ORIGINAL ARTICLE

Factors affecting outcome in poor grade subarachnoid haemorrhage: An institutional study

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ABSTRACT

Context: Poor grade subarachnoid hemorrhage (SAH) is usually associated with unfavorable outcomes and optimal management is deemed complicated. Most centres follow an expectant management strategy or a less aggressive approach till patients improve to good clinical grades. This approach has been associated with higher mortality and morbidity. However, not all patients with poor clinical condition fare badly. Identification and early aggressive management of this select group of patients may lead to favorable outcomes.

Settings and Design: Prospective non-randomized study.

Materials and Methods: We prospectively analyzed 19 cases presented in WFNS grade 4 and 5 and factors affecting their outcome at a tertiary care centre in south India. This study was aimed at identifying those few poor grade patients who are probable candidates for a good outcome.

Statistical Analysis Used: All the variables were analyzed for possible correlations with the SPSS version 13 software. The Chi-square test with a $P < 0.05$ was taken as statistically significant.

Results: Of 19 cases, 13 were operated and good outcome was seen in 53.8% of the patients who underwent surgery and aggressive management. All 7 patients who were managed conservatively died. 15.8% of the patients had low density changes ($P = 0.625$). Absence of such changes was associated with a good long term outcome ($P = 0.004$). 9 patients had intraventricular hemorrhage at presentation and 5 patients having hydrocephalus underwent extra-ventricular drainage. Statistically significant factors precluding good outcome were the presence of infarcts and thick SAH in the cisterns.

Conclusions: Poor grade (WFNS 4 and 5) SAH patients with or without ICH, IVH, if operated within 3 days can give rise to favorable outcome in around 50%. However, presence of patchy infarcts associated with thick subarachnoid blood (Fisher grade 3) precludes long term survival or meaningful recovery. Hence, aggressive management is unlikely to alter the natural history of such patients.

Key words: Aneurysm, poor grade, subarachnoid hemorrhage

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is associated with a mortality of 40-60% due to the initial bleed and further 20-25% seeking medical attention later in poor clinical condition and hence, is termed as poor grade patients.[1] Poor grade SAH management is as complicated as much as it is controversial and its management is directly related to the underlying aetiology including intracerebral hemorrhage (ICH), hydrocephalus (HC), intraventricular hemorrhage (IVH) and vasospasm, with or without cortical and sub cortical infarcts. There is a group of SAH patients who present in poor clinical status without any recognizable imageological cause for the same. Literature has provided enough insights into this intriguing entity with a dismal prognosis. However, timely aggressive management may lead to certain degree of improvement in these patients and early/ultra-early surgical treatment should be instituted in them in order to reverse the clinical state in at least few of them. This study is aimed to identify the factors affecting the outcome and streamline the management protocol for those few poor grade SAH patients who can "*still*" have a better outcome than the rest of the group. We analyze the results of poor grade SAH at our tertiary care centre and review the literature in the light of the same.

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Materials and Methods

Between January 2008 and September 2011, 19 patients were admitted at our centre. We evaluated all patients prospectively with the following inclusion criteria:

1. Diagnosis of SAH, and poor clinical grade, defined as World Federation of Neurological Societies (WFNS) Grade IV or V at admission.
2. SAH confirmed by computerized tomography (CT) and the presence of an aneurysm diagnosed by four-vessel angiography.

Management protocol

All patients were managed according to a standardized policy that included aggressive pre and preoperative resuscitation, surgery, aggressive prevention and treatment of intracranial hypertension and vasospasm.

Preoperative care

Management included intubation, ventilation along with mannitol, phenytoin and nimodipine being administrated in emergency ward or intensive care unit. When the patient was stable immediate plain CT of brain and four vessel angiogram was done. In case of neurological deterioration CT scan of brain was done and any fresh changes were noted. An external ventricular drainage, either by bedside twist drill or reservoir placement in operation theatre was done in patients showing ventriculomegaly or intraventricular hemorrhage (IVH).

