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Original Research

Predicting the outcomes of shunt implantation in patients with post-traumatic hydrocephalus and severe conscious disturbance: a scoring system based on clinical characteristics

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Post-traumatic hydrocephalus is a common complication secondary to traumatic brain injury. It can cause cerebral metabolic impairment and dysfunction. Therefore, timely treatment with shunt implantation is necessary. However, the outcomes of shunt surgery in patients with post-traumatic hydrocephalus combined with disturbance of consciousness are doubtful. The objective was to develop a predictive model that uses the information available before surgery to predict the outcome of shunt implantation in such patients. Retrospectively collected data were used to develop a clinical prediction model. The model was derived from 59 patients using logistic regression analysis, and then it was evaluated by the area under the receiver operating characteristic curve and Hosmer-Lemshow test. A validation cohort verified the model. Four independent predictors were identified: age < 50 years, mild hydrocephalus, Glasgow Coma Scale scores 9-12 at the time of injury, and time interval from trauma to shunting < 3 months. We calculated the total score and defined the patients into three groups: low-probability (0-10 points), medium-probability (11-16 points), and high-probability (17-30 points). The rates of improved outcomes in the three groups were 14.3%, 52.6%, and 94.7%, respectively ($P < 0.0001$). The correlative rates of the validation cohort were 21.4%, 54.5%, and 85.7%. The prognostic model showed good discrimination (area under the receiver operating characteristic curve = 0.869) and calibration (Hosmer-Lemshow test, $P = 0.391$). The developed predictive model can identify patients with post-traumatic hydrocephalus combined with disturbance of consciousness who can benefit from shunt implantation. Therefore, our prognostic model can predict the outcomes of patients with post-traumatic hydrocephalus and disturbance of consciousness after shunt surgery.

Keywords

Post-traumatic hydrocephalus; traumatic brain injury; consciousness disturbance; ventriculoperitoneal shunt; predictive model; cerebrospinal fluid

1. Introduction

Post-traumatic hydrocephalus (PTH) was first reported by Dandy and Blackfan (1964). It is characterized by progressive expansion of the ventricles secondary to cerebrospinal fluid circulation disorders and brain trauma. PTH is a frequent complication of traumatic brain injury (TBI) that affects brain metabolism and neural function. If not treated effectively, this group of patients often show delayed clinical improvement and have poor outcomes (Licata et al., 2001). According to different diagnostic standards, the incidence of PTH reported by other researchers ranges from 0.7% to 50% (Cardoso and Galbraith, 1985; Guyot and Michael, 2000; Mazzini et al., 2003). About 5.48 million people are estimated to suffer from severe TBI every year all over the world (Iaccarino et al., 2018), of which the majority are afflicted with disorders of consciousness. Patients in a minimally conscious state, vegetative state, and those in a persistent coma after head trauma are more likely to develop PTH (Jennett et al., 2001).

Shunt surgery is the primary treatment method for patients with PTH. Unfortunately, for patients with PTH combined with severe disturbance of consciousness, it is difficult to predict the outcome of ventriculoperitoneal shunt by cerebrospinal fluid tap test or lumbar cistern drainage. Several factors have been reported to related to the outcome of shunt implantation, including Glasgow Coma Scale (GCS) score on admission, early cerebrospinal fluid (CSF) shunting, higher preoperative Glasgow Outcome Scale (GOS) score, younger age, lower severity of PTH, disappearance of cisterna ambiens, prolonged duration of unconscious, high plasma fibrinogen levels and the combination of amyloid-β1-42 and total tau-protein levels (Kim et al., 2015; Kowalski et al., 2018; Sun et al., 2019; Tarnaris et al., 2011; Tribl and Oder, 2000; Weintraub et al., 2017; Wen et al., 2009). The measurement of CSF flow using Magnetic Resonance Imaging (MRI) may be potential parameters (Algin et al., 2010; Dixon et al., 2002; Missori et al., 2006). However, according to our understanding, no research has been performed to predict the prognosis of the ventriculoperitoneal shunt (VPS) in patients with PTH combined with severe disturbance of consciousness.

