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# Outcome After Aneurysmal Subarachnoid Haemorrhage: The use of a Graphical Model in the Assessment of Risk Factors

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## Summary

In 102 consecutive prospectively identified patients with subarachnoid haemorrhage (SAH) we have analysed the severity of the initial haemorrhage and the direct and indirect effects of adverse factors on outcome.

The data we recorded included delay in diagnosis, risk groups, Doppler measurements, angiographic findings, surgical events and outcome at 1 year. By using a temporal graphical chain model, the associations between all variables and possible causal pathways were statistically determined.

The severity of the initial haemorrhage, as determined by means of a clinical assessment and CT scanning, allowed low-, medium- and high-risk patient groups and a statistically predictable outcome to be identified.

The overall management mortality was 13.7% at 1 year; 70.6% had a favourable outcome and 15.7% were severely disabled. Outcome was directly associated with risk group ($p = 0.0038$) and rebleeding ($p = 0.0000$). Delayed diagnosis led to a poorer outcome ($p = 0.014$) – an indirect association probably due to rebleeding. Adverse surgical events led to a significantly poorer outcome in high-risk patients.

No significant relationship was found either between age and risk group ($p = 0.7784$) or between age and outcome ($p = 0.6418$). Preoperative clinical (WFNS) grade was unreliable in predicting outcome. It is the particular risk group, determined by the initial SAH, that indicates the individual patient's outcome.

Management strategies can reduce preventable adverse events such diagnostic delay and rebleeding. Future studies should stratify patients according to risk group, delay in diagnosis and rebleeding in order to enable a clearer comparison to be made of treatment methods.

*Keywords:* Aneurysmal subarachnoid haemorrhage; risk groups; graphical modelling; outcome.

## Introduction

Aneurysmal subarachnoid haemorrhage (SAH) is a devastating event with 70% of those affected either dying or being left permanently disabled [9, 32]. This depressing outcome has been improved, compared to the natural history of the event, by refining surgical techniques and applying medical and surgical treatment more aggressively. However the overall management mortality and morbidity of treatment remain disappointing [17, 40].

Following an aneurysmal SAH, a number of interrelated pathophysiological changes and clinical factors dictate the outcome [8, 13, 19, 20, 25, 27, 36, 37, 39]. Therefore, it is not surprising that those attempts to predict outcome which are based on the evaluation of a single factor have failed.

In a previous study, in order to assess the relative predictive strength of individual risk factors, a number of variables were considered. These included age, sex of patient, early neurological grade, systolic and diastolic blood pressure, the presence of blood and its distribution on the CT scan, angiographic vasospasm, the site and multiplicity of aneurysms, the timing of operation, and drug therapy. The best neurological grade recorded within 72 hours and the distribution of blood on a CT scan i.e. the severity of the haemorrhage, emerged as the strongest predictors of outcome. These two indices when combined in the form of a simple "score" further improved the ability to predict outcome. The scoring system allowed patients to be classified as high-risk, medium-risk, or low-risk. The validity of this scoring system was then tested by prospectively placing patients in risk groups in two further series separated in time and place. The probability of full recovery was found to be very likely in the low-risk group whereas the probability of death was the likely outcome in the high-risk category [11].

The present study correlates the severity of the initial insult i.e. the risk stratification, following aneur-

ysmal SAH with the overall outcome in a further series of patients with the aid of a graphical model. It also attempts to determine the relative importance of adverse factors, individually or in combination, in determining outcome within each of the three risk groups.

## Patients and Methods

The neurosurgical unit (NSU) at Southampton, England provides total neurosurgical care for a geographically defined catchment population of 2.8 million people. Hospital physicians refer patients with a SAH to the NSU after initial diagnosis and assessment. The only SAH patients not admitted to the regional NSU are those who die in the community and those who are considered to be unsalvageable. This series consists of 102 consecutive and prospectively identified patients with proven subarachnoid haemorrhage admitted to the NSU between January 1993 and January 1994.

