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Prospective Study of Prognostic Factors in Patients Undergoing Clipping for Aneurysmal Subarachnoid Haemorrhage in a Tier-3 Indian Setup

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Abstract

Purpose: Despite technical and medical advances, aneurysmal subarachnoid haemorrhage (SAH) continues to be a challenging pathology, associated with high rates of morbidity and mortality. The purpose of this study is to describe the various prognostic factors of the clinical outcome in the patients ofaneurysmal clipping for spontaneous SAH.

Methods: It was a prospective study where 48 patients hadmicrosurgical clipping for CT angiography confirmed saccular aneurysm. Various parameters studied were age, sex, hypertension, loss of consciousness, World Federation of Neurosurgical Societies (WFNS) grade and Hunt & Hess grade at admission, time of ictus to surgery, symptomatic vasospasm, Fisher grade of SAH, Hydrocephalus, neck: dome ratio, intra-operative rupture and temporary clipping time. The primary outcome measures were mortality and Glasgow outcome score (GOS) at three-months follow-up. Prognostic study was derived from analysis of these variables.

Results: Parameters found to be associated with unfavourable outcome were increasing age, hypertension, poor WFNS grade on admission, poor Hunt and Hess grade, higher Fisher grade, time of surgery and symptomatic vasospasm. WFNS grade, Hunt and Hess grade and Fisher grade were found having statistically significant correlation with neurological outcome of the aneurysmal SAH patients.

Conclusion: Microsurgical clipping is a safe and time-tested modality for treatment of SAH due to ruptured intracranial aneurysms. Higher WFNS grade, higher Hunt and Hess grade and higher Fisher grade are the factors leading to poor outcome in patients of ruptured intracranial aneurysm presenting with SAH.

Keywords: Prognostic factor; Subarachnoid haemorrhage; Intracranial aneurysm; Microsurgical clipping; Outcome.

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Introduction

Aneurysmal Subarachnoid Haemorrhage (SAH) accounts for 85% cases of spontaneous SAH.[1,2] Despite advancement in understanding of 3-D neurovascular anatomy, microsurgical techniques and intra-operative evaluation of accuracy of the procedure, management of aneurysmal SAH is still associated with high morbidity and mortality. Several studies have been done to delineate the factors responsible for the poor outcome in patients of aneurysmal clipping due to spontaneous SAH.[2-6] All these factors (Age, Hypertension, World Federation of Neurological Societies grade, Fisher grade, time of surgery, aneurysm morphology, temporary clip placement time, vasospasm and hydrocephalus), whether non-modifiable or modifiable, are the patient related factors which have been studied so far. Most of the studies were retrospective and were conducted at the centres of excellence. But in institution like ours which is the prototype of most government hospitals in India there are few institutional factors also, like lack of Digital Substraction Angiography (DSA) lab, improper Intensive Care facilities and lack of trained neurosurgery staff, which may affect the outcome

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of operated patients of aneurysmal SAH. These are the modifiable factors which may be worked upon to improve the outcome of aneurymal SAH. So we have done a comprehensive prospective study at our setup to evaluate all the factors responsible for poor prognosis in patients of aneurysmal SAH.

Material and Methods

This was a prospective longitudinal studyconducted at Post Graduate Institute of Medical Sciences, Rohtak, Haryana from October 2017 to September 2019. The study was done after taking approval of Institutional Ethics Committee Review Board. Majority of patients with spontaneous SAH presented to medical emergency where they were initially evaluated with Computed Tomography (CT) scan brain and routine investigations. A diagnostic CT angiography was performed as early as possible after admission. World Federation of Neurological Societies (WFNS) grading for clinical condition and Fisher grading for SAH on CT scan at the time of admission were done. All the patients were initially kept in neurosurgical ICU. Patients willing for endovascular coiling were referred to higher centre and patients willing for microsurgical clipping were taken up for surgery as soon as possible. After clipping patency of the vessel lumen is confirmed by ensuring distal pulsations under high magnification. All the patients were given HHH therapy and oral Nimodipine (60mg 4hourly). Postoperative CT scan was usually done on day 1 and at the time of discharge of the patient. Outcome was defined in terms of mortality and Glasgow Outcome Score (GOS) at 3 month follow-up.

Inclusion Criteria

1. Patients having CT angiographically confirmed ruptured aneurysm responsible for SAH
2. Patients willing for microsurgical clipping after understanding pros and cons of the surgery.

Exclusion Criteria

1. Patients having fusiform, mycotic, dissecting or traumatic aneurysm
2. Patients with SAH from other causes like ruptured arteriovenous malformation, hypertension, coagulopathy, meningitis or any other unknown cause.

