STUDY OF MORTALITY RISK FACTORS IN PATIENTS WITH SUBARACHNOID HEMORRHAGE WITHIN INDONESIAN POPULATION

Hana JPI[1], Pinzon RT[1].
[1]Faculty of Medicine, Duta Wacana Christian University, Yogyakarta 55224, Indonesia

Correspondence:
Jesi Prilly Imanuella Hana,
Faculty of Medicine, Duta Wacana Christian University
Dr. Wahidin Sudiro Husodo Street
No. 5-25 Yogyakarta 55224, Indonesia
Email: jesiprilly@gmail.com

Abstract

Background: Subarachnoid hemorrhage is a devastating type of stroke with high mortality rate. The understanding of factors that contribute to mortality in patient with subarachnoid hemorrhage can help clinicians in further management of the patients.

Aim: The aim of this study is to identify mortality risk factors in patients with subarachnoid hemorrhage (SH).

Methods: This study is a retrospective cohort study. Data were obtained from the stroke registry and medical records of patients at Bethesda Hospital Yogyakarta. Data were analyzed using univariate, bivariate and multivariate logistic regression analysis.

Results: Data were obtained from 80 subarachnoid hemorrhage patients consisting of 40 males (50%) and 40 females (50%). Result of multivariate analysis show that there are significant associations between mortality in SAH patient with loss of consciousness (OR: 19.722, 95% CI: 1.788- 217.521, *p*: 0.015), elevated systolic blood pressure (OR: 157.4, 95%CI: 2.068- 11990.9, *p:* 0.022), high random blood glucose (OR: 12.457, 95%CI: 2.305- 67.322, *p:* 0.03) and presence of medical complication (OR: 30.539, CI95%: 2.685- 347.377, *p:* 0.006).
Conclusion: This study demonstrated that loss of consciousness, elevated systolic blood pressure, high blood glucose, and presence of medical complication has significant association with mortality of SAH patient.

Keywords: *Clinical Predictor, Mortality, Prognosis, Subarachnoid Hemorrhage*

Introduction

Subarachnoid hemorrhage (SAH) is the least common type of stroke but it accounts for 5% of stroke death. Cerebral aneurysm rupture is the most common etiology of SAH. The mortality rate for aneurysmal subarachnoid hemorrhage (aSAH) is 32-67% make it the most lethal type of hemorrhagic stroke (1). Previous studies showed that there are several risk factors related with mortality in SAH. Some factors have been related with mortality in SAH including older age, aneurysm rebleeding, large aneurysm size, vasospasm, systolic blood pressure >160 mmHg, serum glucose >7 mmol/L, and African Americans/ mixed race (2,3).

Understanding of risk factors of mortality in SAH patient will help clinicians determine proper management of the patients. Previous studies of mortality risk factors for subarachnoid hemorrhage mortality in Indonesia are very limited. The aim of this study is to identify mortality risk factors in patients with subarachnoid hemorrhage.

Methods

Design

This was a retrospective cohort study from stored registry and medical records of Bethesda Hospital, Yogyakarta. The case was patients who died during hospitalization. The control was patients who were alive upon hospital discharge.

Subject

The subjects of this study were patients with Subarachnoid Hemorrhage confirmed with Computed Tomography (CT) Scan. We excluded patients who were referred from other hospital or discharged against medical advice.

Variables

The independent variable in this study is clinical characteristic of the patients. The dependent variable is in-hospital mortality.

Ethics

This study has been approved by the Research Ethics Committee of Duta Wacana Christian University Yogyakarta Number 495/C.16/FK/2017.

Statistical analysis

The statistical analysis was performed using licensed SPSS software. Data were analyzed using univariate, bivariate chi-square, and multivariate logistic regression analysis.

Results

General characteristic and univariate analysis

Data were obtained from 80 subarachnoid hemorrhage patients consisting of 40 males (50%) and 40 females (50%). The general characteristic of these patients were summarized in Table 1.

