



Long-term Outcomes and Risk Factors Related to Hydrocephalus After Intracerebral Hemorrhage

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Received: 31 March 2020 / Revised: 29 April 2020 / Accepted: 13 May 2020 / Published online: 8 June 2020
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Abstract

Hydrocephalus after intracerebral hemorrhage (ICH) is a common and treatable complication. However, the long-term outcomes and factors for predicting hydrocephalus have seldom been studied. The goal of this study was to determine the long-term outcomes and analyze the risk factors of hydrocephalus after ICH. A consecutive series of 1342 patients with ICH were reviewed from 2010 to 2016 to identify significant risk factors for hydrocephalus. Patients with a first-ever ICH without any prior diagnosis of hydrocephalus after ICH were followed up for survival status and cause of death. Risk factors for hydrocephalus were evaluated by using logistic regression analysis. Out of a total of 1342 ICH patients, 120 patients (8.9%) had hydrocephalus. The risk factors for hydrocephalus (≤ 3 days) were infratentorial hemorrhage ($p = 0.000$), extension to ventricles ($p = 0.000$), greater ICH volume ($p = 0.09$), and hematoma expansion ($p = 0.01$). Extension to ventricles ($p = 0.022$) was the only independent risk factor for hydrocephalus (4–13 days), while extension to ventricles ($p = 0.028$), decompressive craniotomy ($p = 0.032$), and intracranial infection ($p = 0.001$) were independent predictors of hydrocephalus (≥ 14 days). Patients were followed up for a median of 5.2 years (IQR 3.3–7.3 years). Estimated all-cause mortality was significantly higher in the ICH patients with hydrocephalus than that without hydrocephalus (HR 3.22, 95% CI 2.42–4.28; $p = 0.000$). Fifty-nine (49.2%) died and 40 (33.3%) had a favorable outcome in patients with hydrocephalus. Of all deaths, 30.5% were from ICH and 64.4% from infection. Hydrocephalus is a frequent complication of ICH and most commonly occurs at the onset of ICH. Patients with hydrocephalus show relatively higher mortality. [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02135783) Identifier: NCT02135783 (May 7, 2014)

Keywords Hydrocephalus · Risk factors · Long-term outcome · Intracerebral hemorrhage

Introduction

Hydrocephalus occurs up to 50% of patients with intraventricular hemorrhage (IVH), which is secondary to intracerebral hemorrhage (ICH) [1, 2]. Recent studies have suggested that hydrocephalus is a predictor of poor prognosis after ICH [2–6]. Both human and animal studies on hydrocephalus after IVH/ICH are rare [7]. Although a few researchers have

reported the therapeutic effect and prognosis of hydrocephalus after ICH with small patient populations [8–13], the long-term outcomes, the prevention, and the association with other complications still remain uncertain. The goal of this study is to assess the risk factors and determine the long-term outcomes of hydrocephalus after ICH.

Materials and Methods

Patients

We identified all patients with ICH between January 2010 and December 2016 from the Department of Neurosurgery in the Southwest Hospital of the Third Military Medical University (Army Medical University). A long-term follow-up of ICH patients was performed. Ethics approval was obtained from the Ethics Committee of the Southwest Hospital of Third

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Military Medical University. Waiver of informed consent was granted for the retrospective cohort.

The patients diagnosed with acute ICH by computed tomography (CT) were included in the study. Patients were eligible for enrollment if they were 18 years of age or older and first-ever ICH. Patients with secondary causes, such as underlying aneurysm, vascular malformation, tumor, head trauma, or hemorrhagic transformation of ischemic infarcts, were excluded. Patients who had hydrocephalus before ICH were also excluded from the study. Any severe pre-existing physical or mental disability or severe comorbidity that might interfere with the assessment of outcome was also excluded.

Hydrocephalus was determined both radiographic evidence and progressive clinical manifestations of hydrocephalus within 1 year after first-ever ICH [14]. The criteria of hydrocephalus on CT or magnetic resonance imaging (MRI) images were as follows: (1) an Evans index (the largest width of the frontal horns of the lateral ventricles/the internal diameter of the skull at the same level) more than 0.3; (2) the enlargement of the anterior horns of the lateral ventricles, temporal horns and third ventricle, and periventricular interstitial edema in the presence of normal or absent sulci [15]. The clinical characteristics of hydrocephalus included neurobehavioral (e.g., inappropriate behavior and depressed mood) and cognitive (e.g., inability to plan or make a decision, memory, or language disturbances) disorders in conscious patients and deterioration of consciousness in the comatose patients [14, 16]. A ventriculoatrial shunt was considered in patients with progressive ventricular dilation and clinical deterioration.

Data Processing

For each patients, information on demographic data (age, sex, smoking history, drinking history), medical history data (hypertension, diabetes mellitus, coronary artery disease, history of stroke), and clinical data at admission (Glasgow Coma Scale score, IVH score [17], systolic blood pressure, diastolic blood pressure); imaging data (ICH volumes and IVH volumes [measured on CT using the ABC/2 [18]], hematoma location [supratentorial and infratentorial], extension to ventricles, hematoma expansion [more than 6 mL or 33% growth compared with the initial ICH volume within 24 h of symptom onset [19, 20]], dilatation of each ventricles of hydrocephalus) were collected; decompressive craniotomy (according to the intracranial pressure (ICP) when the ICP exceeded 20 mmHg by using a ICP monitoring device [Codman, Johnson and Johnson Medical Ltd., Raynham, MA] inserted into the brain parenchyma or cerebral ventricles), hematoma evacuation, rate of clot removal, thrombolysis, extraventricular drainage (EVD), lumbar drainage, ventriculoatrial shunt composed the surgical data. Leucocyte, hemoglobin, platelet, and blood glucose composed the laboratory data. Treatment-related data (time of hydrocephalus ictus, in-hospital outcome, and

complications [gastrointestinal bleeding, pneumonia, ischemic stroke, intracranial infection]) were also collected. All CT scans were evaluated by an experienced investigator who was blinded to patients' clinical and biochemical data.

