Clinical Demographic Association and Outcome in Patients with Aneurysmal Subarachnoid Hemorrhage

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Abstract

Introduction   Even in this modern era of neurosurgery, we could not achieve 0% mortality in operated aneurysmal subarachnoid hemorrhage (SAH) patients. An analysis of factors affecting outcome was never published in detail, and a recent update of guidelines for management of aneurysm SAH noted deficiency in knowledge about this issue.

Objective   The study aims to assess the effect of various factors on the outcome of operated aneurysmal SAH patients.

Methods   The various factors regarding age, sex, associated chronic diseases, clinical condition of patients, surgery interval, and nature of aneurysm were correlated with outcomes of 345 operated aneurismal SAH patients. Statistical analysis was done by chi-square test and logistic regression.

Results   As per grade, patients' survival is 80.16% for fair grade and 21.65 % for poor grade, which was statistically significant ($p < 0.001$). No significant difference was observed for other factors analyzed independently ($p > 0.05$). On comparing with Hunt and Hess (H-H) grade, all the above-mentioned variables showed significantly better survival in fair grade than in poor grade ($p < 0.05$). The Wald criteria demonstrated that only H-H grade made a significant contribution to prediction.

Conclusion   Although a number of factors seem to affect the outcome of aneurismal SAH patients, it is the grade at presentation, which comes out to be an independent variable, influencing the outcome of patients. Patients presented with fair grade tend to have better outcome than those presented with poor grade. All other factors do not have significant impact over the outcome of clipped aneurysm patients with SAH.

Keywords
► aneurysm
► subarachnoid hemorrhage
► clipping
► Hunt and Hess grade

Introduction

The incidence of serious cerebrovascular conditions has substantially decreased in the last three decades,[1] but the incidence of aneurysmal subarachnoid hemorrhage (SAH), however, has not changed and remains approximately 1 per 10,000 people annually.[2,3] SAH because of the rupture of an intracranial aneurysm is a potentially fatal event. Although it accounts for 5% of all strokes but its burden is relevant due to high mortality, high disability, and higher incidence in the young.[4] Among those who suffer aneurysmal SAH, 12% may die before seeking medical attention and 40% die within the first month after the bleeding.[5]

Despite the great advances in diagnostic modalities and availability of dedicated neurosurgical care, mortality of aneurysm surgery is still high and 0% mortality has not been

achieved yet.[6] Case fatality rate for SAH is still reported between 8.3 and 66.7%, with most patients dying as a result of the initial bleed or its immediate complications.[7]

Analysis of factors affecting outcome has never been published in detail.[8] Several studies have been made to examine factors that affect outcome after aneurysmal SAH, but only three included sufficient patients to allow analysis of the effect of multiple independent factors.[8–10] A recent update of guidelines for management of aneurysm SAH noted deficiency in knowledge regarding this issue.[10] There are several reports from India regarding the outcome after surgical clipping or coiling of aneurysms, but few reports present the overall outcome of all patients with SAH.[5,7,11,12]

Most of the previous studies done having inconsistence agreement regarding the influence of various clinicodemographic factors as well as nature of pathology to the overall outcome of the patients but clinical grade admission seems to be the most reliable one.

The study was conducted with the aim to test the effect of various clinicodemographic factors on the outcome of operated aneurysmal patients with SAH and to find out the most reliable factor predicting the outcome (survival).

Patients and Methods

This study is an observational descriptive study. The study was conducted from June 2013 to July 2014 (almost 1 year) and the study was conducted at Department of Neurosurgery of Sawai Man Singh Medical College and Hospital, Jaipur. A total of 345 patients (1985–2013) who underwent aneurysmal clipping (SUGITA CLIP) were included in the study. Data were collected retrospectively through case files.

All patients operated for aneurysmal clipping were included in the study and all those patients not operated either because of very low general medical condition/ hemodynamic instability and preferentially referred patients for endovascular management were excluded from study.

Almost all the cases were operated by single, most experienced neurosurgeon in the department, to compound the expertise and skill bias. All patients were managed in dedicated neurosurgery intensive care unit during postoperative period, treated with intravenous nimodipine. Outcome was analyzed in terms of whether patient survived (irrespective of neurological status) or expired.