Table 1: Baseline characteristic of study subject

Baseline Characteristic	n= 80 (%)
Age (years)	
<40	2 (2.5%)
40-50	14 (17.5%)
51- 60	22 (27.5%)
61- 70	17 (21.5%
> 70	25 (31.3%)
Sex	
Female	40 (50%)
Male	40 (50%)
Consciousness during hospital admission	29 (36.3%)
Unconscious	51 (63.7%)
Conscious	
Onset to hospital admission (hours)	
< 3	14 (17.5%)
3-6	26 (32.5%)
6-12	10 (12.5%)
12-24	6 (7.5%)
>24	24 (30%)
Muscle Strength (MRC Scale)	
5	5 (5.3%)
4	19 (23.8%)
3	6 (7.5%)
2	8 (10%)
1	11 (13.8%)
0	2 (2.5%)
Can not be assessed	29 (36.2%)
Systolic Blood Pressure (mmHg)	
<160	16 (20%)
≥ 160	64 (80%)
Diastolic Blood Pressure (mmHg)	
≤ 84	15 (18.8%)
85-89	3 (3.8%)
≥ 90	62 (77.5%)
Random Blood Glucose (mg/ dL)	
< 140	41 (51.3%)
≥ 140	39 (48.8%)
Sodium Serum (mEq/ L)	
< 136	24 (30%)
136-146	54 (67.5%)
> 146	2 (2.5%)
Leucocyte Count ($x10^{-6}$/L)	
≤ 11 $x10^{-6}$/L	29 (36.6%)
> 11 $x10^{-6}$/L	51 (63.8%)
Seizure	
Present	5 (6.3%)
Absent	75 (93.8%)
Fever	
Present	10 (12.5%)
Absent	70 (87.5%)
Anemia	
Yes	17 (21.3%)
No	63 (78.8%)
Congestive Heart Failure	
Yes	10 (12.5%)
No	70 (87.5%)
Diabetes Mellitus	
Yes	11 (13.8%)
No	69 (86.3%)
Hypertension	
Yes	58 (72.5%)
No	22 (27.5%)
History of COPD	
Yes	5 (6.3%)
No	75 (93.8%)
Previous Stroke	
Yes	22 (27.5%)
No	58 (72.5%)
Urinary Tract Infection	
Yes	4 (5%)
No	76 (95%)
Gastrointestinal Bleeding	
Yes	17 (21.3%)
No	63 (78.8%)
Pneumonia	
Yes	10 (12.5%)
No	70 (87.5%)
Complication	
Yes	51 (63.8%)
No	29 (36.2%)
Rebleeding	
Yes	0 (0%)
No	50 (62.5%)
Can not be assessed	30 (37.5%)
Intraventricular Bleeding	
Yes	22 (27.5%)
No	58 (72.5%)
Hydrocephalus	
Yes	5 (6.3%)
No	75 (93.8%)

Baseline Characteristic	n= 80 (%)
Ventilator Assisted	
Yes	9 (11.3%)
No	71 (88.8%)

Bivariate analysis

Bivariate analysis in Table 2 indicated that consciousness during hospitalization, random blood glucose, natrium serum, leucocyte count, systolic blood pressure, seizure, fever, congestive heart failure, gastrointestinal bleeding, pneumonia, complication, rebleeding, and intraventricular bleeding has a significant relation with mortality in SAH patient (p <0.05).

Table 2: Risk factors of mortality in patient with SAH

Variable	Dead (40)	Alive (40)	OR	CI	*p*
Age (Years)					
<40	1	1	Ref		0.892
40-50	8	6	1.333	0.069- 25.912	
51- 60	9	13	.692	0.038- 12.572	
61- 70	9	8	1.125	0.060- 21.087	
> 70	13	12	1.083	0.061- 19.313	
Sex					0.655
Female	21	19	Ref	0 .508- 2.938	
Male	19	21	1.222		
Consciousness during hospitalization					<0.001
Conscious	13	38	Ref		
Unconscious	27	2	39.462	8.224- 189.357	
Onset to hospital admission (hours)					
< 3	9	5	Ref		0.592
3-6	14	12	0.648	0.170-2.470	
6-12	5	5	0.556	0.106- 2.901	
12-24	3	3	0.556	0.080- 3.858	
>24	9	15	0.333	0.085- 1.312	
Muscle Strength (MRC Scale)					<0.001
5	1	4	Ref		
4	1	18	.125	0.005- 3.225	
3	3	3	.028	0.001- 0.637	
2	3	5	0.500	0.028- 8.952	
1	4	7	0.300	0.018- 4.908	
0	1	1	0.286	0.019- 4.237	
Can not be assessed	29	0	6.500	0.396- 106.712	
Systolic Blood Pressure (mmHg)					0.002
< 160	1	15	Ref		
≥ 160	39	25	23.400	2.907- 188.356	
Diastolic Blood Pressure (mmHg)					0.124
≤ 84	6	9	Ref		
85-89	0	3	0.999	0.000	
≥ 90	34	28	0.306	0.578- 5.739	
Random Blood Glucose (mg/ dL)					<0.001
< 140	9	32	Ref	4.713- 40.281	
≥ 140	31	8	13.778		
Sodium Serum (mEq/ L)					0.001
< 136	19	5	0.143	0.046- 0.443	
136-1461	19	35	Ref		
> 146	2	0		0.000	
Leucocyte Count (x10^{-6}/L)					0.002
≤ 11	8	21	Ref	1.638- 11.930	
>11	32	19	4.421		
Seizure					0.021
Present	5	0	4.750	0.363-0.594	
Absent	35	40	Ref		
Fever					0.043
Present	8	2	4.750	0.941- 23.985	
Absent	32	38	Ref		
Anemia					0.785
Yes	8	9	0.861	0.295- 2.518	
No	32	31	Ref		
Congestive Heart Failure					0.043
Yes	8	2	4.750	0.941- 23.985	
No	32	38	Ref		
Diabetes Mellitus					0.745
Yes	5	6	0.810	0.226- 2.903	
No	35	34	Ref		
Hypertension					0.317
Yes	31	27	1.658	0.614- 4.482	
No	9	13	Ref		
History of COPD					0.644
Yes	3	2	1.541	0.243- 9.754	
No	37	38	Ref		
Previous Stroke					0.133
Yes	14	8	2.154	0.784- 5.920	
No	26	32	Ref		
Urinary Tract Infection					0.305