Operative technique

A standard surgical approach was used. After craniotomy brain relaxation was achieved by diuresis (mannitol 1-2 mg/kg and furosemide 20-40 mg) and cerebrospinal fluid (CSF) drainage and hyper ventilation or in combination. Normotension was maintained throughout the surgery. Standard microvascular techniques and magnification were used in all cases to obliterate the aneurysm. Lax duraplasty was performed when ever brain was tense using pericranial flap and the bone flap was replaced.

Postoperative care

Hypervolemia, hypertension and hemodilution (Triple H therapy) was initiated in all patients. Postoperative CT scan was done routinely and patients showing new hypodensities were considered as having symptomatic vasospasm and intracisternal papavarine (1 mg), which was given eighth hourly until patient showed clinical improvement. Tracheostomy was done to facilitate bronchial toileting if patients required endotracheal tube for more than 4-5 days.

Patient outcome

Outcome was assessed at the time of discharge and at 1, 3, 6 and 12 months according to the glasgow outcome scale (GOS). Patients with a GOS score of 4 and 5 were classified as having a favorable outcome. Patients who died or were not capable of living independently were classified as having an unfavorable outcome.

Results

In the study period, total number of patients admitted at our centre with SAH was 160 and of which 19 were in poor grade. The incidence of poor grade SAH is 11.89% in our study. Most of the patients, i.e., 52.6% fell in the age group of 41-60 years and 26.3% were greater than 60 years. The mean age of the patients was 51.3 years. Of the total cases 11 were females and 8 were males, suggestive of a slight female preponderance with ratio of 1:1.4. The mean age among females was slightly higher than males i.e., 55.3 and 44.4 years respectively. Most of the cases (68.4%) were admitted within 5 days of ictus and the mean duration of ictus was 5.94 days. Only 3 cases presented 20 or more days after ictus. The timing of surgery was classified as acute (<3 days), early (4-7 days) and late (>7 days). 61.5% of cases were operated after 7 days (late) following ictus whereas only 30.8% were operated within 3 days of ictus [Table 1]. The earliest surgery was on the day 1 following the ictus while the maximum duration between the ictus and surgery was 28 days. The mean duration between ictus and surgery was 11.3 days. Grade of SAH was decided based on WFNS grading system and most of the cases (18) were in WFNS grade 4 (94.7%) and only 1 (5.3) patient presented with grade 5. Fishers grading was done based on CT scan imaging and all the cases were in Fishers Grade 3 (36.8%) or Grade 4 (63.2%). None of the cases had Fishers Grade 1 or Grade 2. Out of 19 cases, 13 cases (68.4%) had co-morbidities, hypertension being the most common presentation in 12 cases (63.1%). Other conditions included diabetes mellitus in 5 patients (26.3%), cerebro-vascular accident (CVA) in 2 patients (10.5%), coronary arterial disease in 1 patient (5.3%) and 1 patient had all the 4 co-morbidities together. 17 (89.5%) out of 19 cases under went four vessel cerebral digital subtraction angiogram (DSA) study and 19 aneurysms in 17 cases with 2 cases (11.8%) harboring 2 aneurysms were diagnosed. Of the 19 aneurysms encountered, anterior communicating artery aneurysms were most common i.e., 7 cases (36.8%) and middle cerebral artery (MCA) were 5 (26.3%), internal cerebral artery and posterior circulation were 3 (15.8%) each and 1 case (5.3%) had distal anterior cerebral artery (DACA) aneurysm. Pre operative vasospasm was seen in 8 patients (47%) on angiography. 13 (68.4%) out of 19 cases underwent surgery and 6 cases were not operated due to various reasons. 9 (69.3%) out of 13 patients underwent surgery through pterional craniotomy, 3 cases (23%) underwent fronto-temporo-orbital (FTO) craniotomy and 1 patient harbouring vertebral artery (V-4 segment) aneurysm underwent surgery by far lateral approach. Temporary clipping was done in 84.6% of the cases and 15.4% cases did not require temporary clipping. Intra operatively brain swelling was encountered in only 3 patients (23%). Gyrus rectus resection was done in 2 cases to facilitate clipping of aneurysm. Pre operative interventions in the form of extra ventricular drainage were done in

