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ABOUT COVER

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Retrospective Study

Risk factors for delayed intracranial hemorrhage secondary to ventriculoperitoneal shunt: A retrospective study

Jun-Chen Chen, Shou-Xing Duan, Ze-Bin Xue, Sen-Yuan Yang, Yong Li, Run-Long Lai, Dian-Hui Tan

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Abstract

BACKGROUND

Delayed intracranial hemorrhage (DICH), a potential complication of ventriculoperitoneal (VP) shunts, has been associated with high mortality, but its risk factors are still unclear.

AIM

To investigate the risk factors of DICH after VP shunts.

METHODS

We compared the demographic and clinical characteristics of DICH and non-DICH adult patients with VP shunts between January 2016 and December 2020.

RESULTS

The 159 adult VP shunt patients were divided into 2 groups according to the development of DICH: the DICH group ($n = 26$) and the non-DICH group ($n = 133$). No statistically significant difference was found in age, sex, laboratory examination characteristics or preoperative modified Rankin Scale (mRS) score between the DICH and non-DICH groups ($P > 0.05$); however, a history of an external ventricular drain (EVD) [$P = 0.045$; odds ratio (OR): 2.814; 95%CI: 1.024-7.730] and postoperative brain edema around the catheter ($P < 0.01$; OR: 8.397; 95%CI: 3.043-23.171) were associated with a high risk of DICH. A comparison of preoperative mRS scores between the DICH group and the non-DICH group showed no significant difference ($P = 0.553$), while a significant difference was

found in the postoperative mRS scores at the 3-mo follow-up visit ($P = 0.024$).

CONCLUSION

A history of EVD and postoperative brain edema around the catheter are independent risk factors for DICH in VP shunt patients. DICH patients with a high mRS score are vulnerable to poor clinical outcomes.

Key Words: Delayed intracranial hemorrhage; Ventriculoperitoneal shunt; Hydrocephalus; Risk factor; Retrospective study

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Core Tip: A retrospective study of 109 patients after ventriculoperitoneal shunts indicates that a history of external ventricular drain and postoperative brain edema around the catheter are independent risk factors for delayed intracranial hemorrhage (DICH). The DICH patients are vulnerable to poor clinical outcomes with a high modified Rankin Scale score.

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INTRODUCTION

Ventriculoperitoneal (VP) shunting is a commonly performed surgical procedure for the treatment of hydrocephalus. Reports show that VP shunts are associated with various potential complications, such as infection, shunt obstruction and shunt malformation[1-4]. Delayed intracranial hemorrhage (DICH) refers to a subsequent cerebral hemorrhage that was not found in the first postoperative computed tomography (CT) scan of the VP shunt. Compared with other complications, DICH was regarded as a rare complication of VP shunts[5,6]. In 1985, Matsumura *et al*[7] provided a case report that was the first to describe DICH[7]. Since then, many case reports related to DICH[8] of the VP shunt have been published[9-13]. DICH, a severe complication with a high mortality (50%), has caused concern for neurosurgeons for the past few years. Recognizing the risk factors for DICH, could benefit neurosurgeons and improve treatment for patients. Several retrospective studies related to DICH were recently performed to explore the risk factors and prognosis related to DICH[14-18]. However, the risk factors for DICH have yet to be fully defined and more data are still needed. This retrospective study aims to include more patients and variables and explore the potential risk factors and mechanisms of DICH.

MATERIALS AND METHODS

Study design

This retrospective study was reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Shantou University Medical College (No. 2019034). All data were anonymously analyzed after the patient provided consent. The medical records of the hydrocephalus patients who received VP shunts at the First Affiliated Hospital of Shantou University Medical College between January 2016 and December 2020 were reviewed. The inclusion criteria were as follows: (1) Aged between 18 years and 75 years; (2) Received a Medtronic Strata Adjustable Pressure VP Shunt with the pressure valve set at 2.0; and (3) Intact clinical data including laboratory tests and radiographic imaging. The exclusion criteria were as follows: (1) A history of severe diseases such as coronary artery atherosclerosis, hepatosclerosis, and coagulation dysfunction; (2) Not followed up for more than 3 mo after treatment; (3) Used other brands of adjustable pressure VP shunts; and (4) Used nonadjustable pressure VP shunts. A flowchart of patient selection is summarized in Figure 1. A retrospective study of 159 patients who met the criteria was retrospectively reviewed in this study.

