



Neurosurgical Intervention in Primary Intraventricular Hemorrhage : Experience from a Center in China

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Objective : Primary intraventricular hemorrhage (PIVH) is a rare type of neurologic disorder and remains a challenge for cerebrovascular surgeons. This study intended to investigate the factors associated with neurosurgical intervention and its impact on outcome after PIVH.

Methods : We retrospectively included consecutive patients with PIVH admitted to at a single tertiary academic medical center in China. Conservative treatment or neurosurgical intervention options (including endovascular therapy, craniotomy, stereotactic radiotherapy, endoscopic surgery or external ventricular drain) were assessed. Multivariable logistic regression was applied to determine associations.

Results : In total, 174 patients with PIVH were included in our analysis. There were 79 patients (45.4%) underwent surgery, which was associated with younger age ($p=0.004$), higher baseline Graeb score ($p=0.001$), acute hydrocephalus ($p=0.02$) and underlying cerebrovascular diseases ($p<0.001$) in an adjusted model. In multivariable logistic regression analysis, significant predictors of external ventricular drain after PIVH were higher baseline Graeb score ($p=0.04$), and acute hydrocephalus ($p<0.001$). Furthermore, after adjustment for confounders, our analysis showed that neurosurgical intervention could decrease 90-day mortality after PIVH ($p=0.04$).

Conclusion : After PIVH, younger patients with higher baseline Graeb score, acute hydrocephalus and underlying cerebrovascular diseases were more likely to undergo neurosurgical intervention. Surgical treatment of PIVH patients should be optimized to decrease mortality. However, further clinical trials are still needed to determine which patients would benefit from neurosurgical intervention.

Key Words : Cerebral intraventricular hemorrhage · Neurosurgery · Outcome.

INTRODUCTION

Primary intraventricular hemorrhage (PIVH) is a rare sub-type of neurological disorder, which is defined as bleeding in

the ventricular system without a parenchymal or subarachnoid component^{2,4,6,7,9,10,15}. It comprises only 3.1–9% of all intracerebral hemorrhages (ICHs) in previous findings, and is reported to be caused by a variety of underlying cerebrovascular disor-

• Received : September 19, 2024 • Accepted : January 5, 2025

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ders^{3,10,14,17-19}. However, the clinical characteristics and outcomes have not been well established. Furthermore, treatment of this hemorrhagic stroke remains inconsistent, challenging cerebrovascular surgeons.

The aim of this study was to determine the factors associated with neurosurgical intervention and its impact on outcome in

PIVH at our medical center, which treats approximately 800 spontaneous ICH patients annually. Review of data from this large academic medical center in China may provide a better understanding of the current practices of PIVH treatment and its outcomes.

Table 1. Demographics and clinical characteristics of the patients with and without neurosurgical intervention

Characteristic	Without neurosurgical intervention	With neurosurgical intervention	p-value
No. of patients	95 (54.6)	79 (45.4)	
Age (years)	50.73±14.43	39.96±18.82	<0.001*
Sex, female	40 (42.1)	37 (46.8)	0.53
Admission parameter			
Initial symptoms			
Headache	81 (85.3)	58 (73.4)	0.73
Vomiting	44 (46.3)	22 (27.8)	0.01*
Disturbance of consciousness	14 (14.7)	25 (31.6)	0.01*
GCS on admission	12.57±3.66	11.28±4.16	0.03*
Blood pressure			
Systolic blood pressure (mmHg)	152.28±29.62	143.88±36.16	0.10
Diastolic blood pressure (mmHg)	91.92±17.96	87.01±20.70	0.10
Imaging characteristic			
Baseline Graeb score	3.66±2.23	4.70±2.86	0.008*
Acute hydrocephalus	12 (12.6)	28 (35.4)	<0.001*
Etiological causes			
With cerebrovascular diseases	15 (15.8)	40 (50.6)	<0.001*
Idiopathic	80 (84.2)	39 (49.4)	
Background cerebrovascular risk factors			
Hypertension	53 (55.8)	30 (38.0)	0.02*
Diabetes	6 (6.3)	5 (6.3)	0.99
Smoking	22 (23.2)	19 (24.1)	0.89
Chronic alcoholism	24 (25.3)	14 (17.7)	0.23
Stroke history	5 (5.3)	4 (5.1)	0.95
Anticoagulation or antiplatelet treatment	9 (9.5)	1 (1.3)	0.02*
Laboratory test			
Blood glucose (mmol/L)	7.91±2.75	7.62±2.72	0.48
Hemoglobin (g/L)	136.53±22.95	135.69±18.92	0.80
Platelet (10 ⁹ cells/L)	169.44±66.42	182.55±75.69	0.23
WBC (10 ⁹ cells/L)	11.62±6.91	12.19±5.71	0.60
ANC (10 ⁹ cells/L)	9.29±4.11	10.17±5.69	0.25
ALC (10 ⁹ cells/L)	1.76±5.98	1.35±0.82	0.56
AMC (10 ⁹ cells/L)	0.50±0.26	0.56±0.32	0.16

