pathology to account for the SAH (such as an arteriovenous malformation). Patients were optimized medically and then assessed clinically off sedation.

## Patient Management

Details of patient management as part of the East Anglian Regional Neurosurgical Unit protocol are described elsewhere.<sup>1,5</sup> Briefly, all patients were sedated and paralyzed for transfer to the unit. Fluid and electrolyte resuscitation was carried out, and hydrocephalus was drained with an external ventricular drain. Patients received intrave-

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### Cost Analysis

	Unit Cost, £	Total Cost, £
ITU		
Addenbrooke's	914	1246696
National	501–2085	683 364–2 843 940
Ward (HRG A19)		
Addenbrooke's	142	101 388
National	189	135 125
EVD	237	19 671
Angiogram	481	42 328
Craniotomy and clipping	587	34 633
Coiling*	4836	33 852
Total		
Addenbrooke's	...	1 478 568
National	...	2 000 000

ITU indicates intensive treatment unit; EVD: external ventricular drain. Values shown are based on figures for 2001 supplied by Addenbrooke's Hospital Audit Department and the UK Department of Health Web site (<http://www.doh.gov.uk/nhsexec/refcosts.htm>).

\*Cost based on average of 5 coils per procedure.

nous nimodipine (0.5 to 2 mg/h) or oral nimodipine (60 mg every 4 hours).

After 24 hours, the sedating and paralyzing agents were reversed, allowing clinical assessment. Those patients who were unable to obey commands (GMS <6) were considered to fulfill the criteria for poor grade.

Patients who could not obey commands but were able to flex after painful stimulation (GMS=4 and 5) were selected for angiography with a view to definitive management of culprit aneurysms.

### Outcome

Glasgow Outcome Scale (GOS) scores were assessed at 6 months after SAH from details gleaned from patients' 6-month clinic appointment notes.<sup>8</sup>

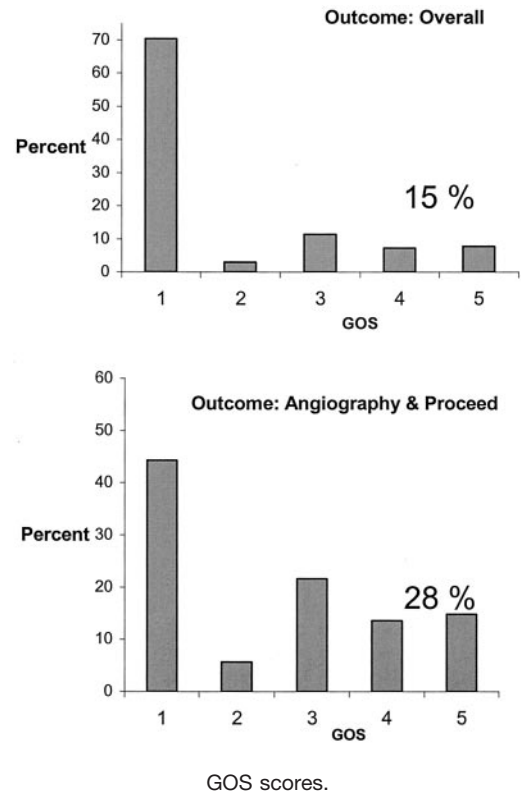
### Cost

The variables used to estimate acute treatment costs are itemized in the Table. Unit costs for stay as an inpatient were obtained from Addenbrooke's Hospital Finance Department for the year 2001 (courtesy of Mike Tapp). The diagnostic criteria code HRG A19 (for hemorrhagic stroke) was used for inpatient ward costs. Hospital stay costs also incorporated medical treatments and simple diagnostic procedures (including radiological investigations). Not included in these values were specific costs for procedures such as external ventricular drain insertion, angiography, coiling, and aneurysm clipping. Unit values for these variables were therefore included in the cost analysis and were obtained from our local Finance Department. To compare these costs nationally, average costs per stay in a neurosurgical ward bed and neurocritical care unit (NCCU) bed were obtained from the Department of Health Web site (<http://www.doh.gov.uk/nhsexec/refcosts.htm>). Applying a method previously used by Pickard et al,<sup>9</sup> we found an estimate of acute cost per QALY that is presented here.