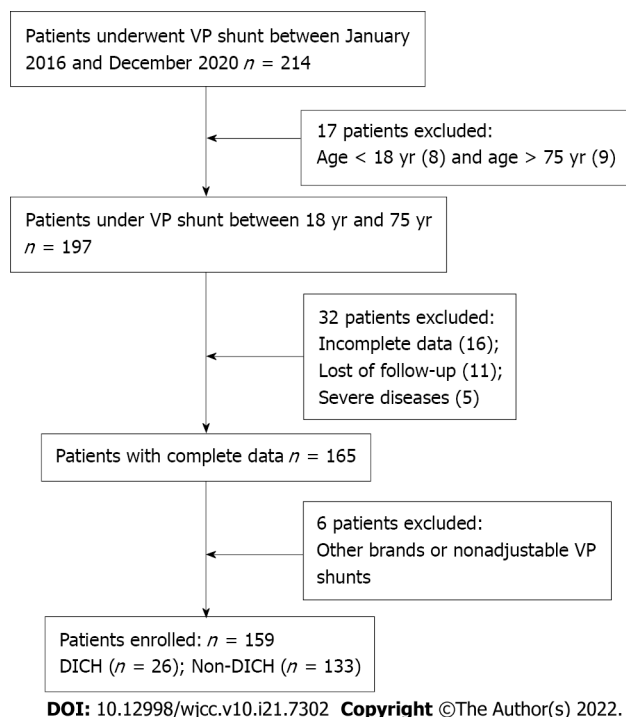


Figure 1 Flowchart of patient selection and groups. VP: Ventriculoperitoneal; DICH: Delayed intracranial hemorrhage.

Data collection

All medical records were reviewed for parameters including age, sex, primary intracranial lesion, history of surgery [craniotomy, decompression, external ventricular drain (EVD), and cranioplasty], history of hypertension, smoking habit, prior blood transfusion, preoperative lumbar puncture, and routine laboratory examinations. The primary intracranial lesion was classified as traumatic brain injury, intracranial hemorrhage, subarachnoid hemorrhage (SAH) (aneurysm rupture), SAH (Arteriovenous malformation), cerebral infarction, tumor, infection, or primary hydrocephalus. All patients underwent lumbar puncture before VP shunting and cerebrospinal fluid (CSF) pressure and laboratory indicators (CSF protein level, glucose level, and nucleated cells) were recorded in detail. Laboratory examinations, such as routine blood tests, were obtained within 3 d before the operation. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio were calculated from routine blood results to explore the relationship with DICH. The two new variables were analyzed independently to prevent bias. Other basic diseases, such as diabetes and gout, were controlled for.

The details of VP shunt surgery included the operation time, location of the VP shunt (frontal or occipital), and other postoperative complications. An initial cranial CT scan was performed within 24 h after the VP shunt was implanted, and a cranial CT scan was performed on postoperative days 5, 6 and 7. A postoperative emergency CT scan was performed if the patients showed signs of neurological deterioration during hospitalization. The radiographic characteristics that were collected were as follows: Presence of DICH, type of hematoma, volume of hematoma, and brain edema around the catheter. The volume of hematoma was calculated based on CT scan results using the volumetric computer on Advantage Windows 3D Workstation 4.1 (Shantou, China). Interreader variability was determined by analyzing the CT images by two independent radiologists who were blinded to the details of the study. Other postoperative complications, such as infection and shunt obstruction, were also recorded.

We assessed the clinical outcomes at the 3-mo follow-up visit. The general postoperative outcomes were evaluated based on the modified Rankin Scale (mRS) score. The mRS score was divided into two categories: Low (0-2) and high (3-5). In addition, the preoperative mRS score was also recorded to evaluate VP shunt clinical outcomes.

Statistical analysis

All statistical analyses were performed using statistical software (SPSS Version 23.0, SPSS, IBM Corp., Armonk, NY, United States). Continuous variables are expressed as the means \pm SD. Comparisons between the 2 groups were analyzed using the χ^2 test (or Fisher's exact test) for categorical data and the *t* test for continuous data. The relationship between each variable and DICH outcome was analyzed by univariate analysis, followed by multivariate logistic regression analysis. *P* values < 0.05 were considered statistically significant.

RESULTS

A total of 159 patients were divided into the DICH group ($n = 26$, 16.4%) or the non-DICH group ($n = 133$, 83.6%) according to the presence of a new hematoma after the first postoperative CT scan. **Table 1** shows the general demographic and clinical characteristics of the patients in this study. For continuous variables, values are expressed as the mean \pm SD; for categorical variables, the values are numbers. No significant differences were found for most variables, such as sex and laboratory examination results. A significant difference was found in the history of EVD between these 2 groups ($P = 0.004$). Regarding radiographic characteristics, a significant difference in the brain edema around the catheter was observed between the 2 groups ($P < 0.01$).

