



Development of a Clinical Nomogram for Predicting Shunt-Dependent Hydrocephalus

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J Health Allied Sci^{NU}

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Abstract

Background Hydrocephalus (HCP) is one of the neurosurgical conditions that can lead to impaired quality of life, disability, and mortality. The nomogram is a clinical prediction tool that has been studied in a variety of medical conditions. Hence, the primary objective of the present study was to establish the nomogram for predicting shunt-dependent HCP in patients with varied etiologies. The secondary objective was to identify predictors associated with shunt-dependent HCP.

Methods In the present study, 382 adult patients with various etiologies of HCP who had undergone ventriculostomy were included retrospectively. Several clinical factors, imaging findings, and ventricular indexes were analyzed for shunt-dependent HCP in both univariate and multivariable analysis. Based on binary logistic regression, the nomogram was created and internally validated from the final model.

Results Shunt-dependent HCP was observed in 25.7% of the present cohort. Initially, progressive headache, preoperative seizure, Evans index, third ventricle index, cella media index, ventricular score, and mass diameter were candidate predictors from univariate analysis. The final model which had the lowest Akaike information criterion comprised the third ventricle index and cella media index. Therefore, the model's performance had an area under the receiver operating characteristic curve (AUC) of 0.712. Moreover, the AUCs of bootstrapping and cross-validation methods were 0.701 and 0.702, respectively.

Conclusion In summary, clinical factors and ventricular measures that were strongly associated with shunt-dependent HCP were used to develop clinical prediction tools that could help physicians make decisions and care for high-risk patients in general practice.

Keywords

- ▶ nomogram
- ▶ prediction
- ▶ intracranial pressure
- ▶ hydrocephalus

Introduction

Hydrocephalus (HCP) is one of the most challenging neurosurgical conditions due to the fact that increased intracranial pressure can lead to impaired quality of life, disability, and mortality.^{1,2} According to Phan et al,³ HCP caused 76% of deaths in patients with intracerebral hemorrhage, while Persson et al found that 47% of children with HCP had

learning disabilities.⁴ Increased intracranial pressure (ICP) causes harm to generalized brain function; thus, cerebrospinal fluid diversion, such as ventriculostomy and ventriculoperitoneal (VP) shunt, is the conventional operation to treat this neurosurgical condition.⁵ Ventriculostomy is a common procedure that was performed to correct acute HCP, and the patient will be tapered off of ventriculostomy once the underlying cause of HCP has been addressed. However, the

DOI <https://doi.org/10.1055/s-0044-1779591>.
ISSN 2582-4287.

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VP shunt operation was required in approximately 13 to 18.75% of patients with acute HCP who were unable to wean off the ventriculostomy or shunt-dependent HCP.^{6,7}

Various risk factors associated with shunt-dependent HCP have been identified from a review of literature as follows: female gender,⁸ increased age,^{8,9} low Glasgow Coma Scale (GCS) score,^{8,10} intraventricular hemorrhage,^{7,8} etiology of HCP,⁹ and ventricular indexes.¹¹

Nomogram is one of the clinical prediction tools that has been studied to predict neurological outcomes in various conditions such as neurotrauma,¹² neuro-oncology,¹³ and surgical complications.¹⁴ Yang et al used a nomogram for predicting shunt-dependent HCP in patients with aneurysmal subarachnoid hemorrhage (SAH) and reported that the tool had an area under the receiver operating characteristic curve (AUC) of 0.895,¹⁵ while Wu et al reported c-statistic of 0.753 for shunt-dependent HCP in aneurysmal SAH.¹⁶ However, HCP is caused by a variety of neurological disorders, including brain tumors, hemorrhagic stroke, and congenital anomalies. Furthermore, nomogram for shunt-dependent HCP prediction has been discussed in a few research, it could be one of the noninvasive ways that real-world practice will be challenged in the future.

Based on the gap in knowledge, the primary objective of the present study was to establish the nomogram for predicting shunt-dependent HCP in patients with varied etiologies. The secondary objective was to identify predictors associated with shunt-dependent HCP.