Values are presented as mean±standard deviation or number (%). *p<0.05. GCS : Glasgow coma scale, WBC : white blood cell, ANC : absolute neutrophil count, ALC : absolute lymphocyte count, AMC : absolute monocyte count

MATERIALS AND METHODS

The Institutional Review Board at West China Hospital, Sichuan University approved our study. All participants gave written informed consent.

Patients and population

We identified all inpatients with PIVH who were diagnosed by brain computed tomography (CT) imaging at the Department of Neurosurgery, West China Hospital, Sichuan University between 2014 and 2020. Subjects were included in the present study if they had intraventricular hemorrhage (IVH) without intraparenchymal or subarachnoid involvement on CT scan. They with a history of head trauma or with parenchymal or subarachnoid hemorrhage on CT scan would be excluded.

Clinical assessment

Data were collected including the demographic information about the patients, initial symptoms, Glasgow coma scale (GCS) score and blood pressure at admission. Radiological characteristics, including initial Graeb score, acute hydrocephalus and the underlying etiological causes by computed tomography angiography and/or digital subtraction angiography were also evaluated. Background cerebrovascular risk factors were reviewed as well. Laboratory parameters, including blood glucose, hemoglobin, platelet, white blood cell (WBC) count, absolute neutrophil count (ANC), absolute lymphocyte count, and absolute monocyte count (AMC) within 24 hours of admission were obtained. Conservative treatment or any neurosurgical intervention options (including endovascular therapy, craniotomy, stereotactic radiotherapy, endoscopic surgery or external ventricular drain [EVD]) were assessed. Variables were analyzed to determine their associations with neurosurgical and EVD.

We also evaluated the clinical outcomes with or without neurosurgical intervention by comparing the discharge or 90-day mortality and poor outcome (defined as modified Rankin scale [mRS] ≥ 3). The discharge status was reviewed from medical records, while the 90-day condition was evaluated at outpatient clinic or through telephone interviews.

Statistical analysis

Statistics were performed with SPSS version 21 (IBM SPSS, Chicago, IL, USA). Student's *t* test was used in normally distrib-

uted continuous variables, while for categorical variables, chi-square testing was applied. Variables that were significant in the univariate analysis were included in the multivariate logistic model to evaluate the associations. The association between factors and neurosurgical intervention or EVD was estimated by the odds ratio (OR) with a 95% confidence interval (CI). A *p*-value of <0.05 was set as the level of statistical significance.

RESULTS

During the 7-year period, 183 patients with PIVH were identified in our center, and nine of them were lost to our follow up. A total of 174 patients were assessed in our final analysis. Among them, 79 subjects (45.4%) underwent neurosurgical intervention after PIVH onset.

The baseline demographic and clinical parameters between patients with and without neurosurgical intervention are presented in Table 1. The neurosurgical intervention group had younger age (39.96 ± 18.82 vs. 50.73 ± 14.43 ; $p < 0.001$), fewer cases with vomiting (27.8% vs. 46.3%; $p = 0.01$), more cases of disturbance of consciousness (31.6% vs. 14.7%; $p = 0.01$), lower GCS score (11.28 ± 4.16 vs. 12.57 ± 3.66 ; $p = 0.03$), higher baseline Graeb score (4.70 ± 2.86 vs. 3.66 ± 2.23 ; $p = 0.008$). They also had higher prevalence of acute hydrocephalus (35.4% vs. 12.6%; $p < 0.001$), underlying cerebrovascular diseases (50.6% vs. 15.8%; $p < 0.001$) and lower rates of hypertension (38.0% vs. 55.8%; $p = 0.02$) and

Table 2. Multivariable analysis including factors associated with neurosurgical intervention