Follow-up

Survival status and cause of death were followed until May 31, 2019. Follow-up was performed by face-to-face interview or telephone call. Cause of death data are classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) and registered in the Cause of Death Registry [20, 21]. The underlying causes of death in this study were categorized into the following groups: (1) cerebrovascular disease (corresponding to ICD-10, I60-69; subdivided into death related to index ICH, new ICH, and ischemic stroke); (2) infection; and (3) other causes of death (for example, renal failure, dementia, and gastrointestinal bleeding). The outcome was measured by modified Rankin scale (mRS). Unfavorable outcome was defined as mRS grades 4–6 (mRS 4 = moderately severe disability; mRS 6 = dead) [18].

Statistical Analysis

Data analysis was performed using the SPSS software for Windows (version 13.0, Inc., Chicago, IL). Data were presented as mean (standard deviation [SD]) or counts (percentages). Quantitative variables were presented as mean \pm SD and compared using Student's *t* test or nonparametric test, whereas categorical variables were expressed as counts with percentages and compared using the χ^2 test or continuity correction test. Significant variables ($p < 0.05$) were entered into the multivariable analysis via the binary logistic regression model of risk factors for hydrocephalus. Survival curves were estimated by the Kaplan-Meier survivor function and compared through log-rank test. Estimated all-cause mortality was tested with Cox proportional hazard regression models. Risk factors for poor outcome within follow-up were tested with Cox proportional hazard regression models, and the variables that had a significant ($p < 0.05$) association in the univariable analysis were included in the multivariable analysis. A $p < 0.05$ indicated statistically significant.

Results

Characteristics of Patients

A total of 1342 patients with first-ever ICH were initially enrolled. Eight patients were lost to follow-up. During 1 year after ICH, 120 (8.9%) developed hydrocephalus and the inter-rater agreement was 0.922 ($p = 0.000$) for the assessing of

hydrocephalus between two experienced investigators. Among 455 patients with IVH secondary to ICH, hydrocephalus occurred in 22.0% (100 of 455 patients). Dilatation of lateral ventricles, third ventricles, and fourth ventricles was 100%, 58.3%, and 30.0%, respectively. Three patients of hydrocephalus with high opening pressure and one patient with normal opening pressure underwent a ventriculoperitoneal shunt. Clinical improvement was seen in 3 cases and 1 case revealed no recovery of clinical signs because of occlusion at the distal catheter. Hydrocephalus appeared within 24 h in 63 (52.5%), within 3 days in 80 (66.7%), 4 days to 13 days in 14 (11.7%), and more than 14 days in 26 (21.6%) (Fig. 1). The baseline characteristics of these patients are shown in Table 1. There was no difference between the patients with hydrocephalus and those without hydrocephalus with respect to age, sex, previous diseases, and lifestyle factors.

Predictors of Hydrocephalus After ICH

Univariate and multivariate logistic regression analyses were used to identify independent predictors of hydrocephalus (Table 1 and Table 2). The independent risk factors for hydrocephalus (≤ 3 days) in the multivariable analysis were infratentorial hemorrhage ($p = 0.000$), extension to ventricles ($p = 0.000$), greater ICH volume ($p = 0.009$), and hematoma expansion ($p = 0.010$). Extension to ventricles ($p = 0.022$) was the only independent risk factor for hydrocephalus (4–13 days), while extension to ventricles ($p = 0.028$), decompressive craniotomy ($p = 0.032$), and intracranial infection ($p = 0.001$) were independent predictors of hydrocephalus (≥ 14 days).

Long-term Outcome of Hydrocephalus After ICH

In hospital, there were 20 deaths (16.7%) and 94 (78.3%) patients of poor outcome for ICH with hydrocephalus. Thirty-four patients (2.8%) died and poor outcome occurred

in 580 (47.5%) patients without hydrocephalus in hospital. There was significant difference between the patients with hydrocephalus and those without hydrocephalus of death ($p = 0.000$) and poor outcome ($p = 0.000$). Among all patients after ICH, 61 (50.8%) patients with hydrocephalus and 962 (78.7%) patients without hydrocephalus survived followed up for a median of 5.2 years (IQR 3.3–7.3 years). Rates of mortality and disability in hydrocephalus of the patients with ICH at discharge and follow-up are shown in Fig. 2. Overall survival for ICH patients is shown in Fig. 3. Estimated all-cause mortality was significantly higher in the ICH patients with hydrocephalus than that without hydrocephalus (HR 3.22, 95% CI 2.42–4.28; $p = 0.000$).