Parameters Studied

The baseline demographic profile and clinical data including age, gender, chief complaints on admission, especially the history of loss of consciousness at ictus, WFNS grade at admission, time from ictus to surgery, concomitant diseases/ risk factors, and a previous history of SAH, were noted. Other significant parameters like Fisher grading of SAH on initial CT scan, presence of hydrocephalus, cerebral infarction, number of aneurysms, aneurysm localization, neck: dome ratio, status of associated vessels, intra-operative brain oedema, intra-operative rupture of aneurysm and temporary clip placement time were recorded. Postoperative complications including operative site hematoma, symptomatic vasospasm, dyselectrolytemia, pulmonary embolism and postoperative length of hospital stay were also recorded. All the variables were analyzed in relation to mortality and GOS score found at the 3 month follow-up.

Statistical Analysis

Data were summarized using descriptive statistics that included number or percentage of patients in each category as well as mean and standard deviation. Student's unpaired't' test, Chi-square test and other appropriate statistics as applicable were incorporated in the study for statistical inferences. Statistical analysis was performed using the Statistical package for the social sciences (IBM) for windows version 22. Two tailed P values were calculated and those less than 0.05 were considered significant.

Results

Total 48 patients had microsurgical clipping and were included in the study. Six patients were having decompressive craniectomy in the same sitting due to extensive brain oedema. Mean age was 51.13±12.2 year with age range 15-75 years. There were 25 female patients (52.08%) and 23 male patients (47.92%) with female to male ratio of 1.08. On comparing age distribution with sex there was female preponderance above the age of 50 years with female to male ratio of 1.9.

Common chief complaints of the patients were headache (68.8%), loss of consciousness (64.58%), hemiparesis (25%) and seizures (12.5%). On the basis of WFNS grading 75% patients were having good WFNS score (1-3) and 25% patients were having poor WFNS score (4 and 5) as shown in Table 1. Maximum number of patients were having

Table 1: Overall Distribution of Descriptive Features (n=48).

Age (years)	**Min-Max (Median)**		**15-75**
	Mean ± SD		**51.13 ± 12.19**
Age-Male (n=23)	Min-Max (Median)		18-65
	Mean ± SD		48.74 ± 10.56
Age-Female (n=25)	Min-Max (Median)		15-75
	Mean ± SD		53.52 ± 13.52
Age (years)	<50		19
	≥50		29
Gender	Male	n (%)	23
	Female	n (%)	25
Headachen (%)			33(68.8%)
Loss of consciousness n (%)			31(64.58%)
Seizures n (%)			6(12.5%)
Hypertension n (%)			13(27.08%)
WFNS score1	Good:	n (%)	36(75%)
	Poor:	n (%)	12(25%)
Fisher grade2	<1 mm		12(25%)
	>1 mm		14(29.2%)
	Bleeding		22(45.8%)
Hunt & Hess Grade3	Low:	n (%)	36(75%)
	High:	n (%)	12(25%)
Number of Aneurysms	Single Aneurysm	n (%)	43(89.6%)
	Multiple Aneurysms	n (%)	5(10.4%)
Localization of Aneurysms	MCA	n (%)	21(39.62%)
	Acom	n (%)	19(35.84%)
	ICA	n (%)	7(13.2%)
	PCOM	n (%)	4(7.54%)
	DACA	n (%)	1(1.88%)
	Basilar Topn (%)		1(1.88%)
Operation after ictus	Immediate (Day 0)	n (%)	0
(Time interval)	Early (Days 1–3)	n (%)	13(27.08%)
	Intermediate (Days 4–14)	n (%)	32(66.67%)
	Late (after 14 days)	n (%)	3(6.25%)
Symptomatic Vasospasm n (%)			9(18.75%)
Intra-operative Rupture	Yes		6 (12.5%)
	No		42 (87.5%)
Hydrocephalus	Yes		5(10.4%)
	No		43 (89.6%)

[1]WFNS score; Good 1-3, Poor 4-5.
[2]Fisher grade; Bleeding includes intracerebral haematoma and intraventricular haemorrhage.
[3]Hunt and Hess grade; Low 1-3, High 4-5.

Fisher grade 4 SAH (45.8%). The most frequent location of ruptured aneurysm was Middle cerebral artery bifurcation (39.6%) followed by anterior communicating artery (35.8%). In the postoperative period 14 patients had symptomatic vasospasm and 5 patients developed hydrocephalus for which Ventriculo-peritoneal (VP) shunt was put. Nine patients got expired in the postoperative period. At the time of 3month follow-up 58.3% patients were having good GOS score(4 and5) and 23% were having bad GOS score (2 and 3) as shown in Table 2.

On statistical analysis of various parameters WFNS grade, Hunt and Hess grade and Fisher grade were found statistically significant (p value <0.05) predictors of mortality. Although age > 50years, hypertension, loss of consciousness, time of

Table 2: Glasgow Outcome Score of the Patients.