Characteristic	OR	95% CI	<i>p</i> -value
Age (years)	0.96	0.94–0.99	0.004*
Vomiting	0.47	0.21–1.07	0.07
Disturbance of consciousness	2.46	0.75–8.03	0.14
GCS at admission	1.13	0.97–1.31	0.13
Baseline Graeb score	1.44	1.16–1.78	0.001*
Acute hydrocephalus	3.36	1.21–9.37	0.02*
With cerebrovascular diseases	6.17	2.40–15.90	$<0.001^*$
Hypertension	1.21	0.50–2.96	0.67
Anticoagulation or antiplatelet treatment	0.14	0.02–1.38	0.09

Adjusted for age, vomiting, disturbance of consciousness, GCS at admission, baseline Graeb score at admission, acute hydrocephalus, with cerebrovascular diseases, hypertension, and anticoagulation or antiplatelet treatment. * $p < 0.05$. OR : odds ratio, CI : confidence interval, GCS : Glasgow coma scale

anticoagulation or antiplatelet treatment (1.3% vs. 9.5%; $p=0.02$). After adjusting for age, vomiting, disturbance of consciousness, GCS at admission, baseline Graeb score at admission, acute hydrocephalus, underlying cerebrovascular diseases, hypertension, and anticoagulation or antiplatelet treatment, neurosurgical intervention was associated with younger age ($p=0.004$; OR,

0.96; 95% CI, 0.94–0.99), higher baseline Graeb score ($p=0.001$; OR, 1.44; 95% CI, 1.16–1.78), acute hydrocephalus ($p=0.02$; OR, 3.36; 95% CI, 1.21–9.37) and underlying cerebrovascular diseases ($p<0.001$; OR, 6.17; 95% CI, 2.40–15.90) (Table 2).

We also evaluated the factors associated with EVD. The patients with EVD had lower incidence rate of presenting with

Table 3. Demographics and clinical characteristics of the patients with and without external ventricular drain

Characteristic	Without EVD	With EVD	p-value
No. of patients	136 (78.2)	38 (21.8)	
Age (years)	45.70±17.32	46.34±17.77	0.84
Female sex	59 (43.4)	18 (47.4)	0.66
Admission parameter			
Initial symptoms			
Headache	118 (86.8)	21 (55.3)	<0.001*
Vomiting	53 (39.0)	13 (34.2)	0.59
Disturbance of consciousness	18 (13.2)	21 (55.3)	<0.001*
GCS on admission	12.91±3.45	8.66±3.79	<0.001*
Blood pressure			
Systolic blood pressure (mmHg)	147.40±32.38	152.54±34.91	0.40
Diastolic blood pressure (mmHg)	89.14±18.90	91.78±21.05	0.46
Imaging characteristic			
Graeb score	3.55±2.27	6.21±2.58	<0.001*
Acute hydrocephalus	17 (12.5)	23 (60.5)	<0.001*
Etiological causes			
With cerebrovascular diseases	42 (30.9)	13 (34.2)	0.70
Idiopathic	94 (69.1)	25 (65.8)	
Background cerebrovascular risk factors			
Hypertension	64 (47.1)	19 (50.0)	0.75
Diabetes	8 (5.9)	3 (7.9)	0.65
Smoking	29 (21.3)	12 (31.6)	0.19
Chronic alcoholism	31 (22.8)	7 (18.4)	0.56
Stroke history	7 (5.1)	2 (5.3)	0.98
Anticoagulation or antiplatelet treatment	9 (6.6)	1 (2.6)	0.35
Laboratory test			
Blood glucose (mmol/L)	7.52±2.77	8.68±2.41	0.02*
Hemoglobin (g/L)	136.56±21.47	134.71±20.35	0.64
Platelet (10 ⁹ cells/L)	175.01±66.24	176.50±86.01	0.91
WBC (10 ⁹ cells/L)	11.12±6.18	14.53±6.48	0.003*
ANC (10 ⁹ cells/L)	8.91±4.05	12.40±6.45	<0.001*
ALC (10 ⁹ cells/L)	1.63±5.04	1.39±0.94	0.77
AMC (10 ⁹ cells/L)	0.50±0.25	0.62±0.38	0.03*