Predictors for Long-term Poor Outcome of ICH

Cox regression analysis showed that higher age ($p = 0.000$), diabetes mellitus ($p = 0.000$), higher systolic BP ($p = 0.014$), greater total ICH volume ($p = 0.000$), extension to ventricles ($p = 0.002$), pneumonia ($p = 0.000$), ischemic stroke ($p = 0.007$), and gastrointestinal bleeding ($p = 0.005$) are independent predictors for poor outcome during follow-up (Table 3). Hydrocephalus (HR 1.446, 95% CI 1.118 to 1.869, $p = 0.005$) was found to be a significant predictor for poor outcome after ICH.

Cause of Death in Patients with Hydrocephalus After ICH

The cumulative numbers of observed deaths during follow-up hydrocephalus after ICH were the following: 18 (30.5%) due to ICH, 38 (64.4%) due to infection (pneumonia and intracranial infection), 2 (3.4%) due to ischemic stroke, 1 (1.7%) due to other causes (dementia). All-cause and cause-specific mortalities (n [%]) in patients for hydrocephalus after intracerebral hemorrhage are shown in Table 4.

Fig. 1 The timing of developing hydrocephalus in the patients with intracerebral hemorrhage. The time was within 1 day, within 3 days, 4 days to 13 days, and more than 14 days in 52.5%, 66.7%, 11.7%, and 21.6% of the patients with hydrocephalus after ICH, respectively

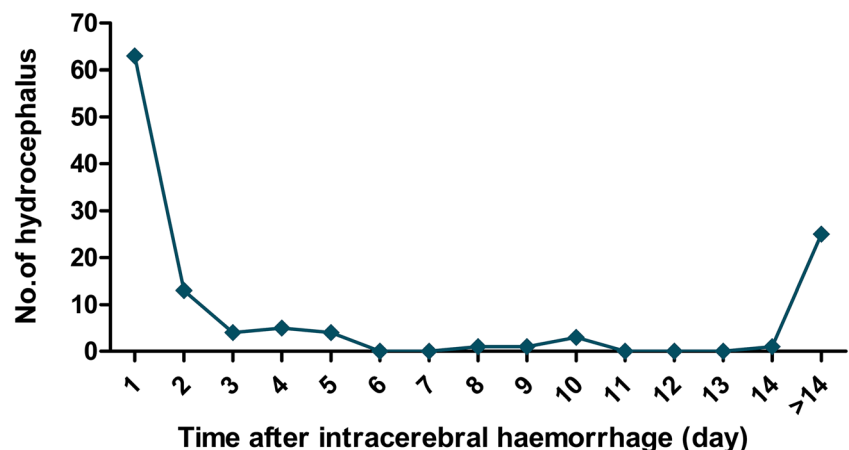


Table 1 The baseline characteristics of the patients with hydrocephalus after ICH