Methods

Study Designs and Study Population

The retrospective cohort study began with a review of the electronic medical records of HCP adult patients admitted to a tertiary hospital and given a ventriculostomy within 24 hours of hospitalization between January 2014 and April 2023. Clinical characteristics, imaging findings, and

various ventricular indexes were collected. Patients who were under 15 years old, lacked a preoperative cranial computed tomography (CT) scan, or lacked operation data were excluded. In addition, patients with normal pressure HCP were also not included in this study.

Operational Definition

Shunt-dependent HCP was defined as patients who received ventriculostomy but were unable to wean off the ventriculostomy. Finally, the VP shunt or other permanent cerebrospinal conversion procedures were performed within 60 days following hospitalization.¹⁰ ICP was recorded intraoperatively after the ventricular catheter placement from the ventriculostomy operation. Consequently, ICP with a unit of a centimeter of water (cm H₂O) was converted to a unit of a millimeter of mercury (mm Hg) with 1 cm H₂O equaling 0.736 mm Hg.¹⁷

Multiple ventricular lines were measured for the ventricular indexes according to the study of Mataró et al,¹⁸ as shown in **Fig. 1A, B**. The following lines were measured from a cranial CT scan at the third ventricle level: the maximum bifrontal distance of the lateral ventricle (A), the distance between the caudate nuclei at the level of the foramen of Monro (B), the maximum width of the third ventricle (C), and the maximum inner diameter of the skull at the level of the maximum bifrontal distance measurement (E), whereas the minimum width of both cella media (D) and maximal outer interparietal diameter was measured at the level of the cella media measurement (F). Then, the following formulas were used to generate the ventricular indexes: Evans index (A/E), third ventricle index (C/E), cella media index (D/F), and ventricular score $((A + B + C + D)/E * 100)$.

Statistical Analysis

Descriptive statistics were performed to describe the baseline characteristics of HCP patients. For descriptive purposes, the proportion means with standard deviation (SD) was determined for continuous variables. The categorical variables were

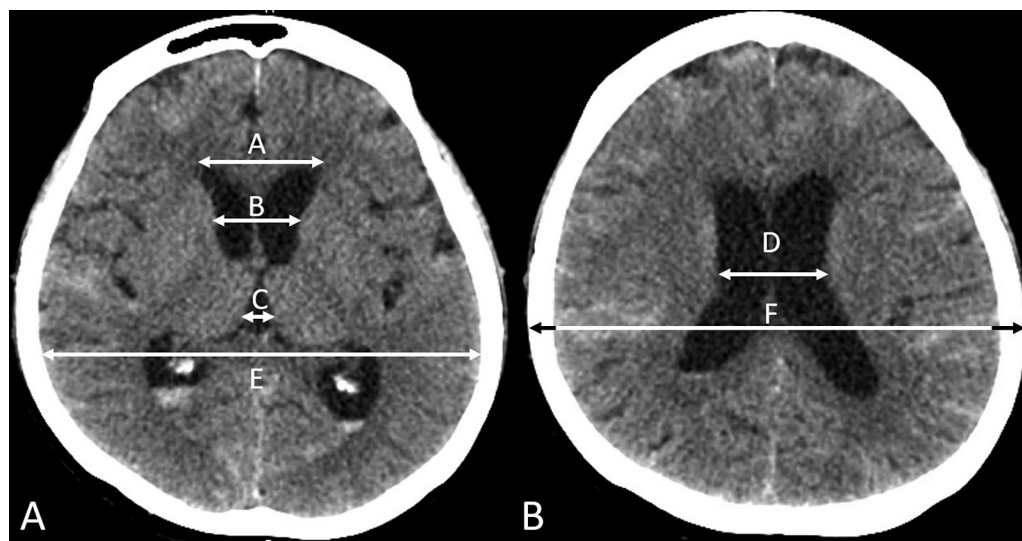


Fig. 1 Measurement of ventricular indexes. (A) Ventricular indexes at the level of the foramen of Monro. (B) Ventricular indexes at the level of cella media.

reported by proportion and percentage. To identify the factors associated with shunt-dependent HCP, univariate and multivariable analyses with binary logistic regression were done. Factors that had a *p*-value less than 0.1 were assigned from univariate analysis as the candidate factors; therefore, these variables were analyzed by multivariable analysis with a backward stepwise method. The final model was considered from the lowest value of the Akaike information criterion (AIC).¹⁹ The statistical analysis was performed using the R version 4.4.0 software (R Foundation, Vienna, Austria).