### *Clinical Assessment and Management*

The initial evaluation included specific details, such as the age and sex of the patient, and a history of current treatment for hypertension. All SAH referrals were assessed prospectively by telephone consultation with the admitting neurosurgeon, and the CT scans were transferred by an image link system. On admission to the NSU the previous information was confirmed and expanded, identifying the sequence of events from the haemorrhage to the eventual admission to hospital with particular attention to the time of the ictus and any subsequent developments. The data from the referring hospital notes, the telephone consultation records and the NSU notes were designed to answer the specific question concerning delay.

''Delay'' was registered if a patient gave a classical history, namely the sudden onset of a severe persistent headache, which was not recognised as SAH by a general practitioner, or by an accident & emergency doctor or a physician if he was admitted to hospital. The diagnosis was ''missed'' and a further clinical event occurred before the appropriate diagnostic investigations were performed.

In the referring hospitals rebleeding was recognised by history, CT scanning and/or lumbar puncture.

The best WFNS grade during the initial 72 hours of the haemorrhage was recorded. A CT brain scan was performed within 96 hours of the haemorrhage in each patient, which was interpreted by an experienced neuroradiologist, in respect of the presence of blood and its distribution or the absence of blood. Using the scoring system described in our previous paper, which is based on the WFNS grade and the number of sites of CT blood, each patient was defined as low-risk, medium-risk or high-risk, and placed in the appropriate risk group [11].

In the NSU the arterial blood pressure (BP) was recorded routinely every 4 hours, and more frequently if required. Antihypertensive medication was given to patients with unstable BP or diastolic readings which remained consistently above 100 mmHg for more than 48 hours. Any patient with a diastolic pressure varying by more than 30 mmHg over the course of 48 hours was classified as having a 'fluctuating' blood pressure [24].

Specific treatment for possible complications of subarachnoid haemorrhage, in particular oral nimodipine, was recorded. Daily assessment of the WFNS grade enabled those patients showing deterioration to be investigated by repeat CT scanning and middle cerebral artery velocity (MCAV) measurement. In this way, rebleeding, hydrocephalus and ischaemia were identified promptly.

### *Pre-Operative Investigations*

*Mean middle cerebral artery velocity.* MCAV was recorded pre operatively through the temporal window using a 2 MHz ultrasound probe (TC-264 Eden Medizinische Elektronik, Uberlingen, Germany). An experienced operator identified the middle cerebral artery (MCA) and the MCAV was taken as the highest velocity detected between 50 and 60 mm; these velocities were expressed as the time-averaged mean in cm/s. A normal MCAV was accepted to be $<100$ cm/s [1]. The pre operative insonation was repeated if the MCAV exceeded 100 cm/s or if the patient deteriorated clinically.

*4 vessel angiography.* The angiograms were performed and interpreted by a neuroradiologist. The timing of angiography was noted. The report identified the site(s) and the number(s) of aneurysms, as well as the presence of spasm. The spasm was defined as ''localised'' if it was restricted to the aneurysm's vessel of origin, or ''diffuse'' if it involved one or more vessels beyond the site of the ruptured aneurysm.

### *Surgical Details*

Our practice in the NSU during this study was to operate on all patients without delay provided they were WFNS grades 1 or 2; therefore a proportion of our patients were operated on within 3 days of the SAH. Other patients who were WFNS grades 3–5 were operated on after 3 days as soon as they were considered to be fit for surgery by the consultant neurosurgeon responsible for their care. Patients whose admission to the NSU was delayed had ''late'' surgery.

The following details were routinely recorded: date of operation, immediate pre operative WFNS grade, and seniority of the operating surgeon. Also, the following adverse intra-operative events (if present) were documented: aneurysm rupture during induction of the patient in the anaesthetic room, brain swelling, aneurysm rupture during dissection, and the time of application and the duration of temporary clipping.

All patients were nursed in high dependency or neurosurgical intensive care beds where as a routine oxygen saturation, arterial blood pressure and central venous pressure were measured continuously. Daily MCAV was recorded and CT scanning was repeated as indicated on clinical grounds. The post-operative management was standardised and included 'triple H' therapy for delayed cerebral ischaemia [2, 14, 26]. Additional physiological monitoring, such as intracranial pressure, cerebral perfusion pressure and pulmonary artery wedge pressure were used when indicated.