## Results

### Patients

One hundred sixty-six patients fulfilled the criteria for poor-grade SAH. Eighty-three patients (50%) demonstrated radiological evidence of hydrocephalus at admission and underwent insertion of an external ventricular drain. After neurological assessment at 24 hours, 78 patients (47%) did



not show purposeful flexion (GMS <4) and were managed conservatively. All 78 eventually died. Time to death for this patient subgroup was  $2.6 \pm 0.8$  days (95% confidence interval [CI]) after admission.

In addition to the final cohort of 166 patients, 18 apparently poor-grade patients improved to a GMS of 6 (obeying commands) after resuscitation and were not included in this study.

Eighty-eight patients (53%) showing purposeful flexion responses ( $4 \leq \text{GMS} < 6$ ) progressed to angiography. A culprit aneurysm was found in 75 patients (85%; 55 patients with an anterior circulation aneurysm, 6 posterior circulation, 14 multiple aneurysms). Early surgery was planned, but 11 (15%) rebled and died before surgery. The remaining 64 progressed to treatment of an aneurysm; 59 of the 64 (92%) received open surgery (2 after a failed endovascular attempt), and 5 (8%) received endovascular treatment.

### Outcome

Overall, 117 patients (70%) died and 49 (30%) survived. Forty-three of 59 patients (73%) who underwent clipping and 1 of 5 (20%) receiving endovascular treatment survived, resulting in a procedural mortality of 31.3%. Five patients without demonstrable aneurysms also survived.

GOS at 6 months is shown in the Figure. Overall, 25 of 166 (15%) achieved a favorable outcome (GOS=4 and 5). Of those receiving an angiogram, 25 of 88 (28%) achieved a favorable outcome, and of those undergoing definitive aneurysm treatment, 22 of 64 (34%) achieved a favorable outcome. The overall NNT for 1 favorable outcome was 7.

### Influence of Age

Age ranged from 14 to 85 years (average age, 53.4 years). Of the 166 patients, 37 (22.3%) were >65 years of age. Of these

elderly patients, 5 were of favorable outcome. There was no difference in outcome between patients >65 years of age compared with the younger age group (Fisher's exact test,  $P=0.8$ ). No patients >80 years of age achieved a favorable outcome.

### ***Influence of Sex***

Favorable outcomes were observed in 20 of 94 female patients (21.3%) but in only 5 of 72 male patients (6.9%; Fisher's exact test,  $P<0.05$ ). The NNT for 1 favorable outcome was 5 for women and 15 for men.

### ***Length of Stay***

Length of stay of patients in the NCCU ranged from 1 to 89 days (95% CI,  $4.2\pm 0.7$ ). For surviving patients, the mean length of stay was  $15\pm 3.5$  days (95% CI). Forty-six of the surviving patients stayed from 3 to 42 days (95% CI,  $15.5\pm 2.8$ ) in the general neurosurgical ward before discharge.

### ***Acute Treatment Costs***

The cost for acute treatment is given in the Table. The total cost for acute treatment of the SAH cohort was £1 478 568 (£211 224 per year). The cost for an identical cohort of patients over 7 years of admissions to an average regional neurosurgical center would be £2 000 000 (£285 714 per year).

The cost of intensive care treatment for the above patients represented  $\approx 84\%$  of the total costs. Given that that was the single most significant variable affecting cost, a national average cost has been calculated from the range of NCCU costs provided by the Department of Health. Using the average value, we found that the acute care cost per patient was £12 048, the cost per life saved was £40 816, and the cost required to avert 1 bad outcome was £84 336. These costs proved to be sex but not age dependent (cost per female favorable outcome, £60 240; cost per male favorable outcome, £180 720).

## **Discussion**

This article reports a favorable outcome (GOS=4 to 5) in 28.4% of selected patients suffering from a poor-grade SAH. Mortality remains high, but half of surviving patients achieved independence by 6 months. Despite an aggressive treatment protocol, rebleeding represented a significant source of mortality during the wait for definitive treatment, indicating the need to expedite aneurysm treatment in these individuals once they satisfy the criteria for active management.

A striking and novel finding was the significant outcome difference according to sex, which is independent of age. Women tend to have a higher mortality than men for all other stroke conditions.<sup>10</sup> Female patients also have higher postoperative rates of stroke and mortality after carotid surgery.<sup>11</sup> In contrast, men are believed to develop symptomatic coronary artery disease earlier than women.<sup>12</sup> Although women are reported to have a higher prevalence of berry aneurysms compared with men, the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease stroke study revealed no overall difference in mortality

between the sexes for SAH.<sup>13</sup> That study, however, did reveal wide geographical differences between the sexes in both incidence and mortality of SAH, with women having a poorer outcome in Denmark and Finland but data from Lithuania and Beijing demonstrating an increased mortality for male SAH patients. Furthermore, there are reports of an increased incidence of vasospasm in Danish female SAH patients.<sup>14</sup> Female sex also affords relative neuroprotection and better outcome in animal models for cerebral ischemia and trauma, a possible consequence of estrogens and progestogens.<sup>15</sup> Of the 20 favorable-outcome female patients, 9 (45%) were >55 years of age and can be assumed to have been postmenopausal.

