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The determinant of poor prognostic factors in patients with primary intracerebral hemorrhage

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ABSTRACT

Background: Stroke is leading cause of death in Indonesia. The mortality rates of patients' hemorrhage stroke are higher than ischemic stroke. The understanding of prognostic factors can help the clinician for further management. The previous studies of a prognostic factor for hemorrhagic stroke in Indonesia are still very limited. **Aim:** The aim of this study is to measure determinant factors of mortality in patients with primary intracerebral hemorrhage. **Methods:** A nested case–control method is used in this study. The study subjects were obtained from the stroke registry from stroke unit at Bethesda Hospital Yogyakarta between 2015 and 2017. Data were analyzed using univariate, bivariate, and multivariate logistic regression analysis. **Results:** The data obtained from 128 intracerebral hemorrhage stroke patients which consist of 74 males (57/8%) and 54 females (42.2%). This study showed that significant prognostic factors are level of consciousness (Glasgow Coma Scale level ≤8) (OR: 22.41, 95% confidence interval [CI]: 4.461-112.587, $P < 0.001$), leukocyte count (odds ratio [OR]: 4.894, 95% CI: 1.480–16.179, $P = 0.009$), and the presence of complications (OR: 3.502, 95%CI: 1.103–11.117, $P = 0.033$). **Conclusion:** This study showed that unconsciousness, high leukocyte count, and the presence of complications will increase the risk of inhospital mortality.

Key words: Clinical predictor, Intracerebral hemorrhage stroke, Mortality, Prognosis

INTRODUCTION

Stroke is leading cause of death and disability worldwide. The ischemic stroke rate is higher than hemorrhagic stroke.[1] Even the rate is lower compared with ischemic stroke, the mortality rate is much higher in hemorrhagic stroke.[2] The previous study showed that there are several prognostic factors in primary intracerebral hemorrhage.[3] Some previous studies determined the scoring system for poor prognosis in hemorrhagic stroke.[4] The data about intracerebral hemorrhagic prognosis are limited.

Understanding about prognostic factors in hemorrhagic stroke will help clinician for appropriate management of the patients.[3] It will also facilitate clinician to give education about the prognosis for the family. Previous studies about the prognostic factors in hemorrhagic stroke in Indonesia are very limited. The aim of this study is to measure the determinant factors of mortality in patients with hemorrhagic stroke.

METHODS

Design

The design of this study is nested case–control. The outcome of this study is inhospital mortality. The case is defined as patients who died during hospitalization. The control group is patients who alive in hospital discharge. We only use complete data. Patients who discharge against medical advice and patients who being refer to other hospital were excluded from the study.

Subject

The subjects of this study are patients with hemorrhagic stroke that confirmed with clinical and radiological finding. The inclusion criteria are as follows: Hemorrhagic stroke patients, age > 40 years old, and first-time stroke. We exclude patients with a history of previous stroke. We also exclude patients that being referred from other hospital. Patients with incomplete data are excluded. We use OpenEpi software to calculate the sample size with a significance level <0.05 and power 0.8.

Variables

The dependent variable in this study is inhospital mortality. The independent variables are demographic profile and clinical characteristics. The data about demographic profile consist of age and sex. The data about clinical characteristics profile consist of onset to hospital admission, comorbidities, and stroke risk factors. We also consider clinical symptoms and inhospital complications as independent variables.

Ethic

This study used secondary data. Research Ethics Committee of Duta Wacana Christian University School of Medicine has approved the study.

Statistical Analysis

The statistical analysis was performed by licensed SPSS software. We considered that significance level is $P < 0.05$. The data analyzed univariate and bivariate. The bivariate analysis was performed

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with Chi-square. The multivariate analysis was performed with logistic regression.

RESULT

The data obtained from 128 patients with hemorrhagic stroke that consist of 74 male (57.8%) and 54 female (42.2%). The most common age ranges from 51 to 60 years old (35.2%). The most common onset to hospital admission is between 3 and 6 h after onset (30.5%). Almost half (42.2%) of the patients are unconscious (Glasgow coma scale [GCS] <8) in hospital admission. High leukocyte count in hospital admission was present in 56.3% of cases. The most prominent risk factor is hypertension and present in 79.7% of cases. Table 1 summarized the baseline characteristic of the study subjects.

Table 2 presented the risk factors of mortality in patients with primary intracerebral hemorrhage. This table showed that elderly, unconsciousness, and the presence of complications will increase the risk of mortality.

The significant risk factors will be further analyzed in multivariate analysis. Logistic regression approach will be used for multivariate analysis. The significant prognostic factors in bivariate analysis are as follows: Age, level of consciousness, leukocyte count, and the presence of complications Table 3.