Immediate and subsequent post-operative complications were listed.

### *Outcome Evaluation*

Outcome was assessed by independent observers in the out patient clinic using the Glasgow Outcome Score (GOS) [15], at 3 months, 6 months and 1 year after discharge.

### *Statistical Method*

*Factors studied.* As a consequence of our previous study describing risk factors in 3 series of SAH patients, the factors examined in this study were those previously identified to be the most important.

*Graphical chain model.* A graphical chain model was fitted to the data. This was performed using the MIM statistical package [6, 7]. This model allows associations between all the variables in the study to be assessed, and possible causal pathways to be found [5, 41, 42, 43].

The first step when fitting a graphical chain model is to partition

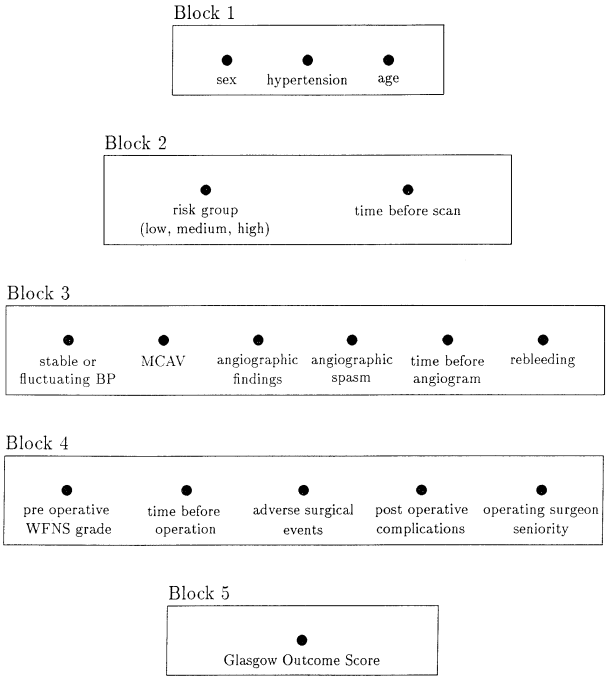


Fig. 1. Blocks. Time before CT scan is the time between haemorrhage and day of CT scan time before angiogram is the time between CT scan and day of angiogram time before operation is the time between angiogram and day of operation

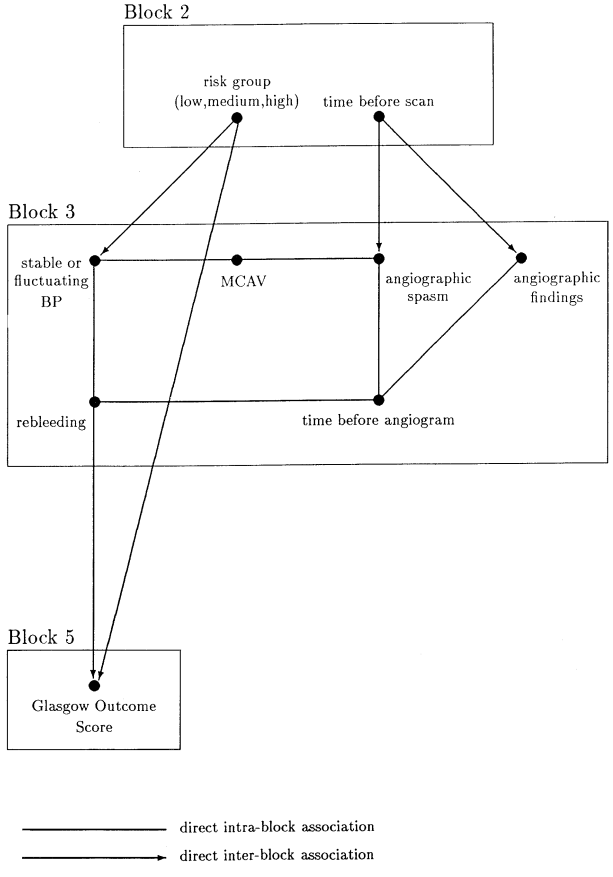


Fig. 2. Chain graph

the variables into a number of ordered blocks (Fig. 1). The variables in the first block are viewed as purely explanatory variables, whereas the variables in the second and subsequent blocks are viewed as responses to the variables in the preceding blocks and as explanatory variables for the variables in the succeeding blocks. The ordering of the blocks is temporal, with the variables in the first block being determined first and those in the last block last.