Variables	No hydrocephalus (<i>n</i> = 1222)	Hydrocephalus				P ₁	P ₂	P ₃	P ₄
		Total (<i>n</i> = 120)	≤ 3 days (<i>n</i> = 80)	4–13 days (<i>n</i> = 14)	≥ 14 days (<i>n</i> = 26)				
Age (years, mean ± SD)	59 ± 12	59 ± 12	61 ± 12	58 ± 13	52 ± 12	0.680	0.035	0.749	0.009
Male (<i>n</i> (%))	863 (70.6)	85 (70.8)	51 (63.8)	14 (78.6)	23 (88.5)	0.961	0.193	0.723	0.120
Medical history (<i>n</i> (%))									
Hypertension	826 (67.6)	82 (68.3)	55 (68.8)	9 (64.3)	18 (69.2)	0.869	0.83	1.000	0.860
Diabetes mellitus	72 (5.9)	11 (9.2)	8 (10.0)	-	3 (11.5)	0.155	0.214	0.717	0.434
Coronary artery disease	35 (2.9)	7 (5.8)	6 (7.5)	-	1 (3.8)	0.132	0.049	1.000	1.000
History of stroke	87 (7.1)	12 (10.0)	9 (11.3)	1 (7.1)	2 (7.7)	0.249	0.171	1.000	1.000
Lifestyle factors (<i>n</i> (%))									
Smoking	473 (38.7)	47 (39.2)	28 (35.0)	6 (42.9)	13 (50.0)	0.921	0.509	0.751	0.243
Drinking	470 (38.5)	48 (40.0)	32 (40.0)	5 (35.7)	11 (42.3)	0.741	0.784	0.834	0.69
Clinical features									
Temperature (°C, mean ± SD)	36.6 ± 0.4	36.6 ± 0.4	36.7 ± 0.4	36.6 ± 0.3	36.6 ± 0.4	0.999	0.726	0.764	0.772
Systolic BP (mmHg, mean ± SD)	166 ± 27	173 ± 28	172 ± 29	179 ± 32	172 ± 22	0.015	0.073	0.075	0.279
Diastolic BP (mmHg, mean ± SD)	94 ± 16	94 ± 18	92 ± 19	98 ± 19	98 ± 13	0.977	0.303	0.353	0.209
GCS score (<i>n</i> (%))									
3–8	179 (14.6)	55 (45.8)	41 (51.2)	4 (28.6)	10 (38.5)	0.000	0.000	0.186	0.001
9–12	246 (20.1)	26 (21.7)	15 (18.8)	4 (28.6)	7 (26.9)				
13–15	797 (65.3)	39 (32.5)	24 (30.0)	6 (42.8)	9 (34.6)				
IVH score (<i>n</i> (%))									
0–7	1092 (89.4)	60 (50.0)	32 (40.0)	9 (64.3)	19 (73.1)	0.000	0.000	0.010	0.021
8–23	130 (10.6)	50 (50.0)	48 (60.0)	5 (35.7)	7 (26.9)				
Radiological data									
Left (<i>n</i> (%))	621 (50.8)	621 (50.9)	37 (46.3)	8 (57.1)	13 (50.0)	0.603	0.429	0.638	0.934
Location (<i>n</i> (%))									
Supratentorial	1188 (97.2)	93 (77.5)	55 (68.8)	12 (85.7)	26 (100.0)	0.000	0.000	0.081	0.800
Infratentorial	34 (2.8)	27 (22.5)	25 (31.2)	2 (14.3)	-				
IVH volume (mL, mean ± SD)	1.7 ± 4.7	9.2 ± 11.4	11.1 ± 12.5	6.3 ± 8.1	4.7 ± 7.4	0.000	0.000	0.000	0.049
Total volume (mL, mean ± SD)	26.3 ± 23.7	38.7 ± 26.0	36.1 ± 24.2	35.3 ± 30.0	48.5 ± 28.1	0.000	0.000	0.156	0.000
Extension to ventricles (<i>n</i> (%))	355 (29.1)	100 (83.3)	71 (88.6)	13 (92.9)	16 (61.5)	0.000	0.000	0.000	0.000
Hematoma expansion (<i>n</i> (%))	66 (5.4)	20 (16.7)	12 (15.0)	3 (21.4)	5 (19.2)	0.000	0.001	0.044	0.005
Laboratory data									
Leucocyte (10 ⁹ /L, mean ± SD)	9.2 ± 3.7	11.5 ± 4.7	11.8 ± 4.7	10.6 ± 3.1	11.2 ± 4.1	0.000	0.000	0.165	0.006
Hemoglobin (g/L, mean ± SD)	137 ± 19	141 ± 20	140 ± 21	134 ± 14	149 ± 18	0.024	0.173	0.57	0.001
Platelet (10 ⁹ /L, mean ± SD)	180 ± 67	181 ± 660	179 ± 63	165 ± 45	192 ± 56	0.926	0.957	0.405	0.377
Blood glucose (mmol/L, mean ± SD)	7.6 ± 2.9	8.3 ± 3.1	8.7 ± 3.4	7.0 ± 1.8	7.9 ± 2.8	0.006	0.001	0.498	0.552
Treatment-related data									
Surgery (<i>n</i> (%))	316 (25.9)	99 (82.5)	67 (83.8)	11 (78.6)	21 (80.8)	0.000	0.000	0.000	0.000
DC (<i>n</i> (%))	198 (16.2)	44 (36.7)	22 (27.5)	5 (35.7)	17 (65.4)	0.000	0.009	0.110	0.000
Hematoma evacuation (<i>n</i> (%))	262 (21.4)	50 (41.7)	29 (36.3)	4 (28.6)	17 (65.4)	0.000	0.002	0.726	0.000
Craniotomy (<i>n</i> (%))	236 (90.1)	47 (94.0)	29 (100.0)	4 (100.0)	14 (82.4)	0.542	0.151	1.000	0.548
MIS (<i>n</i> (%))	26 (9.9)	3 (6.0)	-	-	3 (17.6)				
Rate of clot removal (<i>n</i> (%))									
≥ 90%	147 (46.5)	34 (34.3)	19 (28.4)	5 (45.4)	10 (47.6)	0.002	0.000	0.331	0.960
75–89%	129 (40.8)	38 (37.4)	27 (40.3)	3 (27.3)	8 (38.1)				
< 75%	40 (12.7)	27 (27.3)	21 (31.3)	3 (27.3)	3 (14.3)				

Table 1 (continued)

Variables	No hydrocephalus	Hydrocephalus				P ₁	P ₂	P ₃	P ₄
	(n = 1222)	Total (n = 120)	≤ 3 days (n = 80)	4–13 days (n = 14)	≥ 14 days (n = 26)				
Urokinase/rt-pa (n (%))	262 (21.4)	12 (10.0)	7 (8.8)	2 (14.3)	3 (11.5)	0.000	0.000	0.003	0.000
EVD (n (%))	108 (8.8)	83 (69.2)	62 (77.5)	10 (71.4)	11 (42.3)	0.000	0.000	0.000	0.000
Lumbar drainage (n (%))	73 (6.0)	46 (38.3)	32 (40.0)	7 (50.0)	7 (16.9)	0.000	0.000	0.000	0.000
Ventriculoperitoneal shunt (n (%))	-	4 (3.3)	1 (1.3)	1 (7.1)	2 (7.7)	0.000	0.068	0.000	0.000
Complications (n (%))									
Pneumonia	549 (44.6)	105 (87.5)	72 (90.0)	12 (85.7)	21 (80.8)	0.000	0.000	0.002	0.000
Gastrointestinal bleeding	55 (4.5)	21 (17.5)	15 (18.8)	1 (7.1)	5 (19.2)	0.000	0.000	1.000	0.003
Ischemic stroke	37 (3.0)	8 (6.7)	5 (6.3)	2 (14.3)	1 (2.8)	0.065	0.210	0.104	1.000
Intracranial infection	19(1.6)	19 (15.8)	12 (15.0)	2 (14.3)	5 (19.2)	0.000	0.000	0.009	0.000

p_1 , hydrocephalus (≤ 3 days) vs. no hydrocephalus; p_2 , hydrocephalus (4–13 days) vs. no hydrocephalus; p_3 , hydrocephalus (≥ 14 days) vs. no hydrocephalus; *ICH*, intracerebral hemorrhage; *SD*, standard deviation; *BP*, blood pressure; *GCS*, Glasgow Coma Scale; *IVH*, intraventricular hemorrhage; *SAH*, subarachnoid hemorrhage; *DC*, decompressive craniotomy; *EVD*, extraventricular drainage