DISCUSSION

The multivariate analysis showed that GCS <8, high leukocyte count on hospital admission, and the presence of complications significantly increase the mortality. The mortality of patients with GCS ≤8 is significantly higher compared with conscious patients on hospital admission (odds ratio [OR]: 22.41, 95% confidence interval [CI]: 4.461–112.587, $P < 0.001$). The patients with complications have higher mortality rate compared without complications (OR: 3.502, 95% CI: 1.103–11.117, $P = 0.033$). The medical and neurological complications in patients with stroke are common (gastrointestinal [GI] bleeding, pneumonia,

Table 1: Baseline characteristics of study subjects

Baseline characteristics	*n*=128 (%)
Sex	
Male	74 (57.8)
Female	54 (42.2)
Age (years)	
40–50	26 (20.3)
51–60	45 (35.2)
61–70	29 (22.7)
>70	28 (21.9)
Onset to hospital admission (hours)	
<3	20 (15.6)
3–6	39 (30.5)
6–12	26 (20.3)
12–24	11 (8.6)
>24	32 (25.5)
Level of consciousness	
15	40 (31.3)
13–14	12 (9.4)
9–12	22 (17.2)
≤8	54 (42.2)
Systolic Blood Pressure (mmHg)	
≤129	8 (6.3)
130–139	9 (7.0)
≥140	111 (86.7)
Diastolic blood pressure (mmHg)	
≤84	28 (21.9)
85–89	0 (0)
≥90	100 (78.1)
Random blood glucose on hospital admission	
<200	112 (87.5)
≥200	16 (12.5)
Leukocyte count	
≤11	56 (43.8)
>11	72 (56.3)
Atrial fibrillation	
Yes	4 (3.1)
No	124 (96.9)
Diabetes mellitus	
Yes	26 (20.3)
No	102 (79.7)
Hypertension	
Yes	102 (79.7)
No	26 (20.3)
Dyslipidemia	
Yes	10 (7.8)
No	118 (92.2)
Complications	
Present	62 (48.4)
Absent	66 (51.6)
Side of weakness	
None	20 (15.6)
Left	54 (42.2)
Right	42 (32.8)
Both side	12 (9.4)
Muscle strength (MRC Scale)	
Normal (5)	8 (6.3)
4	16 (12.5)
3	13 (10.2)
2	43 (33.6)
1	27 (21.1)
0	21 (16.4)
Smoking	
Yes	29 (22.7)
No	99 (77.3)
Length of hospital stay (days)	
≤3	49 (38.3)
>3	79 (61.7)
Metabolic encepalopathy	
Yes	14 (10.9)
No	114 (89.1)
Heart failure	
Yes	4 (3.1)
No	124 (96.9)
Ventilator assisted	
Yes	12 (9.4)
No	116 (90.6)

MRC: Medical research council

Table 2: The risk factors of mortality in patients with primary intracerebral hemorrhage

Variable	Dead (64)	Alive (64)	OR	CI	P
Sex					
Female	41	31	Ref		0.152
Male	23	33	0.597	0.294–1.121	
Age (years)					
40–50	17	9	Ref		0.009
51–60	14	31	4.18	1.34–13.37	
61–70	19	10	0.99	0.28–3.50	
>70	14	14	1.89	0.55–6.57	
Onset (hours)					
<3	14	6	Ref		0.500
3–6	19	20	2.46	0.69–9.07	
6–12	12	14	2.72	0.68–11.26	
12–24	5	6	2.80	0.48–17.26	
>24	14	18	3	0.80–11.71	
GCS on admission					
15	7	33	Ref		<0.001
13–14	5	7	3.367	0.824–13.764	
9–12	7	15	2.2	0.654–7.396	
≤8	45	9	23.571	7.964–69.763	
Systolic blood pressure					
≤129	1	7	Ref		<0.42
130–139	0	9	2.5	0.13–85.46	
≥140	63	48	0.11	0–0.93	
Diastolic blood pressure					
≤84	9	19	Ref		0.38
85–89	0	0			
≥90	55	45	0.39	0.15–1.02	
Random blood glucose					
<200	62	60	Ref		0.033
≥200	12	4	3.462	1.052–11.389	
Leukocyte count					
≤11	15	41	Ref		<0.001
>11	49	23	5.823	2.692–12.596	
Atrial fibrillation					
Yes	3	1	3.098	0.314–30.608	0.310
No	61	63	Ref		
Diabetes mellitus					
Yes	12	14	0.824	0.348–1.954	0.660
No	52	50	Ref		
Hypertension					
Yes	54	48	1.8	0.746–4.342	0.187
No	10	16	Ref		
Dyslipidemia					
Yes	2	8	0.226	0.046–1.108	0.068
No	62	56	Ref		
Complications					
Yes	43	19	4.850	2.295–10.248	<0.001
No	21	45	Ref		
Side of weakness					
None	9	11	Ref		0.07
Left	14	24	1.25	0.35–4.43	
Right	11	28	1.85	0.51–6.80	
Both side	11	1	0.07	0–0.71	
Muscle strength (MRC)					
5	6	2	Ref		0.325
4	7	9	3.86	0.45–39.76	
3	8	5	1.88	0.19–20.76	
2	17	26	4.59	0.70–37.70	

(Contd...)