The variables in this study which are determined before or at the time of the SAH are the patient's sex, hypertension and the patient's age. Therefore, these variables are placed in Block 1 and are viewed as purely explanatory variables. The variables which are determined on the patient's admission to the NSU are placed in Block 2 and are viewed as responses to the variables in Block 1 and as explanatory variables to those determined later in the study, e.g. angiographic vasospasm and Glasgow Outcome Score. The variables in Block 3 are determined at some time prior to the operation whereas those in Block 4 are determined immediately before or during surgery. Block 5 contains the final response variable.

A graphical chain model displays the independencies between variables conditioned on all the other variables in the current and previous blocks. In a graphical chain model any direct association between two variables in the same block is assumed to be non-causal and is represented by an undirected edge (line) in a mathematical graph (Figure 2). Any direct association between two variables from different blocks is assumed to be potentially causal and is represented by a directed edge (arrow). The absence of a line or arrow between two variables in the graph indicates that there is no direct association between the variables, i.e. the variables are independent after controlling for all the other variables in the same and previous blocks.

The graphical model is fitted in a number of stges. First, the significant direct associations between the variables in Block 1 are determined. For each pair of variables the null hypothesis when tested shows that the variables are independent given all the other variables in Block 1 and the generalised likelihood ratio test statistic is used [7, 10, 42]. Second, the significant direct associations between the variables in Block 2 and between Blocks 1 and 2 are determined. For each pair of variables the null hypothesis when tested shows that the variables are independent given all the other variables in Blocks 1 and 2 and again the generalised likelihood ratio test statistic is used. The fitting continues, block by block, by determining all the significant direct associations between the variables in the current block and between all the variables in the current and previous blocks. The null hypothesis is now independence given the other variables in the current and previous blocks and again the generalised likelihood ratio test statistic is used. All these tests were carried out at the 5% level using generalised likelihood ratio statistics [7, 10, 42].

## Results

Tables 1–4 summarise the patients' details. Included in Table 1 is information pertaining to delay in diagnosis and the timing of CT scanning and angiography. In these tables the time intervals given are those between haemorrhage and scan, haemorrhage and angiogram, and haemorrhage and operation, rather than the intervals between these events which are required when fitting the graphical chain model. All but one

Table 1. *Series Data: Overall Pattern*

| | | |
|---|---|---|
| Number of patients | 102 | |
| Mean age | 50.4 years | |
| Age range | 26–72 years | s.d. 12.6 years |
| Hypertension | 16 | |
| Sex | 37 males | |
| Delayed diagnosis | 34 patients | median 6 days; maximum 60 days |
| Time before CT scan <4 days | 98 | |
| Angiography | 99 | <4 days 66<br>4–8 days 15<br>>8 days 18 |

Table 2. *Series Data: CT Blood, WFNS Grade and Risk Group*

| CT scan blood | | Risk group | |
|---|---|---|---|
| 1 site | 36 | low | 28 |
| 2 sites | 47 | medium | 41 |
| 3 sites | 17 | high | 33 |
| 4 sites | 1 | | |
| No blood | 1 | | |
| WFNS grade | | | |
| 1 | 12 | | |
| 2 | 71 | | |
| 3 | 7 | | |
| 4 | 7 | | |
| 5 | 5 | | |

Table 3. *Series Data: BP, MCAV and Angiography*

| Blood pressure | | Aneurysms | |
|---|---|---|---|
| Stable | 30 | ACoAA | 26 |
| Fluctuating | 72 | carotid A | 22 |
| | | MCAA | 22 |
| TCD (MCAV) | | multiple | 24 |
| insonations | 310 | posterior circulation | 5 |
| Average/patient | 3 | | |
| Range | 1–15 | rebleeding | 17 |
| <100 cms/s | 48 | angiographic spasm | |
| 100–150 cms/s | 20 | diffuse | 16 |
| >150 cms/s | 34 | focal | 9 |