Table 1: Summary of the patient data

Age	Gender	Day of surgery	Site of aneurism	Vasospasm	Fishers grade	IVH/ ICH	INFARCTS	Brain swelling	Temporary clipping	GOS discharge	1 month	3 month	6 months	1 year
60	F	3	A.com	No	4	IVH	No	No	Yes	3	3	4	4	5
62	F	14	A.com	No	4	IVH	No	No	Yes	3	3	4	4	5
35	M		A.com	Yes	3	NO	No	No	No	1	1	1	1	1
65	F	18	Left M1	Yes	4	IVH	No	No	Yes	2	1	1	1	1
42	M	2	A2	No	4	ICH	No	No	Yes	3	1	1	1	1
65	M	28	A.com	No	4	ICH	No	Yes	Yes	5	5	5	5	5
40	M	9	Right P1	Yes	3	NO	No	No	Yes	2	3	1	1	1
54	F	16	Left M1	Yes	3	NO	Yes	No	Yes	2	1	1	1	1
60	F		Right P.com Left MCA	No	4	IVH/ ICH	No			1	1	1	1	1
45	F		Basilar	Yes	4	IVH	No			1	1	1	1	1
35	F	3	Left M1	Yes	4	ICH	No	No	No	3	3	3	4	4
63	F	4	Right V4	No	3	NO	No	No	Yes	4	4	4	1	1
52	M	17	A.com	Yes	4	IVH/ ICH	No	No	Yes	4	4	5	5	5
50	F		Left P.com	No	3	NO	No			1	1	1	1	1
63	M	1	Left M1	No	4	ICH	No	Yes	Yes	4	5	5	5	5
58	F	22	Left ICA	No	4	IVH	No			1	1	1	1	1
57	F	10	Left A1, Left DACA	Yes	3	IVH	No	Yes	Yes	4	5	5	1	5
55	F				4	IVH	Yes			1	1	1	1	1
14	M				3	NO	Yes			1	1	1	1	1

DACA – Distal anterior cerebral artery; GOS – Glasgow outcome scale; IVH – Intraventricular hemorrhage; ICH – Intracerebral hemorrhage; MCA – Middle cerebral artery

5 cases (26.3%) and 4 of them showed improvement following the procedure. Outcomes of all the patients at various intervals were analyzed at the time of discharge and during follow up at 1, 3, 6 and 12 months according to Glasgow outcome scale [Tables 1-3]. The GOS grade at the time of discharge was analyzed and the most common score was Grade 1 in 9 cases (47.5) and followed by grade 4 in 4 cases (21%) and rest of the 6 cases were distributed equally in grade 2, 3 and 5 [Figures 1 and 2]. Moreover, the GOS score of 4 and 5 was seen in 7 out of 13 patients (53.8%) who underwent surgery. All the cases with GOS 1, 2 and 3 were grouped under unfavorable outcome and those with 4 and 5 were grouped under favorable outcomes respectively. The 6 cases that were not operated had multiple factors like lack of consent, absent brain stem reflexes and poor hemodynamic status. The details are summarized in Table 1.

Statistical analysis

All the variables were analyzed for possible correlations with the SPSS version 13 software. The Chi-square test with a $P < 0.05$ was taken as statistically significant. There was no correlation between the age of the patient and the outcome at discharge or at 6 months follow up ($P = 0.568$). Most of the patients were in the age group of 41-60 years, but their outcomes were not showing any significant difference from the other age groups ($P = 0.421$). There was no significant difference in the outcomes based on the gender ($P = 0.267$). 17 out of 19 cases underwent pre-operative angiogram and vasospasm was evident in 42.1% (8) of cases. However, no significant correlation was seen in the overall outcome at the time of discharge ($P = 0.667$) or at 6 months ($P = 0.75$). 7 (36.8%) cases had Fishers grade 3 and 12 (63.2%) patients had Fishers grade 4 SAH and no correlation was found in outcome at the time of discharge or at 6 months. 31.6% of patients had intracerebral hematoma and there was no correlation in outcome at the time of discharge ($P = 0.67$) or at 6 months.