Preintervention Assessment

All patients presented in Sawai Man Singh hospital emergency as either case of stoke or head injury. All these patients initially got plain computed tomographic (CT) head and CT angio brain done. Four-vessel digital subtraction angiography was done for those patients in whom either CT angiography was negative and suspicion was high or further information with respect to aneurysmal morphological configuration and spatial orientation was desired by the treating neurosurgeon.

The various clinicodemographic factors, that is, age, sex, and associated chronic illness in patients were assessed.

Surgical delay was calculated by considering difference between onset of ictus and date of surgery. Characteristic of aneurysm were defined regarding number and site of aneurysm. The sites considered were aneurysms involving either anterior circulation (anterior communicating artery [ACOM], internal carotid artery [ICA], middle cerebral artery [MCA], distal anterior cerebral artery [DACA], and posterior communicating artery [PCOM]) or posterior circulation (posterior inferior cerebellar artery [PICA] and vertebral arteries [VCA]). Preoperative clinical condition was graded from 0 to 5, according to Hunt and Hess grading scale (H–H grade), further categorized into fair grade (H–H grades 1, 2, and 3), and poor grade (H–H 4 and 5).

All the patients underwent baseline work-up and preanesthetic check-up, and they were optimized for the intervention. The patients in the poor grade were managed initially with conservative measures with supportive measures, including ventilatory support (if required). Any cause for poor neurological status was addressed; for example, hydrocephalus was managed with either a ventriculoperitoneal shunt or external ventricular drain.

A few patients with poor grade come to us after a considerable delay (referral delay), in later half of vasospasm period, we managed them conservatively initially till subsidence of expected vasospastic period and then were considered for surgical intervention if found appropriate.

Statistical Analysis

The qualitative or categorical variables were described as frequencies, proportion and percentage, and the quantitative data were presented as mean ($\pm$ standard deviation [SD]). Difference in proportions was compared using chi-square test. Logistic regression analysis was performed to predict the survival of aneurysmal patients with SAH with various variables. All statistical tests were two-sided and a probability value < 0.05 was taken as significant.

Results

This study included 345 patients operated for aneurysmal clipping, of which 176 were males (51%) and 169 were females (49%) with a mean age of 45.43 ± 12.47 years (►Fig. 1), and 180 patients presented with associated comorbidities such as hypertension, diabetes, etc.

Among 345 operated patients, 284 patients were in fair grade and 61 were in poor grade. In our study, most common site for aneurysm was found to be situated at ACOM followed by MCA, and then ICA. Multiple aneurysms constituted 8.11% of the total.

Most of our patients (199) presented within vasospastic period (5–20 days), with 136 patients presented less than 4 days and a few presented after a considerable delay (> 21 days). Mean surgical interval was 6.5 days with SD ± 4.3 (►Table 1).

A logistic regression analysis was done to predict survival for 345 patients of aneurysmal SAH using age, sex, number of aneurysm, H–H grade, treatment delay, and comorbidity as predictors. A test of full model was statistically significant

indicating that the predictors as asset reliably distinguish between survival and death outcome. (chi-square, 62.127; df, 6; $p < 0.000$). Also, the Hosmer and Lemshow test shows a good fit by high p-value and low chi-square value (chi-square 15.384, df 8, $p < 0.052$). NegelKerke R^2 of 0.237 indicates fair relationship between predictors and grouping. Prediction success overall was 78.6% (for survival 93.2% and for death 40.2%). The Wald criteria demonstrated that only H–H ($p > 0.00$) made a significant contribution to prediction. Other predictors were found to be not significant.

H–H as predictor: exponential value 0.428 indicated that when H–H is raised by one unit, the odds ratio is 0.428 times as large and therefore patients are 0.428 times more likely to survive (►Table 2).

