Predictors of outcome of aneurysmal subarachnoid hemorrhage

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Abstract

Introduction: Aneurysmal Subarachnoid Hemorrhage (aSAH) is a devastating condition with high mortality and morbidity. Significant factors influencing the prognosis of aneurysmal subarachnoid hemorrhage (SAH) include the severity at presentation of the disease and delayed cerebral ischemia (DCI).

Methods: This is a prospective study conducted in Upendra Devkota Memorial National Institute of Neurological and Allied Sciences (UDM-NINAS), Bansbari, Kathmandu, Nepal among patients who underwent clipping of aneurysm for subarachnoid hemorrhage. Various clinical and radiological prognostic factors were registered on admission and during the intensive care stay. Outcome was recorded. GOS>3 was considered good outcome and GOS ≤3 was considered poor outcome.

Results: Seventy-two patients with ruptured aneurysm were surgically clipped. Good outcome was observed in 51 (70.83%) patients while poor outcome was seen among 21 (29.17%) patients including death among 16 (22.2%) patients. In univariate analysis, WFNS>2, Fisher grade >2, EVD placement for hydrocephalus and delayed cerebral ischemia (DCI) were found to have statistically significant in poor outcome. On Multivariate logistic regression model showed delayed cerebral ischemia was statistically significant predictor of poor outcome at p= 0.032 (OR= 7.34; 95% CI=1.280 to 17.702).

Conclusion: WFNS >2, Fisher grade>2, EVD placement and DCI were found to have statistical significance in poor outcome while only DCI was an independent predictor of poor outcome following aneurysmal Subarachnoid Hemorrhage (aSAH).

Key words: Aneurusmal SAH(aSAH), delayed cerebral ischemia(DCI), Glasgow coma scale (GCS), Outcome

Introduction

Aneurysmal Subarachnoid Hemorrhage (aSAH) is a devastating condition with high mortality and morbidity rates which range from 8% to 67% with a significant morbidity among survivors.[1]

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Various studies have explored the prognostic factors that affect the outcome of aSAH. Older age, female sex, severity of clinical presentation, WFNS grade, size of aneurysm, re-bleeding, pre-existing severe medical illness, global cerebral edema, intraventricular and intracerebral haemorrhage, symptomatic vasospasm, delayed cerebral infarction, hyperglycaemia, fever, anaemia, leucocytosis, comorbidities other systemic complications such as pneumonia and sepsis also affect the outcome of patient.[1-6]

The aim of this study is to analyse various clinical and radiological variable and identify the predictor of poor outcome.

Methods

This is a prospective study conducted in Upendra Devkota Memorial National Institute of Neurological and Allied Sciences (UDM-NINAS), Bansbari, Kathmandu, Nepal among patients who underwent clipping of aneurysm for subarachnoid hemorrhage for last 3 years. Demographic profile, comorbidities and risk factor of SAH patients were included. Clinical parameters like symptoms and signs including blood pressure, focal neurological deficit (FND) were assessed and clinical

condition registered according to WFNS grade at hospital admission. The amount of subarachnoid blood on the admission CT scan was graded according to Fischer's scale. Complications during hospital stay were recorded including hydrocephalus, symptomatic vasospasm or re-bleeding and delayed cerebral ischemia.

All patients were treated according to standardized protocol, which closely follows international guidelines.[7,8] Patient presenting with ruptured aneurysm underwent clipping with standard pterional approach. Intraoperative technical complications including premature rupture of aneurysm and brain swelling were recorded. Post operatively patient was managed in Intensive care unit (ICU) with adequate hydration to maintain central venous pressure (CVP) around 12mmHg if needed. Supportive medication with analgesics, Nimodipine, anti-epileptic drug was administered as indicated. Symptomatic hydrocephalus or IVH were addressed with immediate External ventricular drain (EVD) placement. Patient were followed up post operatively and GOS at the time of discharge were recorded.

Demographic profile, comorbidities, clinical presentation, radiological variables, in hospital complication, clinical and radiological variable were compared between two groups (GOS ≤3 and GOS >3) of outcome using 1- and 2- tailed student t-tests, Mann-Whitney-U test for continuous variable and fisher exact test or chi square test for categorical variables were applied. Univariate analysis was used to create a multivariable model for independent predictors of outcome. Admission predictors were added individually to these models to calculate adjusted odds ratios for the strength of association of outcome. Tests for interactions were performed for all of the significant variables in the multivariable models. *P* value of 0.05 or less was considered statistically significant. SPSS version 20 was used as data computation tool. Outcome was recorded on the basis of GOS. GOS>3 was considered good outcome and GOS ≤3 was considered poor outcome.