2. Materials and Methods

2.1 Research population

This retrospective study included patients admitted to the neurosurgery ward of our institute from January 2015 to December 2016. All enrolled patients suffered from severe disturbance of consciousness with the GCS scores $\leq$ 12 before shunt implantation. Glasgow Outcome Scale Extend (GOS-E) score and Coma Recovery Scale-Revised (CRS-R) were used to evaluate their clinical status. We assessed the prognostic value of several clinical characteristics to formulate a comprehensive predictive model. And the model was developed after statistical analysis. Then the verification of this model was tested in a validation cohort of patients with PTH and disturbance of consciousness.

The inclusion criteria were as follows: (1) diagnosis of PTH; (2) complete medical records including history of treatment, personal characteristics, radiographs, and surgical information; (3) persistent unconsciousness after TBI (with no other causes, no lucid interval, and GCS score $\leq$ 12); and (4) ventriculoperitoneal shunt procedure performed in our institute. Exclusion criteria: (1) patients with known severe neural deficits before the TBI, and (2) those who died because of any other diseases before the end of our two-year follow-up.

2.2 Radiological evaluation and clinical technology

Each patient underwent a brain Computed Tomography (CT) scan upon arrival at our department, as well as a follow-up scan after VPS surgery. The CT images evaluated the diagnosis of PTH, the severity of PTH, and the location of the proximal catheter. In all patients, intracranial pressure (ICP) was measured by lumbar punctures before and after the shunt surgery. VPS was performed, and the Miethke proGAV or Medtronic Strata II with the delta chamber was inserted. For proGAV values, the initial pressure was set at the level that about 20 mmH_2O lower than the ICP. And for Medtronic Strata II, the valves were set one level lower than the measured ICP. Subsequent adjustments were performed according to the alteration of patients' clinical symptoms and imaging examinations.

2.3 PTH diagnosis

The diagnosis of PTH was based on clinical symptoms and radiographic evidence. The detailed standards were as follows: (1) the value of Evans' index greater than 0.3; (2) the enlargement of the third ventricle, the temporal and anterior horns of lateral ventricles, and the periventricular interstitial edema without brain atrophy; (3) clinically progressive degradation of neurological function or no evidence of significant clinical improvement; and (4) development of hydrocephalus within 12 months of trauma. The ratio of the cerebral ventricle diameter (the maximum transverse diameter in the middle of the ventricle) to the biparietal diameter (V/BP) was used to evaluate the severity of hydrocephalus; 26-40% indicated mild, 4-60% indicated moderate, and 61-90% indicated severe hydrocephalus.

2.4 Data collection

Data were collected retrospectively from our electronic medical record system. A team of radiologists reviewed all previous imaging data. Our medical team compiled the following clinical data: necessary information (age and gender), cause of injury, severity of hydrocephalus, status of the cisterna ambiens, GCS scores at the time of injury and before shunt placement, ICP measured by lumbar puncture, skull defect (unilateral or bilateral), time interval from injury to cranioplasty, and the time interval from injury to shunt implantation. The GOS-E and Coma Recovery Scale-Revised (CRS-R) scores were evaluated before shunt implantation and at every follow-up appointment. The causes of injury included falls, road traffic accidents, violence, and other reasons. For convenience in establishing the prognostic model, we converted some of the variables into dumb variables (0, 1, 2…). The details of the patients' characteristics and variable transformation are presented in Table 1.

2.5 Outcomes after shunt implantation

The neurological outcomes were evaluated at 6, 12 months, and 2 years after shunt implantation using the GOS-E (Teasdale et al., 1998) and CRS-R scores. An increase in the GOS-E score after shunt implantation was considered as an improvement. For a patient whose GOS-E score remained unchanged, an increase in the score of any single subscale of the CRS-R was recognized as an improvement in the patient's outcome. We obtained the outcome assessment from the patient's medical examination in our institution or medical records from other rehabilitation centers. To those who received rehabilitation treatment at home, the referent physician or legal guardian was contacted. GOS-E scores, part of the CRS-R scale (motor scores and arousal scores), were evaluated when performed by a legal guardian.