Table 2: Outcome following surgery

Outcome	Frequency	Percentage
Good	7	53.8
Poor	6	46.2
Total	13	100

Table 3: Patients with GOS scores at various periods of follow up

Months after discharge/ GOS grade	1 month	3 months	6 months	12 months
GOS 5	3	4	4	6
GOS 4	2	3	3	1
GOS 3	4	1	0	0
GOS 2	0	0	0	0
GOS 1	10	11	12	12
Total	19	19	19	19

GOS – Glasgow outcome scale

47.4% (9) of the patients had intraventricular hemorrhage and no correlation was found in outcome at the time of discharge ($P = 0.667$). Even though good outcome was seen at 6 months in those patients, statistical significance could not be attained. 15.8% (3) of the patients had low density changes [Figure 3] and no correlation was found at the time of discharge ($P = 0.625$). However, absence of these changes was associated with good outcome at 6 months ($P = 0.004$). 9 (47.4%) out of 19 patients had intraventricular hemorrhage and 5 patients had intervention in the form of extra-ventricular drainage. 3 patients improved in GCS while 1 patient had good outcome at discharge and 2 had good outcome at 6 months (no statistical significance was attained though). Route of surgery did not affect the outcome at the time of discharge or at 6 months but all the patients who did not undergo surgery died at the time of discharge and positive correlation with surgery was found at 6 months. Brain swelling was encountered in 25% (3) of the cases and all the 3 cases had good outcome at the time of discharge and also, at 6 months but it was not found to be statistically significant ($P = 0.222$). Intraoperatively, temporary clipping was used in 11 of 13 cases and no correlation was found in the outcome at the time of discharge ($P = 0.228$) or at 6 months ($P = 0.538$).