Nomogram Development

The nomogram predicting the shunt-dependent HCP was created from the final model by “regplot” package.²⁰ Therefore, the goodness-of-fit (GOF) test was estimated using the Hosmer–Lemeshow test, while the discrimination of the nomogram was assessed by AUC. Based on binary logistic regression, AUC equals the *c*-statistic which is a standard measure of the predictive performance of the model.²¹ Therefore, AUCs evaluated those values ≥ 0.9 are “excellent,” ≥ 0.80 “good,” ≥ 0.70 “fair,” and < 0.70 “poor.”²² Additionally, an internal validation was performed to detect the overfitting problems of the nomogram by the bootstrap validation with 500 replicates and 5-fold cross-validation. The bias-corrected AUCs of internal validation were reported.²³

Results

The baseline clinical characteristics of patients are shown in ►Table 1 and a total of 382 patients were considered for this study. The obstructive HCP was observed in 63.4%, whereas 40.8% of all HCPs occur from brain tumor. The majority (95.3%) of ventriculostomy operation was an emergency operation, and 60.2% of HCP patients had GCS score of 3 to 8. In addition, the average values of ventricular indexes and other imaging findings are demonstrated in ►Table 2.

The average Evans index was 0.322 (SD 0.563), while the mean third ventricle index, cella media index, and ventricular score were 0.087 (SD 0.034), 0.257 (SD 0.084), and 91.222 (SD 17.697), respectively. Moreover, the average diameter of intracranial mass was 9.623 mm (SD 17.002), and the mean degree of midline shift was 1.312 mm (SD 2.613).

Factors Associated with Shunt-Dependent Hydrocephalus

The results of univariate and multivariable analysis are demonstrated in ►Table 3. Initially, progressive headache, preoperative seizure, Evans index, third ventricle index, cella media index, ventricular score, and mass diameter were candidate factors in univariate analysis. Therefore, these variables were analyzed by multivariable analysis with backward stepwise elimination. As a result, the final model which had the lowest value of AIC comprised the third ventricle index and cella media index.

Nomogram Development

The nomogram was developed from the final model in the multivariable analysis, as shown in ►Fig. 2. The nomogram is

Table 1 Baseline clinical characteristics (N = 382)

Characteristics	N (%)
Gender	
Male	164 (42.9)
Female	218 (57.1)
Mean age, y (SD)	58.34 (17.63)
Age group, y	
≤ 60	192 (50.3)
> 60	190 (49.7)
Underlying disease	
Hypertension	126 (33.0)
Diabetes meatus	48 (12.6)
Dyslipidemia	42 (11.0)
Renal failure	26 (6.8)
Liver disease	6 (1.6)
Signs and symptoms	
Progressive headache	122 (31.9)
Motor weakness	286 (74.9)
Ataxia	8 (2.1)
Preoperative seizure	30 (7.9)
Preoperative Glasgow Coma Scale score	
13–15	54 (14.1)
9–12	98 (25.7)
3–8	230 (60.2)
Pupillary light reflex	
Fixed both eyes	52 (13.6)
React one eye	30 (7.9)
React both eyes	300 (78.5)
Disease	
Tumor	156 (40.8)
Subarachnoid hemorrhage	128 (33.5)
Hemorrhagic stroke	88 (23.0)
Other	10 (2.6)
Type of hydrocephalus	
Communicating hydrocephalus	140 (36.6)
Obstructive hydrocephalus	242 (63.4)
Basal cistern obliteration	176 (46.1)
Emergency operation	364 (95.3)
Mean intracranial pressure from ventriculostomy, mm Hg (SD)	31.50 (9.40)
Shunt-dependent hydrocephalus	98 (25.7)

Abbreviation: SD, standard deviation.