2.6 Derivation and validation of the predictive model

The predictive model was developed using binary logistic regression, with the outcome after shunt implantation at the end of the two-year follow-up as the dependent variable and the analyzed clinical characters as independent variables. The weighted scores were assigned to each factor based on their β-regression coefficient values and then were transformed to the nearest integer to develop a practical and uncomplicated prognostic score. The prognostic score was calculated by summing all the scores for each patient, and then the patients were grouped into three groups based on their score percentile: low probability (0-33rd percentile), intermediate probability (34th-67th percentile), and high probability (68th-100th percentile) of improvement after shunt implantation. The validation was then launched to assess the accuracy of this scoring model. The β-regression coefficient values and the transformation of the weighted scores are presented in Table 2.

2.7 Statistical analysis

We used the SPSS (Version 17.0, Chicago, IL, USA) for analyses. Pearson's chi-square or Fisher's exact test was used for univariate analysis. Variables associated with the outcome of shunt implantation ($P < 0.05$) were included in the logistic regression model to identify the independent predictors of outcome and were

Table 1. Clinical characteristics of the patients and univariate analysis of the association between the improved and non-improved group.

Characteristics	Category	Transformation	Total patients (n, %)	Patients in the improved group (n, %)	Patients in the non-improved group (n, %)	*P* value
Age (years)	≤ 50	0	19 (32.2%)	15 (78.9%)	4 (21.1%)	0.005
	> 50	1	40 (67.8%)	16 (40.0%)	24 (60.0%)	
Gender	Male	0	30 (50.8%)	15 (50.0%)	15 (50.0%)	0.691
	Female	1	29 (49.2%)	16 (55.2%)	13 (44.8%)	
Cause of injury	Fall	0	18 (30.5%)	15 (83.3%)	3 (16.7%)	0.001
	Road traffic accidents	1	33 (55.9%)	10 (30.3%)	23 (69.7%)	
	Violence and other causes	2	8 (13.6%)	6 (75.0%)	2 (25.0%)	
Severity of hydrocephalus (V/BP)	26-40%	0	31 (52.5%)	22 (71.0%)	9 (29.0%)	0.004
	41-60%	1	28 (47.5%)	9 (32.1%)	19 (67.9%)	
ICP (mmH_2O)	≤ 150	0	24 (40.7%)	12 (50.0%)	12 (50.0%)	0.746
	> 150	1	35 (59.3%)	19 (54.3%)	16 (45.7%)	
Status of cisterna ambiens	visible	0	30 (50.8%)	17 (56.7%)	13 (43.3%)	0.519
	not-visible	1	29 (49.2%)	14 (48.3%)	15 (51.7%)	
GCS scores at the time of injury	3-8	0	41 (69.5%)	16 (39.0%)	25 (61.0%)	0.002
	9-12	1	18 (30.5%)	15 (83.3%)	3 (16.7%)	
GCS scores before shunt implantation	3-8	0	27 (45.8%)	10 (37.0%)	17 (63.0)	0.028
	9-12	1	32 (54.2%)	21 (65.6%)	11 (34.4%)	
Skull defect	unilateral	0	40 (67.8%)	24 (60.0%)	16 (40.0%)	0.096
	bilateral	1	19 (32.2%)	7 (36.8%)	12 (63.2%)	
Time interval from injury to cranioplasty (months)	≤ 6	0	38 (64.4%)	23 (60.5%)	15 (39.5%)	0.254
	> 6	1	16 (27.1%)	6 (37.5%)	10 (62.5%)	
	no cranioplasty	2	5 (8.5%)	2 (40%)	3 (60%)	
Time interval from injury to shunt implantation (months)	≤ 3	0	39 (66.1%)	25 (64.1%)	14 (35.9%)	0.013
	> 3	1	20 (33.9%)	6 (30.0%)	14 (70.0%)	

Abbreviations: ICP, intracranial pressure; GCS, Glasgow coma score.

Table 2. Binary logistic regression analysis and the scoring transformation.

Predictors	Category	OR	*P* value	β-regression coefficient	Scores
Age	< 50 years	18.9	0.004	2.94	10
Severity of hydrocephalus	mild hydrocephalus	5.5	0.025	1.7	6
GCS scores at the time of injury	9-12	6.46	0.029	1.87	6
Time interval time from injury to shunt implantation	< 3 months	10.1	0.017	2.31	8

A linear transformation of the corresponding β-regression coefficient was used to assign points to the predictive factors: the coefficient of each variable was divided by 1.70 (the lowest β-value, corresponding to mild hydrocephalus), multiplied by a constant (6), and then rounded to the nearest integer.