Discussion

To predict the outcome in patients operated for aneurysmal SAH, surgeons have investigated the factors influencing the treatment outcome, but there are still disputes in literature about the majority of such factors.[13] No agreements have yet been reached about the ideal timing for surgery[8–10,14] nor about the dependence of the postoperative outcome associated with aneurysmal size and site[13,15–17] patient's gender and age[8,9,11,13,15] chronic diseases[9,13,15] preoperative clinical condition (►Fig. 2).[5,7,10,11,15,17–22]

As per grade, patients' survival is 80.16% for fair grade and 21.65% for poor grade which was statistically significant ($p < 0.001$). As H–H grade increases, survival becomes significantly poorer. This fact is supported by most of the studies done in past.[5,7,10,11,15,17–22]

Bonilha et al in 2001[18] performed a prospective study in patients with ruptured aneurysm and observed that the clinical condition (H–H scale) assessed upon the moment of surgery showed significant correlation ($p = 0.0002$) with outcome.

Rosengart et al in 2007[15] analyzed data from 3,567 patients with aneurysmal SAH enrolled in four randomized clinical trials and concluded that unfavorable outcome was associated with worsening neurological grade.

A recent prospective study was conducted in Post Graduate Institute of Medical Education & Research,

Chandigarh, by Harsimrat Bir Singh Sodhi,[7] during 10-month period, including 330 patients, taken for intervention for ruptured aneurysm. The study shows that higher the grade at presentation was predictor of poor outcome (odds ratio [OR]: 35.1, 95% confidence interval (CI): 10.8–114.7).

This study showed that survival becomes poorer as age advances. But statistical analysis showed no significant difference in outcome among different age group per se. When outcome was analyzed as per different grades, there was significantly good outcome in more than 20 years age group, in fair grade (80%) then poor grade (30%) (p-value < 0.05), but younger than 20 years, grade does not have any impact ($p = 0.16$ NS).

Duong et al[23] reported good outcome in 87% of patients older than 60 years, 91% of those ranged between 30 and 59 years and in all the patients younger than 30 years.

Lanzino et al in 1996,[24] Rosengart et al in 2007,[15] and Shingare et al in 2011[11] concluded that poor outcome is associated with increasing age of patients whereas Roganović and Pavlićević in 2002[13] contradict the issue by saying that age does not affect the outcome of the patients.

Better results younger than 20 years of age are probably because of the fact of better regenerative capacity/neural plasticity compared with adult ones.

Although overall survival seems to be better in male patients, 74.43% in comparison to 69.23% in females, statistically no significant difference was observed. Although significant differences were observed while comparing fair H–H grade as compared with poor H–H grade. Literature has contradictory opinion about the association of sex with outcome in patients with aneurysmal SAH. Some studies support the view[7,16,25] while some oppose it.[26]

Of 345 patients, 180 patients presented with associated comorbidities such as hypertension, COPD, diabetes etc. Overall survival appears to be better in absence of comorbidities (72.22%) as compared with its presence (71.51%), but statistically no significant difference was observed between the two. When outcome compared according to grade, significant difference was observed in fair grade (80.98%) as compared with poor grade (29.52%) of H–H scale ($p < 0.001$ HS).

Various congenital as well as acquired causes have been implicated in the etiology of aneurysm formation, among which hypertension is the most frequently studied risk factor associated with an increased risk of aneurysmal SAH as well as unruptured intracranial aneurysm. Patients with hypertension had a nearly sevenfold higher risk of aneurysmal SAH.[26,27] Previous studies also having conflicting opinion about its association. Some study negatively correlate,[13,15] and some does not reveal any association.[18]

No significant difference was observed according to time interval between the date of ictus and the date of surgery with the outcome, but significant difference was observed in fair grade as compared with poor grade of H–H scale in less than 20 days as compared with more than 20 days duration.
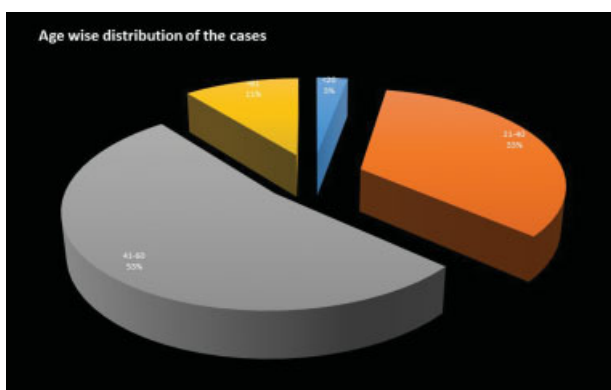

Fig. 1 Age wise distribution of the cases.