easy to utilize for predicting shunt-dependent HCP in new patients. For example, a 57-year-old male developed HCP from thalamic hemorrhage with GCS score of 14. To use the nomogram, draw a straight line upward from the patient’s characteristics of the third ventricle index (Third_index) and

Table 2 Average of central nervous system indexes

Parameter/index	Mean (SD)
Evans index	0.322 (0.563)
Third ventricular index	0.087 (0.034)
Cella media index	0.257 (0.084)
Ventricular score	91.222 (17.697)
Midline shift (mm)	1.312 (2.613)
Mass diameter (mm)	9.623 (17.002)

Abbreviation: SD, standard deviation.

the cella media index (Cella_index) to the upper points scale for scoring each variable (dashed lines) and the sum of the scores of all variables (solid arrow). As a result, he will receive a total score of 40.7, which means that there is a 25.4% chance that he has shunt-dependent HCP within 60 days following hospitalization.

For the model performance, the Hosmer–Lemeshow GOF test for the model’s calibration gave a *p*-value = 0.074, which indicated good calibration. Moreover, the calibration plot was created, as shown in **Fig. 3**. The plot shows that the concordance between the predicted probability and response is satisfactory. Therefore, the domain of the model’s

Table 3 Factors associated with shunt-dependent hydrocephalus

Factor	Univariate analysis		Multivariable analysis	
	Odds ratio (95% CI)	<i>p</i> -Value	Odds ratio (95% CI)	<i>p</i> -Value
Gender				
Female	Ref			
Male	1.39 (0.87–2.20)			
Mean age, y	0.99 (0.93–1.009)	0.57		
Underlying disease				
Hypertension ^a	0.86 (0.52–1.41)	0.56		
Diabetes meatus ^a	0.96 (0.47–1.93)	0.96		
Dyslipidemia ^a	0.89 (0.43–1.89)	0.77		
Renal failure ^a	1.31 (0.55–3.12)	0.53		
Liver disease ^a	1.45 (0.26–8.08)	0.66		
Signs and symptoms				
Progressive headache ^a	0.61 (0.36–1.03)	0.06		
Motor weakness ^a	0.90 (0.53–1.52)	0.71		
Ataxia ^a	2.97 (0.73–12.14)	0.12		
Preoperative seizure ^a	2.06 (0.95–4.45)	0.06		
Preoperative Glasgow Coma Scale score				
13–15	Ref			
9–12	1.15 (0.56–2.36)	0.70		
3–8	0.66 (0.34–1.28)	0.21		
Pupillary light reflex				
Fixed both eyes	Ref			
React one eye	2.10 (0.75–5.86)	0.15		
React both eyes	1.47 (0.70–3.08)	0.30		
Type of hydrocephalus				
Communicating hydrocephalus	Ref			
Obstructive hydrocephalus	0.99 (0.61–1.60)	0.98		
Basal cistern				
Patent	Ref			
Obliteration	1.30 (0.82–2.06)	0.25		
Emergency operation				
Nonemergency	Ref			
Emergency	2.86 (0.64–12.69)	0.16		

Table 3 (Continued)

Factor	Univariate analysis		Multivariable analysis	
	Odds ratio (95% CI)	p-Value	Odds ratio (95% CI)	p-Value
Ventricular indexes				
Evans index	777.86 (10.89–5523.38)	0.002		
Third ventricular index	10560.07 (82.45–135200.29)	< 0.001	8114.91 (2.75–25090.67)	0.02
Cella media index	1028.14 (88.80–11921.22)	< 0.001	732.90 (16.67–1440.26)	0.005
Ventricular score	1.03 (1.01–1.04)	< 0.001		
Midline shift (mm)	1.05 (0.97–1.14)	0.21		
Mass diameter (mm)	1.01 (0.98–1.02)	0.055		
Disease				
Nontumor group	Ref			
Tumor	1.39 (0.88–2.23)	0.15		
Intracranial pressure (mm Hg)	1.01 (0.99–1.03)	0.23		

Abbreviation: CI, confidence interval.

^aData show only “yes group” while reference groups (no group) are hidden.

