ORIGINAL ARTICLE

Factors Associated with Intraventricular Hemorrhage in Patients with Intracerebral Hemorrhage

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Objective: To evaluate risk factors for intraventricular hemorrhage (IVH) in patients with intracerebral hemorrhage (ICH).

Materials and Methods: The present study was a post-hoc analysis of the previously published article. Adult patients with ICH were enrolled. The eligible patients were divided into two groups, presence or absence of IVH. Clinical factors predictive of IVH were computed by using multivariable logistic regression analysis.

Results: Among 110 patients with ICH, 59 patients (53.64%) had IVH. There were five factors in the predictive model for IVH by multivariable logistic regression analysis. Of those, only age was independently associated with the presence of IVH with adjusted odds ratio of 1.035 (95% confidence interval of 1.002 to 1.070).

Conclusion: Over half of the patients with ICH had IVH. Only age was associated with IVH.

Keywords: Intraventricular hemorrhage; Intracerebral hemorrhage; Prevalence; Mortality; Associated factors

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Intracerebral hemorrhage (ICH) is a serious condition with high morbidity and mortality[1]. It has an incidence rate of 24.6 per 100,000 person-years[2]. The incidence of ICH may differ among countries. China had the highest incidence of ICH at 159.81 cases per 100,000 person-years in 2010. In the same year, over five million people worldwide had ICH. The major issue of ICH is the high mortality rate. A global burden of disease study found that an age-standardized mortality rate of ICH in 2021 was 39.1 per 100,000 people causing 3.308 million deaths globally[3].

Surgical treatment is an option for specific types of ICH such as those with worsening symptoms[4]. A previous study showed that surgical treatment may not be effective in patients with ICH[5]. The mortality rate between those treated with surgical treatment versus non-surgical treatment was comparable at 47.06% versus 39.47% (p=0.532). Note that the indication for surgical treatment in this study was based on indications of the 2015 ICH guideline and patient preference[4]. The same study also found that intraventricular hemorrhage (IVH) was associated with mortality with the high adjusted odds ratio of 5.30 (95% confidence interval (CI) of 1.65 to 17.01), particularly, those with IVH volume over 3 mL[6]. Similarly, another study[7] also showed that IVH was associated with hospital mortality in patients with subarachnoid hemorrhage with adjusted odds ratio of 12.128 (p=0.028). Causes and risk factors for IVH in adult patients are unclear[8]. The present study aimed to evaluate risk factors for IVH in patients with ICH.

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Materials and Methods

The present study was a post-hoc analysis of a previously published article[4]. Adult patients with ICH admitted to the neurosurgery ward and required surgical treatment[4]. The study was conducted at a tertiary referral hospital in the northeast Thailand between 2012 and 2021. The study protocol received approval from the Ethics Committee of Khon Kaen Hospital, Thailand (KEXP65078). Baseline clinical

Table 1. Baseline characteristics of patients with intracerebral hemorrhage categorized by presence of intraventricular hemorrhage (IVH)

Factors	No IVH (n=51)	IVH (n=59)	p-value
Age (years); mean [SD]	59.76 [13.24]	66.76 [12.72]	0.006
Male sex; n (%)	29 (56.86)	31 (52.54)	0.650
Current alcohol drinking; n (%)	13 (25.49)	8 (13.56)	0.112
Current smoker; n (%)	12 (23.53)	4 (6.78)	0.013
Co-morbid diseases; n (%)			
Hypertension	20 (39.22)	40 (34.80)	0.003
DM	2 (3.92)	15 (25.42)	0.002
Liver disease	0 (0.00)	3 (5.08)	0.103
Chronic kidney disease	0 (0.00)	3 (5.08)	0.103
Dyslipidemia	1 (1.96)	5 (8.47)	0.134
Barthel index; mean [SD]	22.20 [26.54]	9.32 [18.72]	0.004
Glasgow Outcome Scale (GOS); n (%)			0.006
Death	0 (0.00)	0 (0.00)	
Persistent vegetative state	4 (10.00)	14 (36.84)	
Severe disability	18 (45.00)	18 (47.37)	
Moderate disability	15 (37.50)	6 (15.79)	
Good recovery	3 (7.50)	0 (0.00)	
Glasgow Coma Scale (GCS); n (%)			<0.001
GCS 13-15	32 (62.75)	11 (18.97)	
GCS 5-12	10 (19.61)	11 (18.97)	
GCS 3-4	9 (17.65)	36 (62.07)	
SBP (mmHg); mean [SD]	173.25 [35.59]	184.51 [29.37]	0.072
DBP (mmHg); mean [SD]	100.76 [23.09]	102.08 [25.79]	0.779
Hypertensive emergency; n (%)	35 (68.63)	50 (84.75)	0.044