Discussion

Hydrocephalus is associated with ICH, especially IVH secondary to ICH [1]. Research from Bhattathiri and colleagues has shown that the likelihood of positive outcome is decreased from 15.1 to 11.5% because of the presence of hydrocephalus in a subanalysis of the STICH trial [4]. Although increasing studies have reported the incidence rate of posttraumatic hydrocephalus, varying from 0.7 to 29% [22–25], up to 50% of patients with IVH secondary to ICH may develop hydrocephalus [2]. The incidence of hydrocephalus after ICH was seldom addressed. Of the 1342 patients with ICH in this study,

hydrocephalus occurred in 8.9% of patients after ICH and 22.0% of patients with IVH secondary to ICH. The incidence of hydrocephalus with IVH secondary to ICH is lower than that of the previous study [1]. Agreements on diagnostic method and criteria for hydrocephalus are still not achieved to date [22]. The diagnosis of hydrocephalus in the present research was based on patients' clinical and imaging data.

Hydrocephalus after ICH occurs in about two-thirds of patients mainly within 3 days. Hematoma mass effect/IVH may be related to early obstructive hydrocephalus. However, the time course for ictus of communicating hydrocephalus due to traumatic brain injury and/or subarachnoid hemorrhage (SAH) is from 2 weeks to 1 month [16]. Extension of hemorrhage into the ventricles can prevent normal CSF flow and, with mass effects of blood clot, lead to acute obstructive hydrocephalus in hydrocephalus after IVH secondary to ICH [3–5]. Surgery, such as the insertion of EVD, can be effective when the condition is severe [1, 26]. But, about one-fifth of hydrocephalus occurred more than 14 days. Persistent iron overload from intracerebral hematoma and intracerebral infection from invasive operation after ICH/IVH may contribute to the occurrence of hydrocephalus [7]. Ventriculitis, surgical complications, mass effect due to edema, recurrent ICH, or fibrosis of the ventricles maybe also relate to late hydrocephalus.

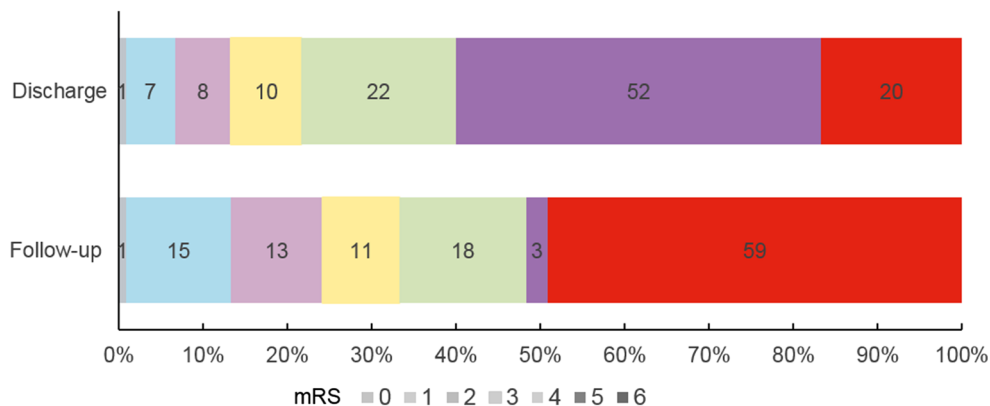
The risk factors for hydrocephalus (≤ 3 days) in the multi-variable analysis were infratentorial hemorrhage, extension to ventricles, greater ICH volume, and hematoma expansion. Extension to ventricles was the only independent risk factor for hydrocephalus (4–13 days), while extension to ventricles, decompressive craniotomy, and intracranial infection were

Table 2 Predictors of hydrocephalus after ICH

Variable	Odds ratio	95% CI	<i>p</i>
Hydrocephalus (≤ 3 days)			
Location (infratentorial)	30.019	13.543, 66.539	0.000
Total ICH volume	1.013	1.003, 1.023	0.009
Extension to ventricles	15.637	7.433, 32.981	0.000
Hematoma expansion	2.831	1.284, 6.245	0.010
Hydrocephalus (4–13 days)			
Extension to ventricles	12.692	1.442, 111.723	0.022
Hydrocephalus (≥ 14 days)			
Extension to ventricles	2.706	1.115, 6.565	0.028
Decompressive craniotomy	4.204	1.135, 15.571	0.032
Intracranial infection	7.917	2.253, 27.819	0.001