Surprisingly, outcome was not influenced by age. This contrasts to our previous experience, a disparity that may reflect a change in policy within our unit.<sup>1</sup> The proportion of patients >65 years of age (22%) in the present study is less than that in the previous one (32%). Although it did not exclude patients >65 years of age, this unit has adopted a more conservative approach to the treatment of the poor-grade elderly patient when the outlook is bleak.

Acute treatment costs are significant and estimated at £2 000 000 for an average neurosurgical unit dealing with the same cohort of patients over a 7-year period (£285 714 per year). This corresponds to approximately £12 000 per patient and £84 000 per bad outcome averted. Using methodology similar to that used by Pickard et al,<sup>9</sup> we found that the cost per QALY for the given cohort of patients equates to £4269 for poor-grade SAH. Previous reports for all cases of SAH have suggested an acute cost per year of £326 602 and a cost of £7258 to avoid a bad outcome.<sup>9</sup> The same report also estimates a cost per QALY for all SAH as £310, although this includes all patient grades. Clearly, the cost per QALY is more expensive for the poor-grade SAH patient when considered in isolation. This figure, however, would appear to be cost effective when considering that reported costs per QALY for clopidogrel treatment in stroke prevention approach £17 000.<sup>16</sup> Furthermore, costs per QALY after lumbar discectomy have been reported to be as high as £22 000.<sup>17</sup>

Acute costs for treatment have only been considered here. No attempt has been made to calculate real costs for poor-grade SAH that would include the cost of rehabilitation and further neurosurgical admissions. Pickard et al<sup>9</sup> speculate that real cost may approach 10 to 15 times the acute cost values for neurosurgical conditions.

Outside the United Kingdom, several studies have explored the cost for treating stroke and cerebrovascular events together, but few have considered poor-grade SAH patients alone.<sup>18,19</sup> Roos et al<sup>20</sup> report the direct costs per year as 2 687 898 Euros (approximately £1.7 million pounds, £15 000 per patient) for 110 patients with a ruptured cerebral aneurysm in the Netherlands. This figure includes nursing costs and out-of-hospital transport costs but does not specifically relate to poor-grade patients who accounted for only 30% of their studied population. Yundt et al<sup>21</sup> separated poor-grade patients in their study and estimated an acute cost of \$37 800 (approximately £24 000) and \$14 200 (approximately £9000) per (Hunt and Hess) grade 4 and 5 patient, respectively. However, only 19 poor-grade patients were

included in this study. Elliott et al<sup>22</sup> have studied 159 Hunt and Hess grade 4 and 5 patients and have estimated a mean cost of \$108 690 (approximately £69 000) and \$96 194 (approximately £61 000) per grade 4 and 5 patient, respectively. These high costs probably reflect fundamental differences between the reported health economics of the United States and the United Kingdom. Although these figures may represent actual differences, it is important to emphasize that North American studies are based on actual billed health cost receipts, whereas UK studies such as the present one have to rely on estimates in the absence of more sophisticated and detailed data. Interestingly, their study revealed that the cost of intensive care management was found to represent <50% of the total cost, with a higher proportion of cost attributed to pharmacy and laboratory tests. These latter variables have not been independently analyzed here because these costs were incorporated into the unit costs of ward and intensive care stay as generated by the UK Department of Health.

In summary, the management of poor-grade SAH patients described here is expensive, with major demands on critical care resources and sometimes prolonged hospital stays. However, our analysis suggests that such aggressive management is not only clinically justified in a significant subset of this cohort of patients but also cost-effective overall. The benefit of such an approach may be particularly apparent in women but does not seem to be modulated by age. Also, these results underline the disastrous effect of early rebleeding, which may be more common in the poor-grade patient who has suffered a high-volume bleed at the primary ictus. The study emphasizes the need to rapidly proceed to definitive therapy in selected patients to avoid the high incidence of early rebleeding in the poor-grade patient.

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