Table 2: The risk factors of mortality in patients with primary intracerebral hemorrhage

Variable	Dead (64)	Alive (64)	OR	CI	*P*
1	16	11	2.06	0.28–18.23	
0	10	11	3.67	0.46–34.99	
Smoking					
Yes	15	14	1.093	0.478–2.502	0.833
No	49	50	Ref		
Length of stay (days)					
≤3	43	6	Ref		<0.001
>3	21	58	0.051	0.019–0.136	
Metabolic encephalopathy					
Yes	10	4	2.778	0.823–9.375	0.089
No	54	60	Ref		
Congestive heart failure					
Yes	1	3	0.323	0.033–3.188	0.310
No	63	61	Ref		
Ventilator assisted					
Yes	8	4	2.143		0.225
No	56	60	Ref	0.611–7.511	

GCS: Glasgow Coma Scale, OR: Odds ratio, CI: Confidence interval, MRC: Medical research council

Table 3: The determinant risk factors of mortality in patients with primary intracerebral hemorrhage

Variable	OR (adjusted)	95% CI	*P*
GCS 15	Ref	Ref	0.002
GCS 13–14	4.661	0.632–34.348	0.131
GCS 9–12	4.390	0.745–25.883	0.102
GCS <8	22.410	4.461–112.587	<0.001
High random blood glucose	5.473	0.865–34.614	0.071
High leukocyte count	4.894	1.480–16.179	0.009
Complications	3.502	1.103–11.117	0.033
Length of stay	0.029	0.006–0.141	<0.001

GCS: Glasgow Coma Scale, OR: Odds ratio, CI: Confidence interval

and urinary tract infection). This study confirmed the finding of previous studies that complications will increase the risk of death.[3,5] Patients with low GCS score have a higher risk of complications and more massive hematoma.[3,5,6]

The adjusted OR for high random blood glucose is not significantly increase the risk of death. The previous review showed that hyperglycemia is related with other ischemic event in patients with hemorrhagic stroke.[7] Hyperglycemia also increases the risk of hematoma expansion.[8] Hyperglycemia in patients with hemorrhagic stroke is related with cytokine activation from the blood extravasation. High cytokine (tumor necrosis factor and interleukin-1) levels are related with higher inflammatory process. High inflammatory process will lead to hyperglycemia condition.[9]

Our study confirmed that high leukocyte count increases the risk of death. The previous study showed that high leukocyte count is correlated with lower GCS, higher disability, and death.[10] High leukocyte count is related with higher inflammatory process and parenchymal brain damage.[11] High leukocyte count in hemorrhagic stroke is a product of stress phenomenon, catecholamine release, and steroid hormone production.[12]

Our study also confirmed that complications increase the death in patients with hemorrhagic stroke. Medical complications (GI bleeding and urinary tract infection) are common in patients with stroke. GI bleeding will cause hypotension and low hemoglobin level. These two conditions will increase the risk of death and disability.[13] Urinary tract infection is a poor prognosis of stroke. The UTI increases the risk of death, disability, and prolonged length of stay.[14] Dysphagia and pneumonia also increase the risk of death and disability. Pneumonia also significantly increases the hospital cost and length of stay.[15]

This study showed that there is an inverse relationship between lengths of stays and mortality. This phenomenon is caused by early death in patients with hemorrhagic stroke. The result is confirmed with previous studies that prolonged length hospital stay is not the risk of death in patients with hemorrhagic stroke.[16,17] The risk of death in patients with hemorrhagic stroke in prolonged hospital stay is associated with the presence of medical complications and not related with the nature of the hemorrhagic stroke.[18,19]

The limitation of our study is the short-term follow-up. We only observed the inhospital mortality and do not follow-up the patients. We only studied patients that not being operated. The use of electronic stroke registry and systematic review of electronic medical record are the strength of this study. Further studies should have longer follow-up.

CONCLUSION

This study showed that lower GCS, high leukocyte count, and the presence of complications would increase the risk of mortality. Prevention of complications should be systematically performed for better prognosis.

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