Univariate analysis between each variable and the DICH outcome in the original 159 patients revealed that a history of EVD and brain edema around the catheter were significantly correlated with DICH outcome (**Table 2**). Multivariate analysis showed that these two variables were significantly correlated with DICH outcome: History of EVD [$P = 0.045$; odds ratio (OR): 2.814; 95%CI: 1.024-7.730] and presence of brain edema around the catheter ($P < 0.01$; OR: 8.397; 95%CI: 3.043-23.171) (**Table 3**).

Table 4 shows the clinical data summary of 26 DICH patients after VP shunt. Among these patients, 3 had a subdural hematoma, 9 had an intraventricular hemorrhage, and 14 had an intracerebral hemorrhage around the catheter (**Figure 2**). No epidural hemorrhage or other types of intracranial hemorrhage were noted. The mean onset day of DICH was 4.19 ± 3.35 d, which ranged from 1 to 11 d. The mean hematoma volume was 10.92 ± 14.53 mL, which ranged from 2 to 56 mL. Two DICH patients with severe neurological deterioration underwent secondary surgical intervention for intracranial hematoma evacuation; 24 patients received conservative treatment because of the low-volume hematoma. A comparison of preoperative mRS scores between the DICH group and the non-DICH group showed a significant difference ($P = 0.553$). Seventeen of 26 (65%) DICH patients and 55 of 133 (41%) non-DICH patients were included in the high postoperative mRS group. A significant difference was found in the postoperative mRS score at the 3-mo follow-up visit ($P = 0.024$).

DISCUSSION

We performed a literature review of retrospective studies on DICH that was associated with VP shunts, and then we summarized these previous studies (**Table 5**). From these 6 studies, the incidence of DICH ranged from 1.6% to 23.7%. In our study, the incidence of DICH was 16.4%, which corresponded to the incidence range of previous studies. The wide range of incidence may be related to the neglect of minor hematoma volume, lower frequency of postoperative CT scan examinations, and different inclusion and exclusion criteria in different studies[6,19]. We suppose that the real incidence range of DICH will be more accurate with careful surveillance, such as imaging and unified standards, in the future.

Thirty-seven variables were included to achieve a better comparison between the DICH group and the non-DICH group in our study, which is more than other prior retrospective studies. The analysis of these variables provides a better description of the actual baseline demographic information and clinical characteristics better. In our study, a history of EVD and the presence of brain edema around the catheter were significantly correlated with DICH in a univariate analysis. The selection of covariates for the multivariate analysis was based on previous studies that assessed the risk factors for DICH and our univariate analysis. In these studies, advanced age, craniotomy history, presence of brain edema around the catheter, manipulation of the valve system, location of the shunt (frontal or occipital), delayed partial thromboplastin time, postoperative low-molecular-weight heparin (LMWH) therapy, dual antiplatelet therapy and elevated levels of postoperative NLR and preoperative NLR were found to be positively associated with DICH[18-20]. Considering our available data, 6 variables (age, craniotomy history, EVD history, prothrombin time, location of shunt, and presence of brain edema around catheter) were consequently selected for the multivariate analysis. The variables in the logistic regression multivariate model that were significantly different were EVD history and presence of brain edema around the catheter.

A history of EVD was regarded as an independent risk factor for DICH in our study, which was first reported and not found in previous studies. We also found that the presence of brain edema around the catheter on the first postoperative CT scan increased the risk of DICH, which corresponded with the report by Guo *et al*[15]. An EVD and VP shunts are inserted using the same frontal approach, which is an invasive brain procedure that may cause neural injury in patients[21]. Some authors have proposed that catheter insertion may lead to a disturbance in venous return or hemostasis of a cortical vein and then contribute to subcortical hemorrhage[15,17,22]. Brain edema around the catheter is regarded as a radiographic sign of vascular erosion and could be used to predict DICH.