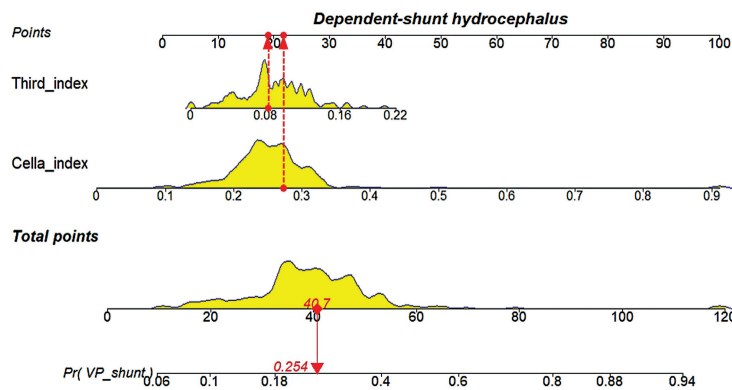


Fig. 2 Nomogram predicting shunt-dependent hydrocephalus.

discrimination had an AUC of 0.712 and the overfitting of the model was considered by 500 bootstrapping and 5-fold cross-validation techniques. Therefore, the AUCs of bootstrapping and cross-validation methods were 0.701 and 0.702, respectively.

Discussion

In the present study, 25.7% of patients had shunt-dependent HCP, and the concordance results were similar to those seen in previous studies. Hao and Wei found shunt-dependent HCP following SAH in 14.3% of the cohort, whereas Dorai et al reported 21.2% of patients with SAH.²⁴ From the literature review, SAH was one of the important neurosurgical diseases associated with shunt-dependent HCP. However, the etiologies of HCP in the present study did not significantly relate to with shunt-dependent HCP. This may be explained by the fact that the study population in the present study consisted of HCP patients who suffered from a variety of etiologies, as

opposed to previous studies, which did not compare HCP patients with other etiologies. Previous studies were conducted on specific SAH patients.^{7,8,24}

Moreover, intraventricular indexes were strongly linked to shunt-dependent HCP, and these findings are consistent with those of other studies. Aboul-Ela et al reported that a high bicaudate index increased the likelihood of the requirement for VP shunt operation.¹¹ Moreover, Weigl et al conducted the scoring system for predicting the failure risk index of the removal of ventriculostomy using various ventricular parameters.^{25,26} Our results are concordant with earlier studies that ventricular indexes were the potential predictors of shunt-dependent HCP, particularly the cella media index.

Nomogram is a clinical prediction tool that has been studied in a variety of medical domains, including neuro-oncology, traumatic brain injury, and others.^{12–14} From a review of the literature, two studies mentioned nomograms for predicting shunt-dependent HCP following aneurysmal SAH. Prior studies indicated predictive performance with