Table 4. *Series Data: Operation*

| Operated cases | 93 | Operating surgeon | |
|---|---|---|---|
| WFNS grade at op | | consultant | 60 |
| 1 | 39 | senior registrar | 26 |
| 2 | 44 | registrar | 7 |
| 3 | 10 | | |
| | | adverse intra operative events | |
| Op <7 days | 32 | none | 59 |
| Op 7–15 days | 35 | rupture | 24 |
| Op >15 days | 26 | temporary clips | 14 |
| | | brain swelling | 2 |
| | | brain swelling – op abandoned | 2 |
| | | aneurysm rupture before dissection | 2 |

patient received nimodipine therefore this variable was excluded from the analysis.

### *Adverse Surgical Events ( Table 4)*

A number of adverse intra-operative events were reported. Intra-operative aneurysm rupture occurred in 24 patients. These included small leaks and major haemorrhage (3) during dissection or clip application. The majority of patients with an intra-operative rupture (19) did well (GOS 4 or 5). No association was found between outcome at 1 year and intra-operative rupture.

When temporary clips were used, they were applied for intervals ranging from 3 to 34 minutes. No relationship was found between duration of application of the temporary clip and outcome.

### *Post-Operative Complications*

49 patients (53%) had post-operative complications. In 19 patients the level of consciousness temporally deteriorated at some point during the post operative course, in another 19 a neurological deficit developed, in 5 cranial nerve palsies occurred, and 6 had several complications including medical complications. All the patients with cranial nerve palsies recovered. The 6 patients with multiple complications died, despite intensive care and aggressive medical management to control cerebral perfusion. Of the remaining 38 patients with cerebral ischaemia (drowsiness, focal neurological deficit), 3 died and 15 were assessed using the GOS as severely disabled at 1 year post operatively.

### *Outcome*

At one year, of the 93 patients who had undergone operation: 56 (60.2%) had made a good recovery (GOS 5), 13 (14%) were moderately disabled (GOS 4), 15 (16.1%) were severely disabled (GOS 3), and the management mortality was 9.7% (9 patients died – GOS 1). At one year, the overall results (102 patients) were: 58 patients (56.9%) had made a good recovery (GOS 5), 14 (13.7%) were moderately disabled (GOS 4), 16 (15.7%) were severely disabled (GOS 3), and the man-

agement mortality was 13.7% (14 patients died – GOS 1). There were no vegetative survivors.

### *Graphical Modelling*

The graphic model describing the data demonstrated that none of the variables in Block 1 (patient's age, sex and hypertension) nor any of the variables in Block 4 were directly or indirectly associated with outcome. Hence these blocks were omitted from the chain graph which shows the relationship between the variables directly or indirectly associated with outcome (Fig. 2).

The arrows from time before scan to angiographic spasm and angiographic findings indicate direct associations between delay, as measured by time before scan, and these variables. Those patients in whom the time interval between CT scan and angiography is 5 or more days are more likely to exhibit diffuse arterial spasm compared with those patients who waited for a shorter period.

The relationship between the variables in Block 3 is complex. Paths are present between all the variables, indicating that all are associated either directly or indirectly with each other. Note that while there is no direct association between risk group and rebleeding, there is an indirect association through the blood pressure variable. This indicates that, after allowing for the differences between patients with and without fluctuating blood pressure, no direct association exists between risk group and rebleeding. A similar conclusion can be drawn for the association between risk group and angiographic spasm.

In Block 5, outcome is directly associated with risk ($p = 0.0038$) and rebleeding ($p = 0.0000$), otherwise given risk and rebleeding it is independent of all other variables. Again note that all the other variables in Figure 2 have an indirect association with outcome but after controlling for risk group and rebleeding there is no direct association between the other variables and outcome.

### *Assessments Within Risk Groups*

An analysis of variables across risk groups revealed several important points.