SD=standard deviation; DM=diabetes mellitus; SBP=systolic blood pressure; DBP=diastolic blood pressure

data, laboratory results, Modified Fisher Scale, and clinical outcome: mortality were evaluated in eligible patients (Table 1, 2). Barthel index, Glasgow Outcome Scale, and Glasgow Coma Scale were evaluated at baseline. Glasgow Outcome Scale was classified according to the disability as death, persistent vegetative state, severe disability, moderate disability, and good recovery. Glasgow Coma Scale was categorized as score of 13 to 15, score of 5 to 12, and score of 3 to 4[4]. Mortality was defined as in-hospital mortality and cases where treatment was denied.

Statistical analysis

The eligible patients were divided into two groups based on the presence of IVH as IVH and no IVH. Descriptive statistics were used to summarize numerical variables as mean with standard deviation (SD) and categorical variables as number (percentage). Differences between the two groups were assessed using inferential statistics, including the Student's t-test or chi-square test, as appropriate. Clinical predictors of IVH were identified using stepwise multivariable logistic regression analysis. Factors with a p-value of less than 0.05 in univariable logistic regression analysis were included in the predictive model, while those with a p-value below 0.25 were retained. The goodness of fit of the final model was evaluated using the Hosmer-Lemeshow chi-square test. All statistical analyses were conducted using Stata Statistical Software, version 18 (StataCorp LLC, College Station, TX, USA).

Results

IVH was present in 59 of 110 ICH patients (53.64%). Table 1 presents the baseline characteristics of patients categorized by the presence of IVH. Eight factors were significantly different between the two groups, age, Barthel index, smoking status, hypertension, diabetes, hypertensive emergency, Glasgow Outcome Score, and Glasgow Coma Scale. Patients in the IVH group were significantly older than those in the non-IVH group at 66.76 versus 59.76 years (p=0.006) and had a higher proportion of

Table 2. Laboratory results of patients with intracerebral hemorrhage (ICH) categorized by presence of intraventricular hemorrhage (IVH)

Factors	No IVH (n=51)	IVH (n=59)	p-value
Hb (g/dL); mean [SD]	12.27 [2.13]	11.86 [2.12]	0.323
Hct (%); mean [SD]	36.24 [5.77]	35.23 [6.19]	0.385
WBC (cells/mm^3); mean [SD]	10582 [5167]	11374 [4045]	0.374
Platelet; mean [SD]	258 [106]	217 [100]	0.041
PT (seconds); mean [SD]	13.14 [5.83]	12.20 [0.92]	0.232
PTT (seconds); mean [SD]	24.40 [3.77]	22.90 [2.31]	0.013
Glucose (mg/dL); mean [SD]	163 [38]	201 [89]	0.346
BUN (mg/dL); mean [SD]	13.59 [6.02]	18.02 [14.28]	0.045
Cr (mg/dL); mean [SD]	0.91 [0.35]	1.19 [1.27]	0.133
eGFR (mL/minute/1.73 m^2); mean [SD]	80.30 [24.34]	76.72 [28.29]	0.487
Radiographic findings; n (%)			
Location			0.533
• Supratentorial	37 (86.05)	46 (90.20)	
• Infratentorial	6 (13.95)	5 (9.80)	
ICH volume ≥30 mL	8 (19.05)	28 (51.85)	0.001
Modified Fisher Scale; n (%)			<0.001
0	44 (86.27)	26 (44.07)	
1	2 (3.92)	0 (0.00)	
2	2 (3.92)	21 (35.59)	
3	3 (5.88)	1 (1.69)	
4	0 (0.00)	11 (18.64)	
Death; n (%)	9 (18.37)	37 (62.71)	<0.001