Result

Seventy-two patients with ruptured aneurysm were surgically clipped. Most of them were female (68.1%) with female to male ration of 2.14:1. Mean age of the patients was 52.5±10.3years with range from 28 to 74 years. Most of the patients were between 40-69 years (62%) age group. Good outcome was observed in 51 (70.83%) patients while poor outcome was seen among 21 (29.17%) patients. In univariate analysis, WFNS>2, Fisher grade >2, EVD placement for hydrocephalus and DCI were found to have statistical significant in poor outcome while age, sex, on admission GCS, ICH, IVE, Cerebral edema, symptomatic vasospasm, and operative timing were not significant in outcome in our study (Table 1).

On Multivariate logistic regression model for predicting outcome in patients with aSAH which was developed from multivariable logistic regression analysis of explanatory variables (P<0.25) namely WFNS, Fischer grade, EVD placement, cerebral edema, rebleeding, delayed cerebral ischemia. The model showed delayed cerebral ischemia was statistically significant predictor of poor outcome. Patients with DCI have 7.34 times higher odds of poor outcome than those without DCI at P= 0.032 (95% CI=1.19 to 45.33) (Table 2).

Characteristics		Total patients (N=72)	Good outcome GOS > 3 (N=51)	Poor outcome GOS ≤3 (N=21)	P value
Age range	<40	8 (11.1%)	7 (13.7%)	1 (4.8%)	0.271
	>40	64(88.9%)	44 (86.3%)	20 (95.2%)	
Sex	Male	23 (31.9%)	7 (33.3%)	16 (31.4%)	0.54
	Female	49 (68.1%)	14 (66.7%)	35 (68.6%)	
On admission LOC	None	46(63.9%)	33 (64.7%)	13 (61.9%).	0.51
	Yes	26 (36.1%)	18 (35.3%)	8 (38.1%)	
WFNS	≤2	34 (47.2%)	28 (54.9%)	6 (%)	0.037*
	>2	38 (52.8%)	23 (45.1%)	15 (71.4%)	
Fisher's grade	1	1 (1.4%)	1 (2%)	0	0.055
	2	23 (31.9%)	21 (41.2%)	2 (9,5%)	
	3	20 (27.8%)	12 (23.5%)	8 (38.1%)	
	4	28 (38.9%)	17 (33.3%)	11 (52.4%)	
Fisher's grade	≤2	24 (33.3%)	22 (43.1%)	2 (9.5%)	0.005*
	>2	48 (66.7%)	29 (56.9%)	19 (90.5%)	

ICH	None	55 (76.4%)	39 (76.5%)	16 (76.2%)	0.60
	Yes	17 (23.6%)	12 (23.5%)	5 (23.8%)	
IVE		24 (33.3%)	15 (29.4%)	9 (42.9%)	0.204
Hydrocephalus		19 (26.4%)	11 (21.6%)	8 (38.1%)	0.126
EVD	None	68 (94.4%)	51 (100%)	17(80.9%)	0.006*
	Yes	4 (5.6%)	0	4 (19.1%)	
Cerebral edema	None	63 (87.5%)	47(92.2%)	16(76.2%)	0.075
	Yes	9 (12.5%)	4 (7.8%)	5 (23.8%)	
Operation timing	≤3days	39 (54.2%)	26 (51%)	13 (61.9%)	0.280
	>3 days	33 (45.8%)	25 (49%)	8 (38.1%)	
Re-bleeding	None	67 (93%)	47 (92.15%)	20 (95.2%)	0.836
	Yes	4 (7%)	3 (7.85%)	1 (4.8%)	
Vasospasm	None	32 (44.4%)	25 (49%)	7 (33.3%)	0.170
	Yes	40 (55.6%)	26 51(%)	14 (66.7%)	
DCI	None	40 (55.5%)	40(78.4%)	7 (33.3%)	0.003*
	Yes	25 (34.7%)	11 (21.6%)	14 (66.7%)	
Post op Complication	None	37 (51.4%)	31 (60.8%)	6 (28.6%)	0.013*
	Yes	35 (48.6%)	20 (39.2%)	15 (71.4%)	

DCI: Delayed cerebral ischemia, LOC: loss of consciousness, IVE: Intraventricular extension