*Age.* If the patient's age is classified according to Lanzino *et al.* [19], namely <41, 41–50, 51–60, 61–70 and >70, there is no significant association between age and the risk group ($p = 0.7784$), or between age and outcome ($p = 0.6418$). The p-values quoted here and below are the exact p-values for the Pearson chi-squared test statistics of independence, calculated using StatXact 3 [23].

Table 5. *Effect of Rebleeding on Glasgow Outcome Score in Different Risk Groups*

| Risk Group | | | | | |
|---|---|---|---|---|---|
| No rebleed | Good | Mod | Sev | Veg | Dead |
| Low | 25 | 2 | 0 | 0 | 0 |
| Medium | 21 | 7 | 4 | 0 | 0 |
| High | 6 | 4 | 10 | 0 | 6 |
| Rebleed | Good | Mod | Sev | Veg | Dead |
| Low | 1 | 0 | 0 | 0 | 0 |
| Medium | 4 | 1 | 0 | 0 | 4 |
| High | 1 | 0 | 2 | 0 | 4 |

Table 6. *Effect of Diagnostic Delay on Glasgow Outcome Score*

| Delay | Good | Mod | Sev | Veg | Dead |
|---|---|---|---|---|---|
| No | 45 | 10 | 7 | 0 | 6 |
| Yes | 13 | 4 | 9 | 0 | 8 |

$X2 = 10.61; p = 0.014$.

*Rebleeding.* Table 5 presents the risk group, outcome and rebleeding status of all 102 patients. Of the medium-risk patients who bled again, 4/9 (44.4%) died. No deaths occurred in the 32 medium-risk patients who did not bleed again. A similar pattern was recognisable in the high-risk patients.

*Diagnostic delay (Table 6).* Delay in diagnosis and referral to the NSU was encountered in 34 (33.3%) patients. Initial assessment indicated no obvious risk factor in these patients. When the association between delay and outcome was assessed, without allowing for the other variables, it was found to be significant ($p = 0.014$). Patients whose admission was delayed had a poorer outcome than those who were admitted without delay. After controlling for the other variables, there is no direct association between delay and outcome. The effect of delay and outcome occurs through the variables in Block 3, especially rebleeding (Fig. 2). Delayed patients are more likely to have adverse states of the variables in Block 3 and hence are more likely to have a poorer outcome than patients who are not delayed.

*Adverse surgical events (Table 7).* If patients are classified as free from, or experiencing adverse surgical

Table 7. *Influence of Adverse Surgical Events on Glasgow Outcome Score*

| | No adverse surgical events | | | | | Adverse surgical events | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome | good | mod | sev | veg | dead | good | mod | sev | veg | dead |
| Low | 18 | 2 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 0 |
| Medium | 12 | 6 | 2 | 0 | 0 | 13 | 1 | 2 | 0 | 4 |
| High | 6 | 3 | 6 | 0 | 2 | 0 | 1 | 5 | 0 | 3 |

events – rather than distinguishing between the types of adverse events as was done when fitting the graphical model – the following two direct associations may be observed. First, patients who have adverse surgical events are more likely to die than those who do not ($p = 0.0222$). However, when the particular risk group of the patient is taken into account, it can be shown that an adverse surgical event does not significantly alter the outcome profile of low-risk patients. The medium-risk and particularly the high-risk patients with adverse surgical events are more likely to die – and less likely to have a good outcome – than those who remain free from adverse events (Table 7). Secondly, patients who rebleed preoperatively are more likely to experience adverse surgical events than those who do not rebleed ($p = 0.0094$).

## Discussion

Neurosurgeons have clear views about managing patients with ruptured intracranial aneurysms based on experience, "common sense" and information available in the literature. However, when faced with the individual SAH patient their ability to predict the outcome at any particular stage of a patient's illness is fraught with difficulty on account of the many factors to be considered.

The graphical model used in this study allows all factors to be considered throughout the time course of an individual patient's illness. In particular, it brings out those factors of high predictive value. Thus, whilst an older patient may fare less well than a young patient, the risk group status is so powerfully predictive that it overrides the age factor, which becomes far less significant. In other words, if a patient's risk group is known, and whether or not he has rebled, it is unlikely that any other information, such as the angiographic findings or blood pressure, will improve prediction of outcome.