Glasgow Outcome Score	No. of patients	Percentage
I	9	18.75
II	2	4.2
III	9	18.75
IV	13	27.1
V	15	31.2

Table 3: Evaluation of Parameters According to Mortality.

Survivor (n=39)		Mortality		P value
		Non-survivor (n=9)		
Age: Mean ± SD		50.72 ± 11.67	53.44 ±15.36	0.555
Age (years)	<50	17	2	0.237
	≥50	22	7	
Gender: n (%)	Male	20	3	0.331
	Female	19	6	
Loss of consciousness n (%)		24(61.53%)	7(77.8%)	0.359
Seizures n (%)		4(10.25%)	2(22.2%)	0.328
Vasospasm n (%)		5(12.82%)	4(44.44%)	0.263
Hypertension (%)		10(25.6%)	3(33.3%)	0.640
Number of Aneurysms n (cases %)	Single Aneurysm	34(87.18%)	9(100%)	0.256
	Multiple aneurysms	5(12.82%)	0	
Localization of Aneurysms n (%)	ACom	14(35.9%)	5(55.5%)	0.163
	MCA	19(48.7%)	2(22.2%)	
Neck Dome Ratio		0.41 ± .498	0.33 ± .50	>.05
Temporary clipping time		8.0 ± 5.54 min	11.22 ± 4.94 min	0.116
Operation After ictus n (%)	Immediate (Day 0)			0.653
(time interval)	Early (Days 1–3)	10(25.6%)	3(33.3%)	
	Intermediate (Days 4–14)	24(61.5%)	6(66.7%)	
	Late (after 14 days)	3(7.7%)	0	
WFNS score	Good (1-3): n (%)	33(84.62%)	3(33.3%)	0.003
	Poor (4&5): n (%)	6(15.38%)	6(66.7%)	
Fisher grade	Grade 1-2	12(30.7%)	0	0.004
	Grade 3	14(35.9%)	0	
	Grade 4	13(33.33%)	9(100%)	
Hunt & Hess grade	Low (1-3): n (%)	33(84.62%)	3(33.3%)	0.008
	High (4&5): n (%)	6(15.38%)	6(66.7%)	
Intra-operative rupture		4(10.25%)	2(22.2%)	0.328
Hydrocephalus		4(10.25%)	1(11.1%)	0.940

surgery (intermediate 4-14 days),vasospasm, intra-operative rupture and postoperative hydrocephalus were associated with poor outcome but correlation was not found statistically significant as shown in Table 3.

Discussion

In the current era of technological and surgical advancement aneurysmal SAH continues to be a challenging pathology associated with high rate of morbidity and mortality. Once the SAH occurs after rupture of aneurysm it sets the cycle of inflammatory mediators, vasospasm, infarction, brain oedema and so on. Although microsurgical clipping completely eliminates the risk of rebleed and drainage of cisternal blood decreases the severity of vasospasm but we can't able to break the said cycle which has already begun. So there is definitive need to identify the factors right from the beginning of ictus which may affect the outcome of patients of aneurysmal SAH. So we have done the prospective studyto evaluate the factors responsible for poor outcome in patients of aneurysmal SAH who underwent clipping at our set-up.

In our study WFNS grade and Hunt and Hess grade at admissionand Fisher grade of SAH on admission CT brain are found having statistically significant correlation with poor prognosis in patients of aneurysmal SAH. These factors are uniformly found associated with poor prognosis in all the previous studies.[2-6] In addition to these factors various other factors like age, hypertension, smoking, time of surgery, symptomatic vasospasm, intra-operative rupture, temporary clip placement time and hydrocephalus were also found significantly associated with poor outcome in various different studies.[2-11] So a detailed literature search is being carried out to evaluate the significance of various important prognostic factors.

Age and Gender

Advancing age is associated with poor neurological grade, thick blood clots, more comorbities and hence more postoperative complications in patients of aneurysmal SAH.[12] Previous studies have shown that advancing age is associated with poor outcome in patients of aneurysmal SAH having microsurgical clipping.[7,12] In our study out of 9 patients who expired, 7 patients were above 50 years. Though the correlation was not statistically significant but it can be concluded that with advancing age mortality increases. Male gender is negatively correlated with the outcome in patients of aneurysmal SAH as anterior communicating artery aneurysms are more common in male patients.[3] But in present study there was no statistical significance between genders in terms of mortality.

Hypertension

Hypertension, smoking and alcohol abuse are the known risk factors for aneurysm formation and SAH.[3,13,14] Kasell et. al. had reported that patients condition at the time of presentation and postoperative results are adversely affected by the presence of hypertension.[15] Diabetes mellitus, hyperlipidemia and atherosclerosis are the other co morbid factors which are associated with poor outcome in patients of aneurysmal SAH.[3,8,16] Except hypertension other risk factors were not included in our study. Hypertension has not found significant correlation with outcome in our study.