Fragile cerebral tissue is considered another underlying mechanism of DICH. Cerebral fragility is not easy to detect and the standard diagnosis is based on features of the fragile arteries surrounding the microbleeds in histological analysis after surgical resection[23]. The microbleed that was confirmed on T2-weighted MR imaging, reflected hemosiderin deposits and could be considered an imaging sign related to fragile cerebral tissue[8,24,25]. In Kwon and Jang[20,26]'s study, two neural tracts (corticore-

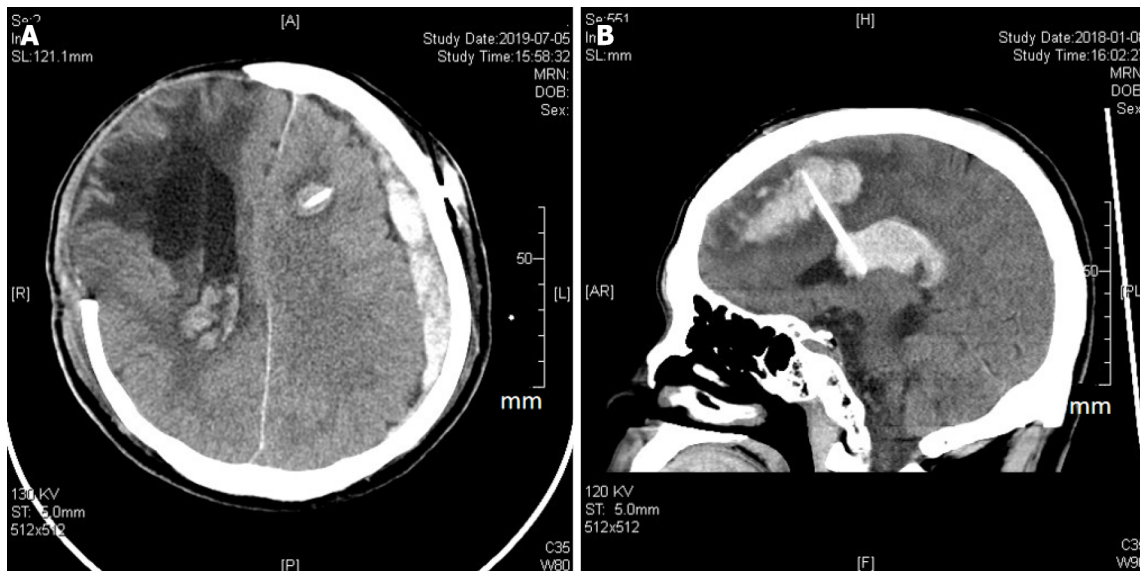
Table 1 Demographical characteristics and clinical data of the patients

Variables	DICH group (n = 26)	Non-DICH group (n = 133)	P value
Age (yr)	51.35 ± 12.08	53.89 ± 15.17	0.422
Male gender, n (%)	17 (65.38)	66 (49.62)	0.141
Primary intracranial lesion, n (%)			0.679
Traumatic brain injury	6 (23.07)	43 (17.29)	
Intracranial hemorrhage	5 (19.23)	30 (22.56)	
SAH (aneurysm rupture)	10 (38.46)	29 (21.80)	
SAH (AVM rupture)	0 (0)	0 (0)	
Cerebral infarction	0 (0)	0 (0)	
Tumor	2 (7.69)	8 (6.02)	
Infection	0 (0)	4 (3.01)	
Primary hydrocephalus	3 (11.54)	19 (14.29)	
Pre-Craniotomy, n (%)	9 (34.62)	56 (42.11)	0.477
Pre-Decompression, n (%)	8 (30.77)	50 (37.59)	0.508
Pre-EVD, n (%)	16 (61.54)	42 (31.58)	0.004 ^a
Pre-Cranioplasty, n (%)	2 (7.69)	23 (17.29)	0.350
LP pressure (mmH ₂ O)	141.54 ± 60.93	139.42 ± 64.94	0.878
CSF protein (g/L)	0.56 ± 0.46	0.64 ± 0.60	0.509
CSF glucose (mmol/L)	3.87 ± 1.45	3.88 ± 1.35	0.980
CSF nucleated cells (10 ⁶ /L)	16.31 ± 20.16	11.68 ± 17.15	0.223
WBC (10 ⁹ /L)	8.37 ± 3.10	7.97 ± 2.82	0.512
Neutrophils (10 ⁹ /L)	5.55 ± 2.97	5.41 ± 2.63	0.810
Lymphocyte (10 ⁹ /L)	1.89 ± 0.55	1.75 ± 0.59	0.237
NLR	3.40 ± 2.79	3.48 ± 2.20	0.869
RBC (10 ¹² /L)	4.04 ± 1.54	3.88 ± 0.69	0.407
HGB (g/L)	112.88 ± 15.44	114.71 ± 18.15	0.631
PLT (10 ⁹ /L)	276.31 ± 68.61	280.92 ± 102.98	0.827
PLR	160.46 ± 69.01	184.02 ± 105.17	0.275
PT(s)	11.64 ± 1.24	11.40 ± 1.26	0.374
INR	1.01 ± 0.11	0.99 ± 0.11	0.382
Fib (g/L)	4.88 ± 7.40	3.67 ± 1.60	0.416
Potassium (mmol/L)	3.85 ± 0.42	3.81 ± 0.43	0.680
Sodium (mmol/L)	136.68 ± 5.19	138.34 ± 5.30	0.144
Calcium (mmol/L)	2.23 ± 0.12	2.22 ± 0.17	0.796
Blood glucose (mmol/L)	5.92 ± 1.45	6.17 ± 2.34	0.591
SBP (mmHg)	137.46 ± 21.35	140.14 ± 24.84	0.609
DBP (mmHg)	86.50 ± 13.22	85.71 ± 14.08	0.791
Hypertension, n (%)	10 (38.46)	49 (36.84)	0.876
Other basic disease, n (%)	3 (11.54)	16 (12.03)	1.000
Smoker, n (%)	7 (26.92)	31 (23.31)	0.693
Prior Blood transfusion, n (%)	6 (23.08)	48 (36.09)	0.200
Operation time (min)	73.46 ± 34.58	74.35 ± 26.86	0.883