The graphical model also offers several advantages over a more traditional approach to assessing outcome, such as inspecting tables of counts, performing chi-squared tests or fitting a single logistic regression model. It permits the association structure of all the variables to be examined and both the indirect and the direct associations between the variables to be identified, and it may reveal possible causal pathways. If only a simple logistic regression model for outcome had been fitted in this study, then no more than the direct effects – namely, risk group and rebleeding – would have been identified, and the indirect effect of diagnostic delay would have been missed.

The overall management mortality at one year (13.7%) and the operative mortality (9.7%) in our patients compares with results reported in the literature where management mortality figures range from 9 to 60% and operative mortality figures are as high as 28% [18, 22, 40].

This study has confirmed our previous three studies in demonstrating distinct risk groups, which are identifiable entities according to their response to the pathophysiological sequelae of SAH and in their outcome characteristics [11]. It is the severity of the initial haemorrhage which determines the patient's risk group, and throughout the course of his illness he remains confined to his particular risk group, irrespective of his clinical state.

Whilst WFNS grading on admission has been shown to correlate with outcome, there are low-risk and high-risk patients in our series within the preoperative grouping of grade 1, 2 and 3 patients – each risk group carrying a significantly different outcome. Our study does not give support to the concept that immediate preoperative Glasgow Coma Score will be reflected in the subsequent Glasgow Outcome Score [12, 17]. We believe that this association, noted by Gotoh and his colleagues, depended on sample size; it may not possess a predictive value. Similarly, the patient's age may attain significance in terms of outcome with larger numbers of patients without having a predictive value [19].

In considering the relationship between risk group-

ing and rebleeding the important observation is that both are independent factors in determining outcome. Risk group does not predict rebleeding. Rebleeding directly affected outcome, particularly in the medium-risk and high-risk groups of patients [17, 33]. Some episodes of rebleeding were a consequence of operative delay which was judged to be necessary to obtain clinical improvement. Our results (Table 5) thus support a policy of early operation for medium-risk and high-risk patients followed by an aggressive regime of post-operative management; a view expressed by others [18, 25]. The conundrum remaining is, of course, the relative risk of early surgery in these patients [30, 31].

The outcome in patients subjected to diagnostic delay was found to be significantly poorer than in patients promptly managed (Table 6). Invariably a further event overtook the delayed patient before his condition was recognised and appropriately treated. It was found in this group that background activity consisting of vasospasm, elevated MCAV and fluctuating blood pressure was a more prominent feature. While our model indicated that this background activity bore no direct relationship with outcome, it exerted an indirect effect, probably through rebleeding. Although others have emphasised the importance of prompt diagnosis and NSU referral, this is the first prospective study, to our knowledge, to have demonstrated statistically a poorer outcome in patients subjected to diagnostic delay [16, 21].

In this study angiographic vasospasm had no direct effect on outcome [28, 29, 34, 38]. Although it was found more frequently in the medium-risk group, its appearance in the low-risk and high-risk groups did not significantly alter the outcome profile which is determined by the severity of the initial haemorrhage.

Similar observations can be made in respect of high MCAV levels and fluctuating blood pressure.

The apparent association of vasospasm, high MCAV and fluctuating blood pressure may be explained by variations in the following; composition of the patient groups (risk-related), the incidence of rebleeding, and the effects of diagnostic delay. In high-risk patients these disturbances will be linked with a poor outcome, while in the low-risk group they are linked with a good outcome. Since outcome is determined by the initial event, these secondary effects remain incidental unless linked with rebleeding and/or diagnostic delay.