Abbreviations: GCS, Glasgow coma score, OR, Odds ratio.

retained in the final model if the P-value was < 0.05. We used the chi-squared test to determine if there was an increased probability of improvement in the patients' outcome among the three categories. The receiver operator characteristic curve (ROC) and the area under the receiver operating characteristic curve (AUC) were used to access the discriminatory power of the scoring system. The AUCs was classified into three levels: good (AUC $>$ 0.8) predictive ability, moderate (AUC = 0.7-0.8) predictive ability, and low (AUC = 0.6-0.7) predictive ability. And then, the H-L test was used to evaluate the model's calibration ability.

3. Results

3.1 Patients' characteristics

A total of 66 patients with PTH combined with disturbance of consciousness were included. Two patients were excluded due to missing data during the 2-year follow-up period. Five patients experienced severe uncontrolled infection after the VPS surgery, and the tubes were finally removed. Of the 59 patients, 12 had a GOS-E score of 2, and the remaining 47 received a score of 3 before the VPS surgery. By the end of the two-year follow-up period, clinical improvements were observed in 31 (52.5%) patients. Among them, 28 patients showed an improved GOS-E score (GOS-E increased from 3 to 4 in 21 patients, 3 to 5 in 4 patients, and 2 to 3 in 3 patients), while the other 3 patients demonstrated an increased CRS-R score (1 showed improvement in motor scores and 2 in arousal scores). No significant difference was observed between the improved and non-improved groups on gender, ICP, skull defect, the status of cisterna ambiens, the time interval from injury to cranioplasty, and GCS score before shunt implantation.

3.2 Formation of the predictive model

By univariate analysis, correlations were revealed between the outcome of shunt implantation and the patients' age, cause of injury, the severity of hydrocephalus, time interval from injury to shunt surgery, and GCS score at the time of injury. Subsequently, a binary logistic regression analysis was performed. After eliminating variables with poor predictive ability, the following factors were included in the final model: age < 50 years, mild hydrocephalus, the time interval from injury to shunt implantation $<$ 3 months, and GCS scores 9-12 at the time of injury. A predictive scoring system was developed according to the logistic regression model, and each predictor was assigned a single score based on its regression coefficient value (Table 2). The total score was calculated by summing the scores of the corresponding predictive factors for each patient. And then, the patients were divided into three groups based on the total score: low-probability (0-10 points), intermediate-probability (11-16 points), and high-probability (17-30 points). The probabilities of improvement after shunt implantation in these three groups were 14.3%, 52.6%, and 94.7%, respectively (Table 3).

3.3 Validation of the scoring system

Patients admitted to our institute from January 2014 to December 2015 were included in the validation cohort. Thirty-two patients with PTH and disturbance of consciousness were added according to the same inclusion and exclusion criteria. There was no statistically significant difference in the patients' characteristics between the derivation and validation cohorts (Table 4). In the validation cohort, 15 patients showed improvement in GOS or CRS-R score by the end of the 2-year follow-up period, while the remaining 17 patients show no improvement. Using our predictive scoring system, the rates of improvement in the three groups were 21.4%, 54.5%, and 85.7%, respectively. The probability of improvement after shunt surgery significantly increased in patients with higher scores in both the derivation and validation cohorts (both chi-square for trend P values < 0.05, Table 3). A ROC curve was created to evaluate the accuracy of the predictive model. The ROC and the AUCs were shown below (Fig. 1). The AUC of the derivation data was 0.869 (95% confidence interval, 0.755-0.942), with a specificity of 64.29% and a sensitivity of 90.32%, indicating that the model performed good predictive power for the outcome. The analysis of the Hosmer-Lemshow (H-L) test (P = 0.391) shows a good calibration.