ICH, intracerebral hemorrhage

Fig. 2 mRS score at discharge and follow-up after hydrocephalus in the patients with intracerebral hemorrhage. mRS scores range from 0 (no disability) to 6 (death). 21.7% (26) at discharge and 33.3% (40) at follow-up had an mRS score of 3 or less. 16.7% (20) at discharge and 49.2% (59) at follow-up had an mRS score of 6



independent predictors of hydrocephalus (≥ 14 days). Many of the risk factors are related to the blood clot which lead to obstruction to normal CSF flow. There was no correlation between the development of hydrocephalus and sex and age. Previous studies have also reported that intraventricular hemorrhage, thickness, distribution of SAH, IVH volume, and Graeb score can be used for predicting hydrocephalus after ICH [4, 9–12, 27], which is similar with our study in the early hydrocephalus, not late hydrocephalus. A greater total hematoma volume was an independent predictor for acute hydrocephalus, not late hydrocephalus. The removal of hematoma which lead to obstruction to normal CSF flow may be a reason. However, our results also show that there is no correlation between rate of clot removal and subsequent hydrocephalus ($p = 0.539$). Maybe, there is no benefit from more clot removal because of ventriculitis, surgical complications, and decompressive craniotomy. Decompressive craniotomy ($p = 0.032$) and intracranial infection ($p = 0.001$) were independent predictors of late hydrocephalus. In the previous study, decompressive craniotomy also seemed to be strongly related to the development of hydrocephalus in previous studies [22, 23].

Decompressive craniotomy is an effective approach to save life. But, a large decompressive craniotomy might aggravate ventricular expansion and reduce the CSF absorption by lower intracranial pressure [23, 28].

In long-term follow-up of study, we recognize the occurrence of late hydrocephalus. Twenty-two (18.2%) patients appeared hydrocephalus after ICH at 1 month later. The mortality was 16.7% at hospital discharge and 49.2% during follow-up. In previous study, 56.4% (679) of patients (1204) died after ICH/IVH [10–12]; the mortality rate was the same as hydrocephalus after ICH [29–31]. However, the mortality of hydrocephalus after IVH/ICH in infants is lower than that in adult [32], 34% and 48.8%, respectively. The cause related to patients death was similar between ICH induced hydrocephalus and ICH, and major causes of death during follow-up were ICH and infection [29].

This study still has some limitations. A major limitation of our work is a retrospective, nonrandomized, and single center study, which may produce information bias because of the unclear data collection. Second, we cannot rule out the additional variables which may influence the outcome of

Fig. 3 Overall survival

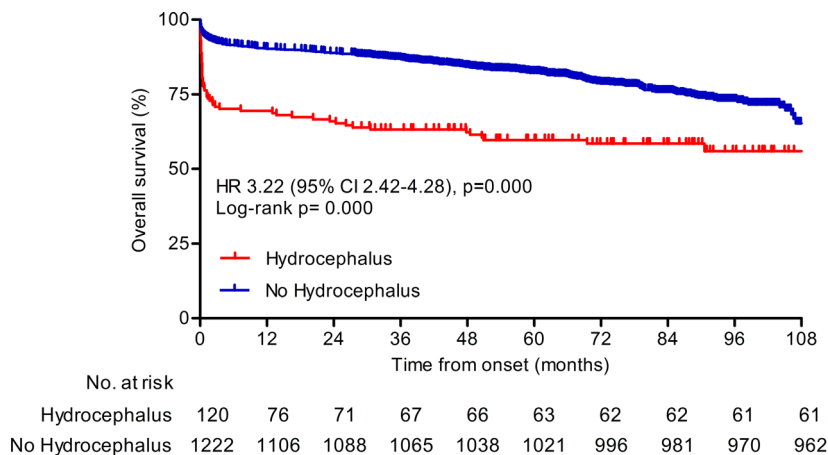


Table 3 Predictors of poor outcome in patients with ICH in long-term follow-up

Variable	Odds ratio	95% CI	<i>p</i>
Age (years)	1.030	1.022, 1.037	0.000
Diabetes mellitus	1.837	1.360, 2.482	0.000
Systolic BP	1.004	1.001, 1.007	0.014
Total ICH volume	1.012	1.009, 1.015	0.000
Extension to ventricles	1.324	1.106, 1.584	0.002
Pneumonia	1.999	1.632, 2.448	0.000
Gastrointestinal bleeding	1.535	1.136, 2.0735	0.005
Ischemic stroke	1.611	1.136, 2.2.285	0.007
Hydrocephalus	1.446	1.118, 1.869	0.005

ICH, intracerebral hemorrhage; BP, blood pressure

hydrocephalus after ICH, such as iron [7]. One study showed that intracerebral hematoma contributed to persistent brain iron accumulation and aggravated hydrocephalus after ICH/IVH. Finally, the information of surgery is incomplete. Therefore, more clinical researches are needed to explore the effectiveness of treatment for ICH.

Summary

Hydrocephalus is a frequent complication of ICH and most commonly occurs at the onset of ICH. Patients with hydrocephalus show relatively higher mortality and disability. Surgery, such as extraventricular drainage, lumbar drainage, and ventriculoatrial shut, may decrease the risk of hydrocephalus. Major causes of death during follow-up were ICH and infection.

Table 4 All-cause and cause-specific mortality (*n* [%]) in patients for hydrocephalus after ICH

	During hospital period	Follow-up (median, 5.2 years)
All-cause mortality	20 (100.0)	39 (100.0)
ICH	7 (35.0)	8 (20.5)
New ICH	0 (0.0)	3 (7.7)
Ischemic stroke	0 (0.0)	2 (5.1)
Pneumonia	10 (50.0)	22 (56.4)
Intracranial infection	3 (15.0)	3 (7.7)
Other	0 (0.0)	1 (2.6)

ICH, intracerebral hemorrhage

Acknowledgments We thank the participants included in our trial for their involvement and enthusiasm.