Table 1 The survival in patients with various clinical grade

S no	Variable		No of patients	Survived	Expired	% Survival	p-Value
1	Sex	Male	176	131	45	74.43	0.340 NS
		Female	169	117	52	69.2	
2	Age	< 20	10	9	1	90	0.228 NS
		21–40	116	82	34	70.68	
		41–60	182	135	47	74.17	
		> 60	37	22	15	59.45	
3	Comorbidities	Present	165	118	47	71.51	0.979 NS
		Absent	180	130	50	72.22	
4	Surgery interval	< 4 d	136	105	31	77.20	0.223 NS
		5–20 d	199	134	65	67.33	
		> 20 d	10	9	1	90	
5	Grade	Fair grade	284	230	54	81.0	< 0.001 HS
		Poor grade	61	18	43	29.50	
6	Site	ACOM	150	102	48	68.0	0.308 NS
		MCA	76	60	16	78.94	
		ICA	40	31	9	77.5	
		DACA	17	12	5	70.58	
		PCOM	29	23	6	79.31	
		PICA	3	2	1	66.67	
		VA	2	1	1	50	
		Multiple	28	17	11	60.71	

Abbreviations: ACOM, anterior communicating artery; DACA, distal anterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCOM, posterior communicating artery; PICA, posterior inferior cerebellar artery; VA, vertebral arteries.

This fallacy can be explained by the fact that after the interval of 21 days, vasospasm subsides, patients are hemodynamically stable and usually having better brain homeostatic conditions and hence resulting in better outcome in both the grades. But this does not give the impression that every patient should be operated after 21 days as there is always a risk of rebleed and deterioration.

The controversy over the optimum timing of surgery for patients with aneurysmal SAH has continued for many years. Early clipping of an aneurysm prevents rebleeding, a
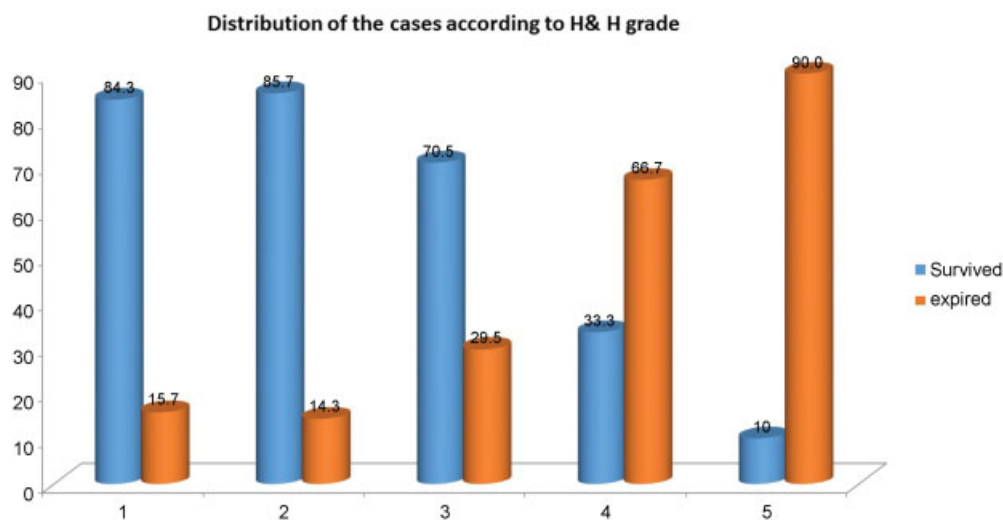

Fig. 2 Distribution of the cases according to H–H grade.