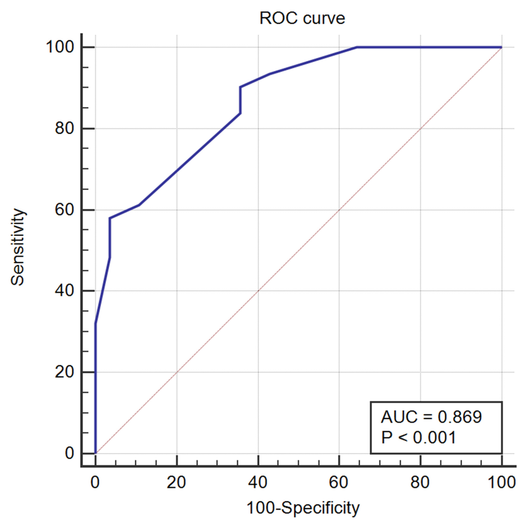

Figure 1. Receiver-operating characteristics curve for the scoring system in the derivation cohort (area under the receiver operating characteristic curve = 0.869).

4. Discussion

PTH is undoubtedly one of the most common and severe complications after TBI. It not only causes disturbance of consciousness but also affects the recovery of neurological function (Weintraub et al., 2017). Standard trauma craniectomy is recommended in severe TBI, as it significantly improves the outcome compared to limited craniectomy (Jiang et al., 2005). Therefore, most TBI survivors suffered from cerebrospinal fluid (CSF) dynamic changes. Along with obstruction of the ventricular system and CSF drainage disorder secondary to traumatic subarachnoid hemorrhage or other causes, PTH has an increasing incidence accompanied by decreasing mortality of severe TBI.

At present, shunt surgery is believed to be the most effective method to treat hydrocephalus. Patients with ICP higher than 200 mmH_2O or with typical symptoms of normal-pressure hydrocephalus (NPH) are more likely to benefit from shunt implantation. However, most patients with PTH have normal ICP, but few of them show typical symptoms of NPH (Cardoso and Galbraith, 1985; Wen et al., 2009). Also, in patients with PTH and uncon-

Table 3. Incidence of improvement of patients in the derivation and validation cohorts according to the predictive scoring system.

Outcome category	Score	Derivation cohort (n = 59)		Validation cohort (n = 32)	
		No. (%)	Improved No. (%)	No. (%)	Improved No. (%)
Low	0-10	21 (35.6%)	3 (14.3%)	14 (43.8%)	3 (21.4%)
Intermediate	11-16	19 (32.2%)	10 (52.6%)	11 (34.4%)	6 (54.5%)
High	17-30	19 (32.2%)	18 (94.7%)	7 (21.9%)	6 (85.7%)
χ^2 for trend		25.892		8.141	
p value for trend		< 0.0001		0.017	

Table 4. Comparison of the variables between the derivation and validation cohorts.

Variables	Category (transformations)	Total patients (n1/n2/...)		Pearson χ^2	P value
		Derivation cohort	Validation cohort		
Age (years)	0/1	19/40	12/20	0.259	0.611
Gender	0/1	30/29	17/15	0.043	0.836
Cause of injury	0/1/2	18/33/8	9/19/4	0.1	0.951
Severity of hydrocephalus	0/1	31/28	18/14	0.115	0.735
ICP	0/1	24/35	12/20	0.088	0.767
Status of cisterna ambiens	0/1	30/29	16/16	0.006	0.938
GCS scores at the time of injury	0/1	41/18	12/20	0.459	0.498
GCS scores before shunt implantation	0/1	27/32	13/19	0.222	0.637
Skull defects	0/1	40/19	22/10	0.009	0.926
Time interval from injury to cranioplasty (months)	0/1/2	38/16/5	19/11/2	0.586	0.746
Time interval from injury to shunt implantation (months)	0/1	39/20	20/12	0.118	0.731

Abbreviations: ICP: Intracranial pressure; GCS: Glasgow coma scale.

scious, assessing symptoms of hydrocephalus or improvement after performing a cerebrospinal fluid tap test is troublesome. Although several parameters are used to predict the outcome of shunt implantation in patients with PTH, the decision is difficult, particularly in patients with consciousness disturbance.

We developed a prognostic model to predict the outcome of shunt implantation after a two-year follow-up in patients suffering from PTH with a disorder of consciousness. This scoring system was useful to predict the probability of an improved outcome, and the AUCs indicated an excellent predictive power.