Location of VP shunt, <i>n</i> (%)			0.250
Frontal	23 (88.46)	101 (75.94)	
Occipital	3 (11.54)	32 (24.06)	
Other VP Complications, <i>n</i> (%)			0.801
Brain edema around catheter, <i>n</i> (%)	15 (57.69)	34 (25.56)	0.000 ^a
Pre-mRS, <i>n</i> (%)			0.281
Low (0-2)	8 (30.77)	56 (42.11)	
High (3-5)	18 (69.23)	77 (57.89)	
Post-mRS, <i>n</i> (%)			0.024
Low (0-2)	9	77	
High (3-5)	17	55	

^a*P* < 0.05.

AVM: Arteriovenous malformation; CSF: Cerebrospinal fluid; DBP: Diastolic blood pressure; DICH: Delayed intracranial hemorrhage; EVD: External ventricular drain; HGB: Hemoglobin; LP: Lumbar puncture; INR: International normalized ratio; NLR: Neutrophil to lymphocyte ratio; mRS: Modified Rankin Scale; PLR: Platelet to lymphocyte ratio; PLT: Platelet; PT: Prothrombin time; RBC: Red blood cell; SAH: Subarachnoid hemorrhage; SBP: Systolic blood pressure; VP: Ventriculoperitoneal; WBC: White blood cell.



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Figure 2 Computed tomography images of the delayed intracranial hemorrhages in our study. A: A postoperative computed tomography (CT) scan showed subdural hematoma in patient 23; B: A CT scan indicated intracranial hematoma along the path of the catheter in patient 7.

ticular pathway and cingulum) were damaged by an EVD and were confirmed by diffusion tensor imaging parameters (fractional anisotropy and fiber number) and the configuration of the neural tracts [20,26]. The fractional anisotropy value refers to the degree of directionality of water diffusion and represents white matter organization, including the degree of directionality and integrity of white matter microstructures such as axons, myelins, and microtubules [21,27]. This evidence provides an anatomical mechanism to explain cerebral tissue fragility after EVD. Neural injury supposedly occurred in a considerable number of patients with an EVD history [21]. Notably, a history of craniotomy was considered an independent risk factor for DICH in some previous studies [15,16]. The possible mechanism is that craniotomy could contribute to brain fragility and the adhesive arachnoid with small cerebral vessels, which is prone to bleeding after the insertion of a catheter [15,16]. However, a history of craniotomy did not increase the risk of DICH in our research.

Other variables were not risk factors in our study but had statistical significance in other retrospective studies (Table 5). Guo *et al* [15] pointed out that advanced age might contribute to the high incidence of DICH because of present complications such as hypertension and cerebral amyloid angiopathy. Coagulation dysfunction, antiplatelet therapy, and the use of LMWH are associated with an increased risk of DICH [14,18,19]. Cerebral amyloid angiopathy was believed to contribute to DICH secondary to

Table 2 Univariate analysis of variable relating to delayed intracranial hemorrhage in ventriculoperitoneal shunt patients