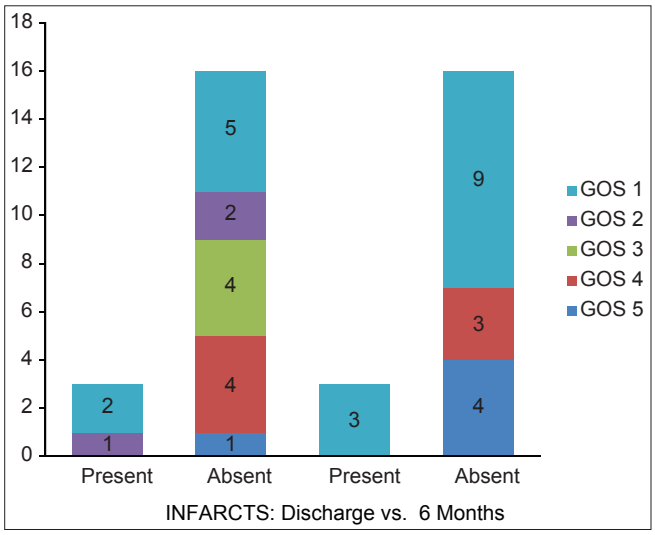

Figure 1: GOS scores at various periods of follow up

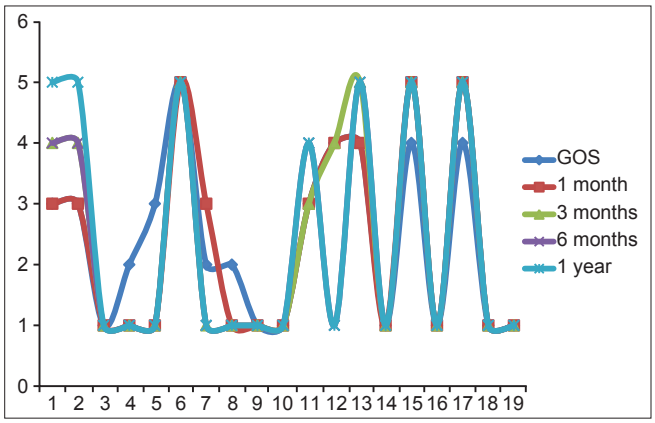

Figure 2: Trends of GOS with time

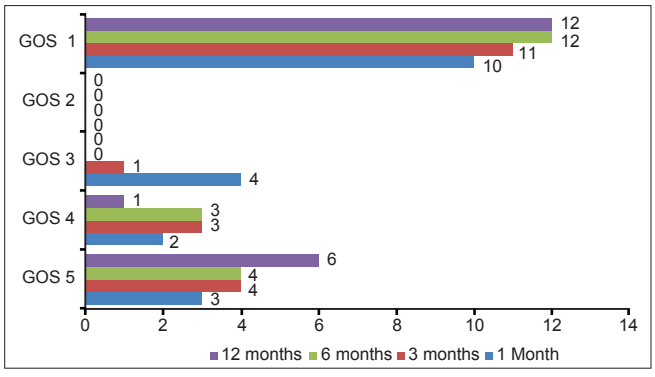

Figure 3: Relation between low densities and GOS at discharge and at 6 months

Discussion

This prospective study describes our experience with the management of 19 random patients of SAH who were classified at admission as WFNS Grade IV or V after aneurysm rupture. Overall 38.3% of WFNS Grades IV and V patients experienced a good outcome while 53.8% of the operated patients had a favorable outcome. Although outcome was largely determined by the initial hemorrhage and its immediate pathophysiological consequences, attempting to select patients who are probable candidates likely to benefit from surgery remains a difficult task.

The incidence of this condition among all the cases of SAH has ranged from 25 to 45%.[2-5] In the present study, the incidence was 12%, which concurs with that reported in the literature. The mean age at diagnosis in our study was 51.3 years, which is slightly lower than that described in literature. Many studies suggest that, advanced age is associated with poor outcome after SAH; other studies demonstrate that old and young people in the same clinical condition experience a similar outcome.[6-9] There are several important considerations when evaluating the association between age and outcome: (1) Patients older than 65 years are frequently excluded from admission or active treatment,[10,11] this exclusion exerting a considerable influence on outcome; (2) Older patients are more frequently in poor clinical grade,[12,13] which has a greater impact on outcome than age;[14] and (3) Other variables such as hypertension or atherosclerosis are more frequent in elderly patients, and these factors taken independently may have an adverse effect on outcome.[6] In our series, bivariate analysis demonstrated no association between advanced age and poor outcome. Co-morbidities especially, hypertension, diabetes and coronary artery disease in SAH patients are known to be associated with poor outcome. In our patients, hypertension was the most common co-morbidity followed by diabetes

mellitus and none of them had a significant correlation to the outcome.

Poor clinical grade is unquestionably associated with unfavorable outcome. Comparison of the results obtained from other studies suggests that outcome is favorably influenced by an aggressive approach, including rapid resuscitation and control of Intra-cranial pressure (ICP), early surgery, optimal intensive care and prophylaxis against delayed ischemia. More than 90% of untreated poor-grade patients die.[13,15-17] When the treatment is delayed in order to expect clinical improvement prior to surgery, unfavorable outcomes are observed.[18-20] The most important and common finding in all the studies has been that in patients who were managed expectantly mortality almost reached 100% and the common cause being either rebleed or ischemic damage to the brain due to vasospasm[2] and hence, early aneurysmal obliteration is the only way to prevent it so that vasospasm can be managed more aggressively with triple H therapy. In our study, 5 cases were operated early and 4 cases had favorable outcome at the time of discharge but at 6 months 3 out of them died. Hence, the long term outcome in these patients was unfavorable although these deaths were not related to the surgery or the disease *per se*. Sasaki *et al*.[21] advocated close monitoring in the first 24 hours for grade change to identify a select group that can benefit from surgery at earlier stage. Ventricular drainage and aggressive management of the selected patients who demonstrated clinical improvement is a common strategy used to manage poor-grade patients.[14,18,22,23] We had 9 cases with intraventricular hemorrhage and resulting ventriculomegaly in 4 cases and all the cases underwent external ventricular drainage and 3 showed improvements in their clinical grades. The outcome at the time of discharge was not affected by the EVD but at 6 months there was improvement in outcome which suggests that early EVD to relieve raised ICP has good results in long term.