WFNS Grade at Presentation

It is a universally accepted fact that poor WFNS grade and poor Hunt and Hess grade at the time of initial presentation of the patients are predictors of poor outcome in patients of aneurysmal SAH. Various meta-analyses have shown that WFNS grade IV and V at the time of presentation have direct correlation with negative outcome of management of aneurysmal SAH patients.[5,17] In our study also mortality in patients with WFNS grade I, II and III patients was 0%, 22.2% and 11.1%, respectively whereas in grade IV and grade V it was 44.4% and 22.2% respectively.Similarly three patients out of nine patients who expired were in Hunt and Hessgrade II and rest of the expired patients were in Hunt and Hess grade IV at the time of presentation. Most of our patients(66%) presented in poor WFNS grade because of poor transportation facilities, ignorance of poor people and lack of proper referral services in rural areas. Many of our patients were having history of rebleed before presentation. So in indirect way improvement in rural health services can improve the outcome of patients of aneurysmal SAH.

Fisher Grade

Thickness of clot in subarachnoid spaces is directly related to extent of vasospasm. Also intracerebral hematoma and intraventricular haemorrhage are associated with poor outcome in patients of ruptured aneurysm.[18] Various meta-analyses and individual

studies have shown that a higher Fisher grade at presentation is associated with poor prognosisin patients of aneurysmal SAH.[19-21] In our cohort study 46% patients were having Fisher grade 4 SAH and all the expired patients were also having higher Fisher grade. The correlation between Fischer grade at presentation and post operative Glasgow outcome score was statistically highly significant.

Time of Surgery

Time of surgery whether early or late is a controversial topic. Early surgery on swollen brain in neurologically poor patients can lead to high morbidity and mortality.[22-24] On the other hand early surgery has significant advantages too. It eliminates the fear of rebleeding by early obliteration of aneurysm. Second removal of blood clots from cisterns alleviates the severity of vasospasm. So in recent years the trend has shifted from late surgery to early surgery. But aneurysm surgery in the intermediate period (4-14 days) during the peak of vasospasm is definitely found associated with high morbidity and mortality with no added advantages. In 1990, the International Cooperative Study demonstrated that earlysurgery was neither more hazardous nor more beneficial thanlate surgery. Z. Yao et. al. in their meta-analyses have found that early surgery is superior to late surgery in terms of good outcome and mortality.[22] In our case series 67% patients were operated in the intermediate period because of late presentation of the patients, constrained Operation theatre facilities and improper intensive care backup. The maximum mortality was found in patients operated in the intermediate period but thedifference in mortality on the basis of time period was not statistically significant in our study.

Vasospasm

Symptomatic vasospasm or delayed ischemic neurological deficit is the aftermath of persistent thick subarachnoid clot. Many studies have proven symptomatic vasospasm as predictor of poor outcome in patients of aneurysmal SAH.[9,10,25] Rosen et. al. found that the presence of angiographic vasospasm at admission is apoor prognostic factor of outcome.[18] So vasospasm needs to be detected early and should be managed as early as possible. In our setup where there is no transcranial Doppler, no DSA lab and lack of proper ICU facilities outcome is mainly based on clinical monitoring and HHH therapy. In this study clinical vasospasm is associated with the poor outcome of aneurysmal SAH patients but the correlation is not found statistically significant.

Hydrocephalus and Cerebral Infarction

Hydrocephalus, vasospasm and cerebral infarction develop side by side in cases of aneurysmal bleed especially in cases of intraventricular haemorrhage. Few studies have shown correlation of hydrocephalus with poor outcome in such patients.[7,11] Cerebral infarction, appearing as scattered hypo densities in cases of aneurysmal SAH, is also predictor of poor outcome according to previous studies.[11,26] In the present study five patients had VP shunt surgery for hydrocephalus but not found significantly correlated with poor outcome in aneurysmal SAH.

So in nutshell time of surgery, hyperglycaemia, hypertension, volume of thick blood clots in subarachnoid spaces and vasospasm are the modifiable factors which if properly managed, can improve the outcome of patients of aneurysmal SAH. Limitations of our study are small sample size, short duration follow-up scoring and minimal inclusion of aneurysmal morphological findings. However it shows definite need for meta-analysis of clinical records of aneurysmal SAH patients managed in low tier set-ups of developing countries to highlight the prognostic factors aggravated due to constrained resources.

Conclusion

Aneurysmal SAH is a critical healthcare emergency associated with high morbidity and mortality. Early surgery, drainage of cisternal blood and HHH therapy are the tools for good outcome of these patients. WFNS grade, Hunt and Hess grade and Fisher grade are having significant correlation with outcome in patients of aneurysmal SAH.

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