Authors' Contributions RH and FH conceived, organized and supervised the study. CZ, JSX, HFG, JZ, and YJZ, CL and LL conducted the research. RH and XYF performed the statistical analysis. RH and CZ prepared and revised the manuscript. All authors approved the final version to be published.

Funding Information This work was supported by the National Key Research and Development Program of China (No. 2017YFC0111900) and National Natural Science Foundation of China (No. 81671228).

Data Availability Please contact with the corresponding author.

Compliance with Ethical Standards

Disclaimer All inferences, opinions, and conclusions drawn in this publication are those of the authors and do not reflect the opinions or policies of the data steward(s).

Conflict of Interest The authors declare that they have no conflict of interest.

Ethics Approval This study adheres to the principles of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the Southwest Hospital of Third Military Medical University, China.

Consent to Participate Obtained.

Consent for Publication Obtained.

Patient Consent Obtained.

References

- Balami JS, Buchan AM. Complications of intracerebral haemorrhage. *Lancet Neurol*. 2012;11(1):101–18. [https://doi.org/10.1016/S1474-4422\(11\)70264-2](https://doi.org/10.1016/S1474-4422(11)70264-2).
- Diringer MN, Edwards DF, Zazulia AR. Hydrocephalus: a previously unrecognized predictor of poor outcome from supratentorial intracerebral hemorrhage. *Stroke*. 1998;29(7):1352–7. <https://doi.org/10.1161/01.str.29.7.1352>.
- Tuhim S, Horowitz DR, Sacher M, Godbold JH. Volume of ventricular blood is an important determinant of outcome in supratentorial intracerebral hemorrhage. *Crit Care Med*. 1999;27(3):617–21. <https://doi.org/10.1097/00003246-199903000-00045>.
- Bhattathiri PS, Gregson B, Prasad KS, Mendelow AD. Intraventricular hemorrhage and hydrocephalus after spontaneous intracerebral hemorrhage: results from the STICH trial. *Acta Neurochir Suppl*. 2006;96:65–8. https://doi.org/10.1007/3-211-30714-1_16.
- Steiner T, Diringer MN, Schneider D, Mayer SA, Begtrup K, Broderick J, et al. Dynamics of intraventricular hemorrhage in patients with spontaneous intracerebral hemorrhage: risk factors, clinical impact, and effect of hemostatic therapy with recombinant activated factor VII. *Neurosurgery*. 2006;59(4):767–73; discussion 73–4. <https://doi.org/10.1227/01.neu.0000232837.34992.32>.
- Xi G, Strahle J, Hua Y, Keep RF. Progress in translational research on intracerebral hemorrhage: is there an end in sight? *Prog*