We inferred that hydrocephalus, amount of blood (Fishers grade) and hypodensities on CT were associated with poorer outcome.[24] Macdonald *et al*. evaluated the factors associated with vasospasm.[25] The SAH on the admission CT scan was classified, based on the maximal amount of blood, as none diffuse thin or thick, or localized thin or thick, and IVH/ICH were recorded as present or absent. Of the 3567 patients, thick SAH was observed on the admission CT scan in 66%, IVH was present in 45%, ICH was present in 23%, and vasospasm developed in 30%. For all patients, significant predictors of vasospasm were: Age (peak incidence among patients 40-59 years old); history of hypertension; neurological grade; cisternal blood clot thickness; aneurysm size; presence of IVH without ICH. However, in our series all the cases were in either Fisher 3 or 4 and those with Fishers 4 had better outcome than Fisher 3 which suggests that thick clots in subarachnoid space is associated with vasospasm and ischemia resulting in an overall poor outcome.

Magnetic resonance (MR) diffusion-weighted imaging (DWI) is a powerful tool for the non-invasive detection of early ischemia[26] and provides higher sensitivity than CT scans for the evaluation of primary brain damage with acute SAH in experimental models.[27] Hadeishi and his colleagues found that five of seven patients with acute poor-grade SAH (WFNS grades 4 and 5) had widespread multifocal patchy infarcts throughout the brain, possibly caused by focal disturbances in cerebral perfusion throughout the brain due to dramatically increased intracranial pressure.[28] In our series none of the patients had MRI due to financial constraints but the patients who had hypodensities on CT scan suggestive of infarcts were associated with poor outcome.

The site of the bled aneurysm dictated the route of approach and most of the aneurysms (69.2%) were operated by the pterional approach. Frontotemporo-orbital route was used in 3 cases and far lateral route in 1 case. The route of approach did not affect the outcome which correlates with study by Le Roux *et al*.[22] Also, the cooperative study has mentioned that there was no significant difference in the outcome based on the timing of surgery.[29,30] Various studies reported similar findings including one by Mizoi *et al.* where the authors mentioned that, though the incidence of good result was the same in both early and late operated cases, the morbidity was lower in the early cases and mortality was higher.[31,32] In a study of 159 patients by Le Roux *et al*.[22] all the patients were managed aggressively and the mortality was low[33,34] and favorable outcome was seen in 38.4%. In an another study by Laidlaw *et al*.,[2] the only series where the authors advocated early surgery in all the patients unselected by age or grade, the mortality was less in grade 4 and 5 patients, a finding observed by other authors as well.[14,18,19,35] In our series those patients who were operated within 4 days of ictus had no effect on the outcome at the time of discharge. But, at 6 months there was a statistically significant difference from those who were operated after 4 days. Ultra early surgery (performed within 24 hrs of ictus) has gained popularity in good grade SAH patients but many surgeons feel that tense brain would increase difficulty in dissection and clipping of the aneurysm.[2] There have been studies demonstrating that the incidence of complications such as failure to occlude the aneurysm, intra-operative ruptures or surgical contusions fared similar in all grades.[2] Le Roux *et al*.[36] concluded that except for cerebral swelling, the risks of complications are same in all grades. In our series we encountered brain swelling in 3 of 13 cases and all the patients had good outcome both at the time of discharge and at 6 months follow up. It was also suggested that wider craniotomy may not only help in overcoming the tense brain but also to tackle the raised intracranial pressure.[37]

Future prospects and present limitations of the study

Infarcts seen as the low density on CT scan are better visualized and earlier identified on MR diffusion and future study with such tools is recommended. The present study consists of small number of patients. This may probably be due to the nihilism and pessimistic attitude towards poor grade SAH patients leading to non-referrals from the secondary, less experienced centres. However, large numbers of patients are required to be included in the study to further substantiate the observations.

Conclusions

Poor grade (WFNS 4 and 5) SAH patients with or without ICH, IVH, if operated within 3 days can give rise to favorable outcome in around 50%. However, presence of patchy infarcts associated with thick subarachnoid blood (Fisher grade 3) precludes long term survival or meaningful recovery. Hence, aggressive management is unlikely to alter the natural history of such patients.

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