Table 2 Predictor of survival of aneurysmal patients with SAH with binary logistic regression

Variables in the equation								95% CI for Exp (B)	
		B	S.E.	Wald	df	Sig.	Exp (B)	Lower	Upper
Step 1[a]	Age	0.009	0.013	0.430	1	0.512	1.009	0.983	1.035
	Sex	−0.147	0.269	0.298	1	0.585	0.863	0.509	1.463
	Delay	−0.001	0.029	0.001	1	0.979	0.999	0.945	1.057
	H–H	0.848	0.124	47.099	1	0.000	2.335	1.833	2.975
	Aneurysm(1)	0.091	0.480	0.036	1	0.850	1.095	0.428	2.805
	Comorbidity	−0.318	0.327	0.951	1	0.330	0.727	0.383	1.379
	Constant	−2.781	1.191	5.453	1	0.020	0.062		

Abbreviations: CI, confidence interval; SAH, subarachnoid hemorrhage; H–H, Hunt and Hess.
[a]Variable(s) entered on step 1: age, sex, delay, H–H, aneurysm, comorbidity.

major cause of death after SAH. However, concerns about the possible deleterious effects of early surgery raise questions about the safety and efficacy of this approach.[26]

For fair grade patients, most of the studies accept that early surgery is going to improve the outcome.[14,16,28] But evidence for the optimum timing of surgery in poor grade patents is still insufficient.[29] The prognosis of poor grade patients is associated with significant morbidity and mortality.[17,30] Without surgical intervention, the mortality rate of poor grade patients can reach more than 90%.[31]

Ohman and Heiskanen[25] randomized 216 patients with SAH in clinical grades I to III (according to the H–H classification) into the following three operational groups: acute (0–3 days after SAH), intermediate (4–7 days after SAH), or late (after day 7). At 3 months post-SAH, clinical outcomes indicated that there was no difference in the prognosis of these three groups. In 2002, Ross et al[32] indicated that there were no significant difference at discharge or 6 months between the early group (day 1–3), intermediate group (day 4–10), and late group (day 11–21). However, this study was only concerned with the prognosis of surgical patient and ignored the relationship between clinical grades, rebleeding, and prognosis.

In 2002, de Gans et al[28], performed a systematic meta-analysis and showed that outcomes were better after early or intermediate surgery than after late surgery, in patients who were in good clinical condition at admission. For patients in poor clinical condition, results suggest only a trend toward a better outcome for early or intermediate surgery when compared with late surgery. So, timing of surgery cannot be designated as independent clinical variable determining the outcome in aneurysmal patients with SAH.

In this study, no significant difference was observed according to site of aneurysm with the outcome. To further refine the conclusion, outcome was assessed to various sites of aneurysm as per two different grades and results are significantly better outcome in ACOM, MCA, and ICA group in fair grade patients and no difference in outcome was found in patients with aneurysm at sites other than those aforementioned. We predict lesser aneurysmal SAH sequel

such as vasospasm and also less brain manipulation while approaching anterior circulation when compared with posterior circulation aneurysms.

Rosengart et al[15] in 2007 concluded that unfavorable outcome was associated with ruptured posterior circulation aneurysm. Shingare et al[11] in 2011 concluded that aneurysmal bleeding from anterior or posterior circulation do not influence the immediate outcome of patients with SAH.

The assumption that surgical outcome in patients with SAH with multiple intracranial aneurysms is actually worse than with single aneurysm is controversial.[23,33–37]

Our result also apparently reflects that multiple aneurysm patients having poorer prognosis then having single aneurysm (single 81.2 % vs. multiple 78.9%) but no significant difference was observed between these two group with the outcome ($p = 0.23$ NS).

Significant difference was observed in fair grade as compared with poor grade of H–H scale in the presence of single or multiple aneurysms.

In the studies by Rinne et al in 1995,[34] Kaminogo et al[19] in 2003, and Gaivas et al[38] in 2011, patients with multiple intracranial aneurysms had a higher mortality than patients harboring single intracranial aneurysms.

However, Orz et al[37] in 1996 reviewed surgical outcome of 221 cases with multiple intracranial aneurysms operated on during the years 1988 to 1994. They reported that there is no significant difference in the outcome of patients with single or multiple aneurysms, if they present with SAH. However, there is a marked difference seen, if presented without SAH.

Conclusion

Although several factors seem to affect the outcome of patients with SAH, it is the grade at presentation, which eligibles to be an independent variable influencing the outcome of patients. Patients presented with fair grade tend to have better outcome as compared with poor grade. All other factor such as age, gender, associated comorbidities, number, and site of aneurysm does not have significant impact in deciding the outcome of surgically clipped patients.

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