Values are presented as mean±standard deviation or number (%). * $p<0.05$. EVD : external ventricular drain, GCS : Glasgow coma scale, WBC : white blood cell, ANC : absolute neutrophil count, ALC : absolute lymphocyte count, AMC : absolute monocyte count

headache (55.3% vs. 86.8%; $p < 0.001$) and higher rate with disturbance of consciousness (55.3% vs. 13.2%; $p < 0.001$) (Table 3). They had lower GCS score (8.66 ± 3.79 vs. 12.91 ± 3.45 ; $p < 0.001$), higher Graeb score (6.21 ± 2.58 vs. 3.55 ± 2.27 ; $p < 0.001$) and higher rates of acute hydrocephalus (60.5% vs. 12.5%; $p < 0.001$). In addition, The EVD group had a significantly higher admission blood glucose (8.68 ± 2.41 vs. 7.52 ± 2.77 mmol/L; $p = 0.02$), WBC count (14.53 ± 6.48 vs. 11.12 ± 6.18 10^9 cells/L; $p = 0.003$), ANC (12.40 ± 6.45 vs. 8.91 ± 4.05 10^9 cells/L; $p < 0.001$), and AMC (0.62 ± 0.38 vs. 0.50 ± 0.25 10^9 cells/L; $p = 0.03$) than that of the non-EVD group. In multivariable logistic regression analysis, significant predictors of EVD after PIVH were higher baseline Graeb score ($p = 0.04$; OR, 1.27; 95% CI, 1.01–1.58), and acute hydrocephalus ($p < 0.001$; OR, 6.50; 95% CI, 2.47–17.10) (Table 4).

Associations of neurosurgical intervention with 90-day outcome are presented in Table 5. Although neurosurgical inter-

vention did not seem to decrease the 90-day poor outcome either in univariable ($p = 0.13$; OR, 1.72; 95% CI, 0.86–3.45) and multivariable analysis ($p = 0.38$; OR, 0.59; 95% CI, 0.18–1.91), it could decrease 90-day mortality after PIVH ($p = 0.04$; OR, 0.22; 95% CI, 0.05–0.92) after adjusting for confounders.

DISCUSSION

The present study represents the largest single cohort of patients with PIVH reported to date. Our data suggest that younger patients with higher baseline Graeb score, acute hydrocephalus and underlying cerebrovascular diseases were more likely to undergo neurosurgical intervention after PIVH. In further analysis, significant predictors of EVD after PIVH were higher baseline Graeb score and acute hydrocephalus. Besides, neurosurgical intervention could significantly decrease 90-day mortality in PIVH after adjustment. Our study indicated that surgical treatment of PIVH patients should be optimized to decrease mortality.

The management of PIVH patients remains a challenge for cerebrovascular surgeons and neurologists. In our study, 45.4% of patients underwent a surgical procedure. However, the rates of patients with neurosurgical intervention ranged from 13.3% to 100% in previous studies which were conducted in seven different countries including United States, China, Germany, Turkey, Spain, India, and South Korea^{3,7,10,14,15,17-19}. This broad range indicated that surgical practice for PIVH varies between countries. As the decision to perform neurosurgical intervention in PIVH is multifactorial, neurosurgeons may choose different treatment strategies according to their experience and acceptance of the clinical evidence.

Table 4. Multivariable analysis including factors associated with external ventricular drain

Characteristic	OR	95% CI	p-value
Disturbance of consciousness	2.26	0.70–7.35	0.18
GCS at admission	0.91	0.76–1.09	0.32
Baseline Graeb score	1.27	1.01–1.58	0.04*
Acute hydrocephalus	6.50	2.47–17.10	<0.001*
Blood glucose	0.85	0.69–1.05	0.13
WBC	1.46	0.82–2.60	0.20
ANC	0.73	0.42–1.26	0.26
AMC	0.74	0.09–6.35	0.78

Adjusted for disturbance of consciousness, GCS at admission, baseline Graeb score, acute hydrocephalus, blood glucose, WBC, ANC, and AMC. * $p < 0.05$. OR : odds ratio, CI : confidence interval, GCS : Glasgow coma scale, WBC : white blood cell, ANC : absolute neutrophil count, AMC : absolute monocyte count

Table 5. Associations of neurosurgical intervention with 90-day outcome

Intervention	Unadjusted		Adjusted	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Neurosurgical intervention				
Mortality	0.96	1.02 (0.43–2.42)	0.04*	0.22 (0.05–0.92)
Poor outcome	0.13	1.72 (0.86–3.45)	0.38	0.59 (0.18–1.91)
EVD				
Mortality	0.001	4.77 (1.93–11.79)	0.94	0.95 (0.26–3.55)
Poor outcome	<0.001	4.63 (2.13–10.03)	0.33	0.52 (0.14–1.94)

Adjusted for age, disturbance of consciousness, GCS at admission, baseline Graeb score at admission, acute hydrocephalus, and with cerebrovascular diseases. * $p < 0.05$. OR : odds ratio, CI : confidence interval, EVD : external ventricular drain, GCS : Glasgow coma scale