SD=standard deviation; Hb=hemoglobin; Hct=hematocrit; WBC=white blood cell; PT=prothrombin time; PTT=partial thromboplastin time; BUN=blood urea nitrogen; Cr=creatinine; eGFR=estimated glomerular filtration rate

Table 3. Factors predictive of intraventricular hemorrhage in patients with intracerebral hemorrhage (ICH)

Factors	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	1.042 (1.011 to 1.074)	0.007	1.035 (1.002, 1.070)	0.038
Smoking	0.236 (0.070 to 0.787)	0.019		
Hypertension	3.263 (1.490 to 7.144)	0.003		
Diabetes	8.352 (1.807 to 38.592)	0.007		
Hypertensive emergency	2.539 (1.008 to 6.397)	0.048		

OR=odds ratio; CI=confidence interval

hypertensive emergencies at 84.75% versus 68.63% (p=0.044). In terms of laboratory results, the IVH group demonstrated significantly lower platelet counts, shorter partial thromboplastin time (PTT), higher blood urea nitrogen (BUN) levels, a greater proportion of ICH volumes of 30 mL or more, a higher Modified Fisher Scale score of 4, and a higher mortality rate at 62.71% versus 18.37% (p<0.001) compared to the non-IVH group.

The predictive model for IVH, derived from multivariable logistic regression analysis (Table 3), included five factors. Among these, age was the only factor independently associated with the presence of IVH, with an adjusted odds ratio of 1.035 (95% CI 1.002 to 1.070). The model demonstrated good fit, as indicated by a Hosmer-Lemeshow test value of 4.26 (p=0.833).

Discussion

A previous study reported that IVH was uncommon in patients with ICH, with only 3.1% of patients (30 out of 905) having IVH in a tertiary care setting in India[7]. In contrast, the present study found a significantly higher rate of IVH in ICH patients at 53.64%. These differences may be attributed to variations in inclusion criteria such as the previous Indian study enrolled only patients without ICH, whereas the current study included those with ICH.

Additionally, the Indian study reported favorable 6-month outcomes in most patients at 83.33%, while both the present study and another prior study found high mortality rates of 62.71% and 36%, respectively[8]. Larger studies are needed to further evaluate and confirm these findings. The occurrence of IVH may be due to an expansion of ICH. A previous study found that those with ICH and IVH had increased ICH volume than those ICH without IVH at 18.0 mL versus 0.7 mL ($p<0.001$)[8].

The present study also investigated the predictors of IVH in patients with ICH. Among the significant factors identified in univariable logistic regression analysis, age was the only independent predictor in multivariable analysis (Table 3). While hypertension, diabetes, and hypertensive emergency were significant in univariable analysis, they were not retained in the multivariable model, suggesting that these factors were not strong predictors of IVH after adjustment for other variables. This contrasts with findings from two previous studies, where hypertension was identified as the main risk factor for IVH[7,8].

In the present study, age was significantly associated with IVH in both univariable and multivariable analyses. A previous study on 12 patients with primary IVH reported an average age of 78.9 years[9], suggesting that older adults are more prone to developing IVH compared to younger individuals. In patients with ICH, the presence of IVH may reflect a larger hemorrhage, indicating more severe disease. Another explanation is the higher risk of ICH in older adults, with a relative risk of 1.97 (95% CI 1.79 to 2.16) as reported in a systematic review of the general population[10]. This increased risk of ICH in older individuals may subsequently lead to a greater likelihood of IVH.

Limitation

The present study has limitations. First, the cases of IVH in this study were not primary IVH. Second, the study was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to other healthcare settings. Third, the predictive model was developed using baseline characteristics alone, without incorporating laboratory data. Finally, the sample size was small, and data was missing such as the specific location of ICH.

Conclusion

More than half of the patients with ICH had IVH, with age being the only factor associated with IVH.

What is already known about this topic?

- IVH is a significant risk factor for mortality in patients with ICH.
- Data on risk factors for IVH remains limited.

What does this study add?

- Approximately 50% of patients with ICH presented with IVH.
- Older age is a risk factor for IVH in patients with ICH.

Conflicts of interest

The authors declare no conflict of interest.

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