Variables	DICH group (n = 26)	Non-DICH group (n = 133)	P value
Demographics			
Age (yr)	51.35 ± 12.08	53.89 ± 15.17	0.420
Male gender, n (%)	17 (65.38)	66 (49.62)	0.145
Primary clinical diagnosis, n (%)			
Traumatic brain injury	6 (23.07)	43 (17.29)	
Intracranial hemorrhage	5 (19.23)	30 (22.56)	
SAH (aneurysm rupture)	10 (38.46)	29 (21.80)	
SAH (AVM rupture)	0 (0)	0 (0)	
Cerebral infarction	0 (0)	0 (0)	
Tumor	2 (7.69)	8 (6.02)	
Infection	0 (0)	4 (3.01)	
Primary hydrocephalus	3 (11.54)	19 (14.29)	
Pre-Craniotomy, n (%)	9 (34.62)	56 (42.11)	0.479
Pre-Decompression, n (%)	8 (30.77)	50 (37.59)	0.510
Pre-EVD, n (%)	16 (61.54)	42 (31.58)	0.005 ^a
Pre-Cranioplasty, n (%)	2 (7.69)	23 (17.29)	0.233
LP pressure (mmH ₂ O)	141.54 ± 60.94	139.42 ± 64.94	0.877
CSF protein (g/L)	0.56 ± 0.46	0.64 ± 0.60	0.509
CSF glucose (mmol/L)	3.87 ± 1.45	3.88 ± 1.35	0.980
CSF nucleated cells (10 ⁶ /L)	16.31 ± 20.16	11.68 ± 17.15	0.229
WBC (10 ⁹ /L)	8.37 ± 3.10	7.97 ± 2.82	0.510
Neutrophils (10 ⁹ /L)	5.55 ± 2.97	5.41 ± 2.63	0.808
Lymphocyte (10 ⁹ /L)	1.89 ± 0.55	1.75 ± 0.59	0.237
NLR	3.40 ± 2.79	3.48 ± 2.20	0.868
RBC (10 ¹² /L)	4.04 ± 1.54	3.88 ± 0.69	0.415
HGB (g/L)	112.88 ± 15.44	114.71 ± 18.15	0.629
PLT (10 ⁹ /L)	276.31 ± 68.61	280.92 ± 102.97	0.826
PLR	160.46 ± 69.01	184.02 ± 105.17	0.276
PT(s)	11.64 ± 1.24	11.40 ± 1.26	0.373
INR	1.01 ± 0.11	0.99 ± 0.11	0.381
Fib (g/L)	4.88 ± 7.40	3.67 ± 1.60	0.183
Potassium (mmol/L)	3.85 ± 0.42	3.81 ± 0.43	0.678
Sodium (mmol/L)	136.68 ± 5.19	138.34 ± 5.30	0.145
Calcium (mmol/L)	2.23 ± 0.12	2.2238 ± 0.17	0.795
Blood glucose (mmol/L)	5.92 ± 1.45	6.17 ± 2.34	0.589
SBP (mmHg)	137.46 ± 21.35	140.14 ± 24.84	0.607
DBP (mmHg)	86.50 ± 13.22	85.71 ± 14.08	0.790
Hypertension, n (%)	10 (38.46)	49 (36.84)	0.876
Other basic disease, n (%)	3 (11.54)	16 (12.03)	0.944
Smoker, n (%)	7 (26.92)	31 (23.31)	0.693
Prior Blood transfusion, n (%)	6 (23.08)	48 (36.09)	0.205

Operation time (min)	73.46 ± 34.58	74.35 ± 26.86	0.882
Location of VP shunt, n (%)			0.170
Frontal	23 (88.46)	101 (75.94)	
Occipital	3 (11.54)	32 (24.06)	
Other VP complications, n (%)	1 (3.85)	10 (7.52)	0.508
Brain edema around catheter, n (%)	15 (57.69)	34 (25.56)	0.000 ^a
Pre-mRS, n (%)			0.523
0-2	8 (30.77)	56 (42.11)	
3-5	18 (69.23)	77 (57.89)	

^aP < 0.05.

AVM: Arteriovenous malformation; CSF: Cerebrospinal fluid; DBP: Diastolic blood pressure; DICH: Delayed intracranial hemorrhage; EVD: External ventricular drain; HGB: Hemoglobin; LP: Lumbar puncture; INR: International normalized ratio; NLR: Neutrophil to lymphocyte ratio; mRS: Modified Rankin Scale; PLR: Platelet to lymphocyte ratio; PLT: Platelet; PT: Prothrombin time; RBC: Red blood cell; SAH: Subarachnoid hemorrhage; SBP: Systolic blood pressure; VP: Ventriculoperitoneal; WBC: White blood cell.