- Neurobiol. 2014;115:45–63. <https://doi.org/10.1016/j.pneurobio.2013.09.007>.
7. Chen Q, Tang J, Tan L, Guo J, Tao Y, Li L, et al. Intracerebral hematoma contributes to hydrocephalus after intraventricular hemorrhage via aggravating iron accumulation. *Stroke*. 2015;46(10):2902–8. <https://doi.org/10.1161/strokeaha.115.009713>.
 8. Hughes JD, Puffer R, Rabinstein AA. Risk factors for hydrocephalus requiring external ventricular drainage in patients with intraventricular hemorrhage. *J Neurosurg*. 2015;123(6):1439–46. <https://doi.org/10.3171/2015.1.jns142391>.
 9. AlShardan MM, Mubasher M, Orz Y, AlYamany M. Factors that predict hydrocephalus following intraventricular hemorrhage. *Br J Neurosurg*. 2015;29(2):225–8. <https://doi.org/10.3109/02688697.2014.960365>.
 10. Zacharia BE, Vaughan KA, Hickman ZL, Bruce SS, Carpenter AM, Petersen NH, et al. Predictors of long-term shunt-dependent hydrocephalus in patients with intracerebral hemorrhage requiring emergency cerebrospinal fluid diversion. *Neurosurg Focus*. 2012;32(4):E5. <https://doi.org/10.3171/2012.2.focus11372>.
 11. Stein M, Luecke M, Preuss M, Boeker DK, Joedicke A, Oertel MF. Spontaneous intracerebral hemorrhage with ventricular extension and the grading of obstructive hydrocephalus: the prediction of outcome of a special life-threatening entity. *Neurosurgery*. 2010;67(5):1243–51; discussion 52. <https://doi.org/10.1227/NEU.0b013e3181ef25de>.
 12. Hanley DF. Intraventricular hemorrhage: severity factor and treatment target in spontaneous intracerebral hemorrhage. *Stroke*. 2009;40(4):1533–8. <https://doi.org/10.1161/strokeaha.108.535419>.
 13. Passero S, Olivelli M, Reale F. Primary intraventricular haemorrhage in adults. *Acta Neurol Scand*. 2002;105(2):115–9. <https://doi.org/10.1034/j.1600-0404.2002.1o118.x>.
 14. Williams MA, Malm J. Diagnosis and treatment of idiopathic normal pressure hydrocephalus. *Continuum (Minneapolis, Minn)*. 2016;22(2 Dementia):579–99. <https://doi.org/10.1212/con.0000000000000305>.
 15. Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. *Neurosurgery*. 2005;57(3 Suppl):S4–16; discussion ii–v. <https://doi.org/10.1227/01.neu.0000168185.29659.c5>.
 16. Tian HL, Xu T, Hu J, Cui YH, Chen H, Zhou LF. Risk factors related to hydrocephalus after traumatic subarachnoid hemorrhage. *Surg Neurol*. 2008;69(3):241–6; discussion 6. <https://doi.org/10.1016/j.surneu.2007.02.032>.
 17. Hwang BY, Bruce SS, Appelboom G, Piazza MA, Carpenter AM, Gigante PR, et al. Evaluation of intraventricular hemorrhage assessment methods for predicting outcome following intracerebral hemorrhage. *J Neurosurg*. 2012;116(1):185–92. <https://doi.org/10.3171/2011.9.jns10850>.
 18. Hanley DF, Thompson RE, Rosenblum M, Yenokyan G, Lane K, McBee N, et al. Efficacy and safety of minimally invasive surgery with thrombolysis in intracerebral haemorrhage evacuation (MISTIE III): a randomised, controlled, open-label, blinded endpoint phase 3 trial. *Lancet (London, England)*. 2019;393(10175):1021–32. [https://doi.org/10.1016/s0140-6736\(19\)30195-3](https://doi.org/10.1016/s0140-6736(19)30195-3).
 19. Brouwers HB, Chang Y, Falcone GJ, Cai X, Ayres AM, Batty TW, et al. Predicting hematoma expansion after primary intracerebral hemorrhage. *JAMA Neurol*. 2014;71(2):158–64. <https://doi.org/10.1001/jamaneurol.2013.5433>.
 20. Paoin W, Yuenyongsuwan M, Yokobori Y, Endo H, Kim S. Development of the ICD-10 simplified version and field test. *Health Inf Manag*. 2018;47(2):77–84. <https://doi.org/10.1177/1833358317701277>.
 21. Brooke HL, Talbäck M, Hörnblad J, Johansson LA, Ludvigsson JF, Druid H, et al. The Swedish cause of death register. *Eur J Epidemiol*. 2017;32(9):765–73. <https://doi.org/10.1007/s10654-017-0316-1>.
 22. Cardoso ER, Galbraith S. Posttraumatic hydrocephalus—a retrospective review. *Surg Neurol*. 1985;23(3):261–4. [https://doi.org/10.1016/0090-3019\(85\)90092-8](https://doi.org/10.1016/0090-3019(85)90092-8).
 23. Czosnyka M, Copeman J, Czosnyka Z, McConnell R, Dickinson C, Pickard JD. Post-traumatic hydrocephalus: influence of craniectomy on the CSF circulation. *J Neurol Neurosurg Psychiatry*. 2000;68(2):246–8. <https://doi.org/10.1136/jnnp.68.2.246a>.
 24. Mazzini L, Campini R, Angelino E, Rognone F, Pastore I, Oliveri G. Posttraumatic hydrocephalus: a clinical, neuroradiologic, and neuropsychologic assessment of long-term outcome. *Arch Phys Med Rehabil*. 2003;84(11):1637–41. [https://doi.org/10.1053/s0003-9993\(03\)00314-9](https://doi.org/10.1053/s0003-9993(03)00314-9).
 25. Poca MA, Sahuquillo J, Mataró M, Benejam B, Arikan F, Báguena M. Ventricular enlargement after moderate or severe head injury: a frequent and neglected problem. *J Neurotrauma*. 2005;22(11):1303–10. <https://doi.org/10.1089/neu.2005.22.1303>.
 26. Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46(7):2032–60. <https://doi.org/10.1161/str.0000000000000069>.
 27. Strahle J, Garton HJ, Maher CO, Muraszko KM, Keep RF, Xi G. Mechanisms of hydrocephalus after neonatal and adult intraventricular hemorrhage. *Transl Stroke Res*. 2012;3(Suppl 1):25–38. <https://doi.org/10.1007/s12975-012-0182-9>.
 28. Shapiro K, Fried A, Takei F, Kohn I. Effect of the skull and dura on neural axis pressure-volume relationships and CSF hydrodynamics. *J Neurosurg*. 1985;63(1):76–81. <https://doi.org/10.3171/jns.1985.63.1.0076>.
 29. Hansen BM, Nilsson OG, Anderson H, Norrving B, Säveland H, Lindgren A. Long term (13 years) prognosis after primary intracerebral haemorrhage: a prospective population based study of long term mortality, prognostic factors and causes of death. *J Neurol Neurosurg Psychiatry*. 2013;84(10):1150–5. <https://doi.org/10.1136/jnnp-2013-305200>.
 30. Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: mechanisms of injury and therapeutic targets. *Lancet Neurol*. 2012;11(8):720–31. [https://doi.org/10.1016/s1474-4422\(12\)70104-7](https://doi.org/10.1016/s1474-4422(12)70104-7).
 31. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol*. 2010;9(2):167–76. [https://doi.org/10.1016/s1474-4422\(09\)70340-0](https://doi.org/10.1016/s1474-4422(09)70340-0).
 32. Sajjadian N, Fakhrai H, Jahadi R. Incidence of intraventricular hemorrhage and post hemorrhagic hydrocephalus in preterm infants. *Acta Med Iran*. 2010;48(4):260–2.