The literature offers a perplexing picture of the effects of intra-opertive events such as aneurysm rupture, temporary clipping, brain swelling and occlusion of perforators, varying from no discernible effect to disastrous results [3, 4, 36, 44]. An attempt to analyse the intra-operative events of patients in this study proved to be confusing without a number of factors being taken into account, and this analysis was facilitated by graphical modelling. Continuous assessment of the variables in the graphical model allowed those factors of significant predictive value to be taken into account throughout the patient's illness and treatment. For example, it could be shown that patients who had rebled were more likely to experience surgical problems and to have a poorer outcome. This result supports the argument for early diagnosis and surgery. Secondly, if an operative event occurred, such as rupture, temporary clipping or brain swelling, patients in the high-risk and medium-risk groups had a significantly poorer outcome. This finding suggests that these patients, although considered clinically fit for operation, probably had a reduced capacity to withstand further pathophysiological challenges. Other surgical strategies may be indicated which avoid temporary clipping or operating in the face of brain swelling.

## Conclusions

Using the most powerful predictors of outcome the model identifies the high-risk patient. Throughout the course of their illness the high-risk patient will be significantly more susceptible to adverse events than the low-risk patient. Thus delay in diagnosis, rebleeding and adverse operative events will result in significant morbidity and mortality in the high-risk patient compared to the low-risk patient. The model enables the examination of various influences on outcome at each stage of a patient's illness, which in turn should identify appropriate treatment and surgical strategies for the individual patient. This is considerably different to the reliance on one or two factors of immediate interest (fluctuating level of consciousness or blood pressure, increasing Doppler velocity, angiographic spasm) while neglecting significant factors that have already occurred (extensive blood on CT scan, decreased level of consciousness in the first 72 hours, previous rebleed) which in effect have determined the patient's outcome profile.

The present study has revealed possible causal pathways of clinical events, as well as their direct and indirect effects, on outcome. If future studies support

these results, it would be possible to construct a model to predict outcome, which would aid the clinician in determining the most appropriate regime of treatment for a particular patient.

It may be advantageous for future workers to stratify their patients according to risk groups, diagnostic delay and rebleeding in the analysis and reporting of results.

The graphic model identified three significant predictive factors; risk grouping, rebleeding and delay in diagnosis. Patients, when the SAH is recognised, were placed in risk groups calculated by the severity of the haemorrhage. Patients remain in their risk groups throughout the period of their illness. Notwithstanding the predetermined nature of the risk groups which predict outcome, the predicted course in medium-risk patients may be altered by prompt diagnosis and early operation combined with aggressive pre and post operative management, so avoiding rebleeding. While the same management strategy may be adopted with the high-risk patients, we suspect that they require immediate and sustained additional intensive therapy support to maintain cerebral perfusion. There were within the study patients some whose initial ictus went unrecognised and they were only diagnosed after an additional event – delayed diagnosis. The outcome in this delayed group of patients was poorer. Aggressive management may improve their outcome. Although clearly, early diagnosis and treatment would be the preferred option.

The legacy of the appalling outcome from the initial haemorrhage and the predicted course following aneurysmal rupture has resulted in no major improvement over the years in the management morbidity and mortality of this condition [17, 35]. Action before rupture leading to the identification and prophylactic treatment of intracranial aneurysms, even with the inherent difficulties of this option, may be the way to achieve a significant improvement in the overall outcome of these patients.

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## Comments

This is a prospective study relating the severity of the initial aneurysmal subarachnoid haemorrhage on the outcome of surgical treatment. The severity of haemorrhage was determined with a method described previously by the authors and based on the clinical assessment and CT criteria. A multiplicity of factors that could influence the outcome were analysed and evaluated using a statistical tool (a temporal graphic chain model) developed in the Southampton University. This method enables identification of associations and causal sequences between various factors influencing the clinical course and final outcome.

A very important finding of the study indicates, that the individual patient's outcome is determined principally by the severity of the initial SAH and the management can only reduce the occurrence of adverse events like diagnostic delay and resulting rebleeding. This is in agreement with the results of my experimental studies on SAH showing that SAH reduces capacity of brain blood circulation to compensate for secondary blood flow reduction. The study showed that preoperative clinical status (grade) was not good predictor of outcome in aneurysmal SAH. This result revises a very common opinion on the prognostic factors in the treatment of SAH.

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This paper from the Southampton group stresses some very important facts. Neither age nor clinical grading is sufficient for predicting outcome after SAH and aneurysm clipping. We will in our institution try to approach our patients in a similar way in order to check the presented results.

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