Table 3 Multivariate analysis of variable relating to delayed intracranial hemorrhage in ventriculoperitoneal shunt patients

Variable	P value	OR	95%CI
Age (yr)	0.162	0.975	0.942-1.010
Pre-Craniotomy	0.548	0.723	0.250-2.085
Pre-EVD	0.045	2.814	1.024-7.730
PT(s)	0.224	1.268	0.865-1.859
Location of VP shunt	0.153	2.775	0.685-11.249
Brain edema around catheter	0.000	8.397	3.043-23.171

CI: Confidence interval; EVD: External ventricular drain; OR: Odds ratio; PT: Prothrombin time; VP: Ventriculoperitoneal.

VP shunt in elderly patients in Wang *et al.*'s research. The discrepancy might be related to the inclusion and exclusion criteria in our study[28]. We included patients aged 18-75 years and excluded patients with coagulation dysfunction to control for confounders and achieve a balanced baseline.

In contrast to the preoperative mRS scores, the postoperative mRS scores for both the DICH group and the non-DICH group were significant in the statistical analysis in our study. Sixty-five percent of DICH patients were involved in the higher postoperative mRS group, which was higher than that of non-DICH patients (41%). This indicates that VP shunt patients with DICH might have worse clinical outcomes. DICH may contribute to severe neurological function deterioration and secondary surgical intervention should be performed in patients with large volume hematoma and intractable intracranial pressure. The average hematoma volume of DICH is 10.92 mL. Only 2 patients with hematomas exceeding 50 mL in volume in our study underwent surgery, and the other 24 patients received conservative treatment. Most DICH patients treated conservatively are asymptomatic due to the low hematoma volume. These observations collectively demonstrate that DICH increases the length of hospital stay and is related to poor clinical outcomes.

Several limitations should be noted in the present study. First, this was a retrospective study that used a multivariate analysis to minimize bias in patient selection. Some confounders mentioned in other studies, such as manipulation of the valve system and same-sided approach as EVD, were not recorded. Second, the low statistical power (0.63) and the small sample size in our study may overestimate the effect measure. The low statistical power increases the likelihood of a false positive result. The small sample was solely comprised of Chinese individuals in a single center. The number of DICH patients was much smaller than that of the non-DICH group. Logistic regression overestimates the OR in studies with small to moderate sample sizes[29]. More samples from different populations and centers should be included in future studies. Third, the follow-up evaluation needs to be replaced by a more objective method to verify the prognosis.

Table 4 Summary of 26 patients with delayed intracranial hemorrhage after ventriculoperitoneal shunt

No.	Age/sex	Primary intracranial lesion	History of EVD	Location of VP shunt	DICH type	Onsetday	Treatment	Pre-mRS	Post-mRS
1	50/F	Aneurysm	Y	Frontal	IVH	2	Conservative	1	1
2	67/M	ICH	Y	Frontal	ICH around catheter	3	Conservative	3	1
3	64/M	Aneurysm	Y	Frontal	IVH	1	Conservative	1	1
4	37/F	Tumor	N	Occipital	ICH around catheter	11	Conservative	5	4
5	56/M	TBI	Y	Frontal	ICH around catheter	3	Conservative	5	5
6	23/M	TBI	N	Frontal	ICH around catheter	4	Conservative	5	5
7	63/F	Aneurysm	N	Frontal	ICH around catheter	7	Surgery	4	5
8	54/M	Aneurysm	Y	Frontal	ICH around catheter	3	Conservative	5	5
9	61/M	Aneurysm	Y	Occipital	ICH around catheter	5	Conservative	2	1
10	47/M	ICH	Y	Frontal	ICH around catheter	7	Conservative	5	5
11	58/M	Aneurysm	Y	Frontal	IVH	7	Conservative	2	2
12	51/F	Aneurysm	N	Frontal	ICH around catheter	3	Conservative	1	1
13	58/M	Tumor	N	Frontal	ICH around catheter	2	Conservative	5	5
14	58/F	Primary hydrocephalus	N	Frontal	Subdural hematoma	7	Conservative	5	5
15	47/M	Primary hydrocephalus	N	Frontal	ICH around catheter	5	Conservative	4	4
16	53/M	TBI	Y	Frontal	IVH	2	Conservative	5	3
17	42/M	Aneurysm	Y	Frontal	ICH around catheter	9	Conservative	5	5
18	32/M	Aneurysm	Y	Occipital	IVH	1	Conservative	2	2
19	45/M	TBI	Y	Frontal	ICH around catheter	1	Conservative	5	5
20	62/M	ICH	Y	Frontal	Subdural hematoma	2	Conservative	5	5
21	47/F	TBI	Y	Frontal	ICH around catheter	2	Conservative	4	4
22	56/M	ICH	N	Frontal	IVH	7	Conservative	5	4
23	47/M	ICH	N	Frontal	Subdural hematoma	4	Surgery	5	5
24	26/F	Primary hydrocephalus	Y	Frontal	IVH	8	Conservative	2	2
25	72/F	Aneurysm	Y	Frontal	IVH	1	Conservative	1	1
26	59/F	TBI	N	Frontal	IVH	1	Conservative	5	5