Table 1: Outcome of patient with Aneurysmal Subarachnoid Hemorrhage

Variables		Reference category	β (SE)	OR (95% CI)	P-value
WFNS grade	≤2	>2	-0.597(0.66)	1.82 (0.492 to 6.701)	0.188
DCI	0 (No)	1(Yes)	1.99(0.929)	7.34 (1.28 to 17.70)	0.032*
Fischer grade	≤2	>2	1.223(0.856)	3.39 (0.635 to18.176)	0.153
Constant			-18.831(0.444)		0.000

*Model χ^2=<0.001, -2Log likelihood=40.735, Cox & Snell R^2=0.260, Nagelkerke R^2=0.371, p=0.994 (Hosmer and Lemeshow test), *Significant at p<0.005.*

Table 2: Regression model for predicting outcome of Subarachnoid hemorrhage.

Discussion

Despite considerable advances in the perioperative management of aneurysmal SAH, patient outcomes remain poor with high mortality and significant morbidity occurring in about 8-67% of those who survive the hemorrhage.[1] Several factors are related through mortality and poor outcome in aSAH (rebleeding, hydrocephalus, symptomatic vasospasm, older age, female, intraventricular and intracerebral hemorrhage, delayed cerebral infarction, aneurysm location, hyperglycemia, fever, anemia, and other systemic complications such as pneumonia and sepsis.[9]

In our study, cerebral vasospasm was seen among 40 (55.6%) patients, while 32 (44.5%) patients developed DCI and 29.1% had poor outcome (GOS ≤3). Mortality rates vary widely across published epidemiological studies, ranging from 8% to 67%. Mortality rates in this study was similar to previous reports (29.17%).[1]

The mean age at diagnosis in our study was 52.5±10.3years with range from 28 to 74 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 consistent with our study in which, there is no significant difference in outcome of patient in relationship to age.[10,11]

SBP and hypertension have been associated with unfavourable outcome after aSAH by Rosengart et al. but different effects were established in 2010 by Cha et al.[9,12]. It is remarkable to mention that a few researches evaluated the relation between blood pressure, rebleeding, and mortality after aSAH when it is recognized that the hypertension is important risk factors for aneurysm rupture. However, we didn't find HTN as a predictor of poor outcome following aneurysmal rupture.[9,12]

The clinical degree of LOC is favoured as a brief evidence for predicting the probability of an unfavourable outcome after aneurysmal SAH.[13] The period of loss of consciousness indicates global ischemia. Hop et al. claim that LOC is a strong predictor of the occurrence of DCI. However, LOC at presentation was unremarkable in our study.[14]

Scholler et al. reported hydrocephalus to be the weakest predictor of outcome, while Lagares et al. reported that the presence of hydrocephalus was related to a poor outcome.[15,16] We found the rate of hydrocephalus did not differ significantly in terms of poor outcome. Though EVD placement for hydrocephalus was significant in poor outcome in univariate analysis it turned out to be insignificant in multivariate analysis.

Cerebral vasospasm (CV) and delayed cerebral ischemia (DCI) are the most important preventable cause of mortality and poor neurological outcome among aSAH patients who survive the initial bleed consistent with our study where DCI was found to be an independent predictor of poor outcome.[17-19] Symptomatic vasospasm and DCI has already been associated with unfavourable outcome.[4] In a review of 1000 reports appearing in the literature, a common OR of 3.05 (95% CI, 2.73 to 3.40) has been calculated, indicating much better odds for a full recovery for a patient without vasospasm.[20] Rebleeding, hydrocephalus, symptomatic vasospasm, older age, female, intraventricular and intracerebral hemorrhage, aneurysm location, hyperglycemia were not found to be statistically significant in our study.

WFNS>2, Fisher grade >2, EVD placement for acute hydrocephalus, post-operative complication including sepsis, pneumonia and brain swelling were significant in univariate analysis, but these variables failed to prove as a predictor of poor outcome in multivariate analysis. Moreover, Haley et al revealed better prognosis in those group who were operated on days 0–3 when compared to the patients who were operated on days 11–32.[21] The outcomes were poorer when surgery was planned for the 7–10-day period, because of the greatest risk for symptomatic vasospasm. However, such significance was not revealed in our study.

Conclusion

Aneurysmal Subarachnoid Hemorrhage (aSAH) is a devastating condition with high mortality and morbidity. WFNS >2, Fisher grade>2, EVD placement, post-operative complication and DCI were found to have association in poor outcome while only DCI was an independent predictor of poor outcome.

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