Currently, no definitive medical treatment has been established for PIVH, among which EVD remains widely available as the primary treatment option for patients with PIVH. EVD placement is a minimally invasive neurosurgical intervention for PIVH, which could provide the potential benefits of monitoring intracranial pressure, draining cerebrospinal fluid, and evacuating intraventricular blood¹⁾. However, no evidence-based consensus for the indication of EVD insertion in PIVH patients has reached. Furthermore, previous evaluations of EVD use in these patients have been limited to small cohorts^{2-4,7,10,14,15,17)}. Although Herrick et al.¹³⁾ determined that the characteristics of patients who were more likely to have an EVD placed were lower GCS, higher IVH severity, and lower ICH volume in secondary IVH, we identified patients with EVD use based on clinical and radiographic criteria in one of the largest PIVH cohorts. In our study, independent predictors of EVD use after PIVH were higher baseline Graeb score and acute hydrocephalus. These characteristics may represent current considerations of neurosurgeons in China to place EVD in PIVH settings. Although variations exist between countries, the rate of EVD use in the present study (21.8%) was higher than previous reports in ICH^{5,12)}. This could be attributable to the presupposed high mortality rate of PIVH based on the neurosurgeons' judgement. In addition, EVD offers the option of concomitant use of intrathecal pharmacotherapy in PIVH. Trials have been conducted to assess the impact of intraventricular thrombolysis therapy in IVH secondary to ICH. A randomized, multicenter trial has already demonstrated the safety of irrigation with alteplase with EVD that in patients with IVH¹¹⁾. Furthermore, a meta-analysis with 316 patients in 12 observational studies included, compared the effect of intraventricular fibrinolysis (IVF) with EVD alone, supported the favor of IVF as an adjunct to EVD in secondary IVH⁸⁾. In addition, neuroendoscopic techniques may have a role in guiding EVD position and the potential therapeutic benefit for aspiration or removal of IVH. However, well-designed randomized trials are still needed to investigate the effect of fibrinolytic agents with EVD and neuroendoscopic techniques in patients with PIVH.

Studies have tested the potential benefits of surgical intervention in secondary IVH. A retrospective review of 183 consecutive IVH patients described a reduced mortality and mRS score towards EVD placement for patients with GCS >3 and hydrocephalus¹³⁾. Furthermore, a large meta-analysis by Nieuwkamp et al.¹⁶⁾ demonstrated a significant decrease of mortality with

EVD utilization in patients with IVH secondary to ICH. However, the impact of surgical treatment has not been evaluated in patients with PIVH as the low incidence rate. As the majority of studies examining the impact of surgery limit their patient sample to secondary IVH, the impact of neurosurgery on PIVH patients remains poorly understood. In our study although neither neurosurgical intervention nor EVD placement could improve the short and long-term outcomes, the neurosurgical intervention was suggested to decrease the 90-day mortality. However, a randomized clinical trial evaluating the use of EVD may be a necessary to further confirm the value of neurosurgical intervention in PIVH.

Our study is the first cohort with both detailed clinical information and outcome variables to investigate the role of neurosurgical intervention in PIVH. However, some limitations still should be considered in our study. First limitation is the retrospective design of our study, which may represent selection bias. In addition, our hospital is an academic medical center with standard neurosurgical training, which may lead to a positive bias towards higher neurosurgical quality. Finally, although our study contained detailed information, some unmeasured confounders such as neurosurgeon's opinions on the possible benefit of surgery in a certain PIVH patient may have been missed in our analysis.

CONCLUSION

In summary, our analysis indicated that neurosurgeons tended to perform interventions on younger patients with higher baseline Graeb score, acute hydrocephalus and underlying cerebrovascular diseases after PIVH. Significant predictors of EVD after PIVH higher baseline Graeb score and acute hydrocephalus. In addition, neurosurgical intervention could significantly decrease 90-day mortality in PIVH. Therefore, early identification of severe PIVH based on age, clinical and radiological parameters may facilitate neurosurgical intervention and reduce the mortality of patients with this serious condition. However, further studies with a large scale are still needed to confirm our findings.

AUTHORS' DECLARATION

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Informed consent

Informed consent was obtained from all individual participants included in this study.

Author contributions

Conceptualization : CF, RG; Data curation : XZ; Formal analysis : XZ; Funding acquisition : CY; Methodology : YL; Project administration : CY; Visualization : RC; Writing - original draft : XZ; Writing - review & editing : CF, RG

Data sharing

None

Preprint

None

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