EVD: External ventricular drain; F: Female; ICH: Intracranial hemorrhage; IVH: Intraventricular hemorrhage; M: Male; mRS: Modified Rankin Scale; N: No; TBI: Traumatic brain injury; VP: Ventriculoperitoneal; Y: Yes.

CONCLUSION

In summary, the incidence of DICH would be more accurate with careful surveillance that includes

Table 5 Summary of the previous studies of delayed intracranial hemorrhage after ventriculoperitoneal shunt

Ref.	Year	DICH	Non-DICH	Number of variables	Proposed risk factors
Hudson <i>et al</i> [18]	2018	8	72	10	DAPT ($P = 0.0001$, OR = 31.23, 95%CI: 2.98-327.32)
Guo <i>et al</i> [15]	2017	20	512	8	Advanced age ($P = 0.027$, OR = 1.048, 95%CI: 1.005-1.092), craniotomy history ($P = 0.025$, OR = 3.874, 95%CI: 1.183-12.693), brain edema around the catheter ($P < 0.001$, OR = 9.056, 95%CI: 3.194-25.675)
Gong <i>et al</i> [16]	2017	12	742	9	Age ≥ 60 yr ($P = 0.0008$), prior craniotomy operation ($P = 0.0001$) and manipulation of the valve system ($P = 0.0017$)
Qian <i>et al</i> [14]	2017	11	140	18	Postoperative LMWH therapy ($P = 0.026$, relative ratio = 4.8, 95%CI: 1.4-17.1)
Jang <i>et al</i> [17]	2018	34	104	9	Old age ($P = 0.037$) and delayed PTT ($P = 0.032$)
Li <i>et al</i> [6]	2021	29	101	21	Elevated NLRR ($P < 0.001$, OR = 2.792, 95%CI: 1.747-4.460); history of craniotomy ($P = 0.010$, OR = 3.394, 95%CI: 1.060-10.869)

DAPT: Dual antiplatelet therapy; NLRR: A ratio of postoperative neutrophil-to-lymphocyte ratio to preoperative neutrophil-to-lymphocyte ratio; LMWH: Low-molecular-weight heparin; OR: Odds ratio; PTT: Partial thromboplastin time; DICH: Delayed intracranial hemorrhage.

imaging and unified standards. Our results indicate that a history of EVD and postoperative brain edema around the catheter are associated with a high risk of DICH in VP shunt patients. DICH patients with a high mRS score are vulnerable to poor clinical outcomes.

ARTICLE HIGHLIGHTS

Research background

Delayed intracranial hemorrhage (DICH), one of the high mortality complications in ventriculoperitoneal (VP) shunt patients, has not been fully recognized.

Research motivation

To explore the risk factors of delay intracranial hemorrhage and reduce the incidence of this complication in VP shunt patients.

Research objectives

To explore the potential risk factors and mechanisms of delay intracranial hemorrhage in VP shunt patients.

Research methods

We collected the demographic and clinical characteristics data of VP shunt patients between January 2016 and December 2020. DICH group and Non-DICH group were compared in a retrospective study.

Research results

A history of an external ventricular drain and postoperative brain edema around the catheter were related to a high risk for DICH statistically. There was a significant difference in the postoperative modified Rankin Scale scores at the 3-mo follow-up in these two groups.

Research conclusions

A history of an EVD and postoperative brain edema around the catheter were risk factors of DICH VP shunt patients. DICH patients are vulnerable to poor clinical outcomes with a high mRS score.

Research perspectives

More samples from different populations and centers should be included in future studies. The follow-up evaluation needs to be replaced by a more objective method to verify the prognosis.

FOOTNOTES

Author contributions: Chen JC was considered as first author; Chen JC, Xue ZB, Yang SY, Li Y, Lai RL and Tan DH participated in the patient treatment; Chen JC, Xue ZB and Yang SY collected the clinical data and performed the literature; Chen JC and Duan SX wrote the manuscript; Tan DH helped to design and revise the paper.

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Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

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