Variable	Dead (40)	Alive (40)	OR	CI	*p*
Yes	1	3	0 .316	0.031- 3.317	
No	39	37	Ref		
Gastrointestinal Bleeding					<0.001
Yes	7	0	0.365	0.264- 0.506	
No	23	40	Ref		
Pneumonia					0.043
Yes	8	2	4.750	0.941-23.985	
No	32	38	Ref		
Complication					<0.001
Yes	24	5	10.500	3.390- 32.523	
No	16	35	Ref		
Rebleeding					<0.001
Yes	0	0		12.556- 841.960	
No	11	39	Ref		
Cannot be assessed	29	1	102.818		
Intraventricular Bleeding					<0.001
Yes	18	4	7.364	2.204- 24.602	
No	22	36	Ref		
Hydrocephalus					0.166
Yes	4	1	4.333	0.462- 40.608	
No	36	39	Ref		
Ventilator Assisted					0.288
Yes	6	3	2.176	0.504- 9.391	
No	34	37	Ref		

Multivariate analysis

Multivariate analysis was done to variables that has p value <0.05 and 95% CI. Stepwise regression with backward elimination approach was used to identify statistically significant variables.

Table 3 shows the result of multivariate analysis. There is a significant association between patient and consciousness (OR: 19.722, 95% CI: 1.788- 217.521, *p*: 0.015), systolic blood pressure (OR: 157.4, 95%CI: 2.068- 11990.9, *p:* 0.022), random blood glucose (OR: 12.457, 95%CI: 2.305- 67.322, *p:* 0.03) and complication (OR: 30.539, CI95%: 2.685- 347.377, *p:* 0.006) with mortality in SAH patient.

Table 3: Determinant risk factors of mortality in patients with subarachnoid hemorrhage

Variable	OR	95% CI	*p*
Consciousness during hospitalization	19.722	1.788- 217.521	0.015
Systolic Blood Pressure	157.4	2.068- 11990.9	0.022
Random Blood Glucose	12.457	2.305- 67.322	0.03
Complication	30.539	2.685- 347.377	0.006

Discussion

Multivariate analysis showed that consciousness, systolic blood pressure, random blood glucose and medical complication has a significant association with mortality of SAH patient.

The mortality of patient with initial loss of consciousness (LOC) has a significant association (OR: 19.722, 95% CI: 1.788- 217.521, *p*: 0.015). This study confirmed that LOC is a significant risk factor of mortality in SAH patient. LOC was associated with larger SAH, intraventricular hemorrhage, and global cerebral edema (4). The mechanism of LOC in SAH patient has been thought to be associated with increased intracranial pressure, decreased cerebral perfusion pressure, and cerebral ischemia (5). This study is in contrast with a previous study reported by Wang *et al* (6) which found that LOC is associated with unfavorable functional outcomes but not with patient mortality.

Elevated blood pressure, particularly in systolic blood pressure in SAH patient might happen due to a stress response. Activation of sympathetic nervous system is an important cause of sustained elevation in blood pressure in SAH patient (7). This study showed that systolic blood pressure ≥ 160 mmHg has a significant association with mortality in SAH patient (OR: 157.4, 95%CI: 2.068- 11990.9, *p:* 0.022. High blood pressure is a risk for aneurysmal rupture and rebleeding (7).

Our study confirmed that hyperglycemia in SAH patients upon hospital admission is a significant risk of mortality (OR: 12.457, 95%CI: 2.305- 67.322, *p:* 0.03). Lee *et al* (2008) found that hyperglycemia is a harmful risk on short-term mortality in SAH patient (8). Elevated glucose level in SAH patient could be a transient stress reaction inflicted by the insult or a pre-existing but unrecognized diabetes mellitus (9).

The presence of medical complication including gastrointestinal bleeding, urinary tract infection and pneumonia significantly increase mortality risk in SAH. It

is common for stoke patients to develop multiple medical complication during hospitalization. Those complications may occur independently or are associated with another (10). Several studies have shown that the presence of non-neurological complication has a significant role in mortality in stroke patients (11, 12).

This study has several important limitations including the use of retrospective cohort design and small sample size. We did not follow up the patients after hospital discharge. We were not able to gain data about the etiology, location, and volume of bleeding in the subjects. Further studies should use prospective design with larger sample size.

Conclusion

This study demonstrated that loss of consciousness, elevated systolic blood pressure, high blood glucose, and presence of medical complications are significantly associated with mortality of SAH patient.

Competing interests

The authors declare no conflict of interest.

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