Patients $<$ 50 years old is an independent predictor for a good outcome in our present study. It is consistent with our previous research (Wen et al., 2009). It may be explained that younger patients show a higher ability for the restoration of CSF circulation. Czosnyka et al. (2001) had reported that meningeal fibrosis seems more severe in older patients than younger patients, which impaired the CSF circulation and decreased the ability of CSF absorption. But Tribl and Oder (2000) found that age at the time of injury did not affect the outcome.

Some studies have demonstrated that GCS at the time of injury was a significant independent risk factor for the development of PTH (Honeybul and Ho, 2012; Mazzini et al., 2003). Patients with lower GCS always mean a more severe primary TBI and brain tissue damage and expected to produce more severe CSF circulation and absorption disturbance. Kim et al. (2015) reported that 11 patients (100%) improved in the GCS 13-15 group and 2 patients (50%) improved in the GCS 5-8 group after shunt surgery. In our present study, 15 patients (83.3%) in the GCS 9-12 group got an improved outcome after shunt surgery. The primary brain injury was thought to remain even though the CSF circulation has been treated by shunt implantation. And the rehabilitation of patients' neurological functions and CSF circulation is a long-term process, especially for those with a more severe primary injury. Also, the majority of enrolled patients had normal ICP. But the severity of hydrocephalus varies by subgroup. The severity of hydrocephalus can intuitively reflect the status of CSF circulation. Therefore, patients with higher GCS scores and less severe hydrocephalus seems more likely to get improvements after the shunt operation.

It is reported that the majority of PTH occurred during the early stages of TBI (Kammersgaard et al., 2013). In earlier work, we demonstrated that early cranioplasty in patients with significant cranial defects after decompressive craniectomy would be safe and helpful for the improvement of the patients ' neurological function and prognosis (Wen et al., 2007). Early restoration of CSF circulation can improve cerebral perfusion and promote recovery of neurological function and consciousness. Patients treated with early shunt implantation showed a higher total score measured by our prognostic model and would more likely have a better outcome.

Finally, our scoring model has limitations. It reveals the relationship between several clinical features and the long-term prognosis of shunt implantation but is not useful for predicting the occurrence of PTH. In recent years, many studies assessing the risk factors for PTH (Hao et al., 2016; Honeybul and Ho, 2012; Shi et al., 2011) have been performed, but no consensus has been determined. Also, most of the data were collected from the clinical record system for such a retrospective study, making it difficult to draw a definite conclusion. However, for patients suffering from PTH and unconsciousness secondary to TBI, shunt implantation was only a part of comprehensive treatment. Rehabilitation exercise and long-term follow-up after shunt surgery are also necessary. Various neurological rehabilitation methods should be included in the treatment of such patients. Therefore, we are presently conducting a prospective, multicenter study to determine the other predictive factors and to include several new parameters such as cerebral perfusion and CSF dynamics before and after lumbar drainage procedure.

5. Conclusions

In conclusion, more than half of the patients included in the present study (52.5%) benefitted from shunt implantation. Using variables such as age, the severity of hydrocephalus, GCS scores at the time of injury, and time interval from injury to shunt implantation, we established a reliable predictive model to predict the outcomes of patients with PTH combined with severe consciousness disturbance.

Abbreviations

AUC: area under the receiver operating characteristic curve; CRS-R: Coma Recovery Scale-Revised; CSF: cerebrospinal fluid; CT: Computed Tomography; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; GOS-E: Glasgow Outcome Scale Extend; H-L: Hosmer-Lemshow; ICP: intracranial pressure; MRI: Magnetic Resonance Imaging; NPH: normal-pressure hydrocephalus; OR: Odds ratio; PTH: Post-traumatic hydrocephalus; ROC: receiver operator characteristic curve; TBI: traumatic brain injury; VPS: ventriculoperitoneal shunt.

Ethics approval and consent to participate

The study was approved by the ethics committee of the First Affiliated Hospital, College of Medicine, Zhejiang University, and was performed based on the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The informed consents signed by legal guardians were obtained from all participants.

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Conflict of Interest

The authors declare no competing interests.

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