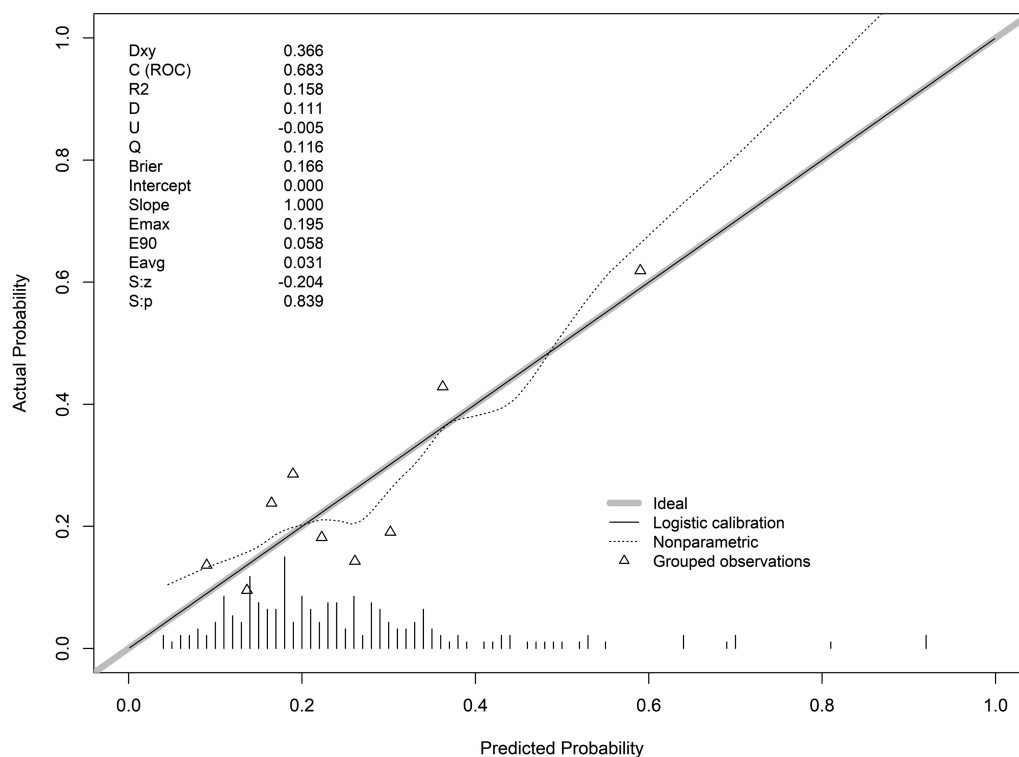


Fig. 3 Calibration plot. The dashed 45° line indicates ideal performance, in which the expected outcome is acceptable in comparison to the actual performance.

AUC ranging from 0.753 to 0.895^{15,16}; however, the present study's AUC was 0.712. The outcome was slightly lower than the literature since the current study's nomogram was intended to use in various etiologies of HCP, whereas prior studies' nomograms were applied only in SAH patients. From internal validation, the AUC of the present study's nomogram was still acceptable and there was no overfitting issue.²⁷

Currently, various clinical prediction tools have been studied in medicine, such as scoring systems, nomograms, and machine learning.^{27,28} Comparison among these tools is a challenge for future research and the tool has the highest predictive performance that could be implicated in clinical practice. Moreover, the tools should be easily applied to aid physician's decision marking in the real-world situation such as web application.²⁷ According to a prior systematic review, web applications are one of the straightforward technologies that may be utilized as a computerized clinical decision support system (CCDSS). In the future direction, CCDSS improved the care process, including screening and treatment, and had an impact on patient outcomes, health care expenditures, and patient safety.^{27,29}

There are some limitations to the research that should be mentioned. The nomogram of the present study needs to be validated with data from new patients. Therefore, external validation would be the next step to evaluate the performance of the prediction tool on unseen data from novel patients at the same centers at which the nomogram was developed, as temporal validation, or patients from centers that were not involved in the tool's development, as geographic validation. Other limitations must be acknowledged.^{27,28} The nomogram was a two-dimensional graphic scoring system that required

scores to be assigned to each variable, making it a challenging tool to use in general practice. A Web-based nomogram or mobile application should be developed and distributed to simplify the tool for the physician's practice.^{29,30} The nomogram in this study was created using the R program's regplot package, which used the built-in nomogram with automatic summation of the total score after each parameter was entered (supplement for R script). Furthermore, because the retrospective study design may generate bias, future multicenter prospective research should be conducted.^{13,30}

Conclusion

In summary, clinical factors and ventricular measures that were strongly associated with shunt-dependent HCP were used to develop clinical prediction tools that could help physicians make decisions and care for high-risk patients in general practice.

Ethical Considerations

The present study was approved by the human research ethics committee (REC.65-249-10-1). Informed permission of the patients was not necessary for the present study because it was a retrospective analysis. But before analysis, patient identity numbers were encoded.

Declarations

All procedures performed in the study that involved studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee or both and with the 1964

Helsinki Declaration and its later amendments or comparable ethical standards (REC.65–249–10–1).

Authors' Contributions

A.T. and T.T. conceived the study and designed the method. T.T. supervised the completion of the data collection. A.T. and T.T. undertook the recruitment of participating centers and patients and managed the data, including quality control. T.T. provided statistical advice on the study design and analyzed the data, while T.T. drafted the manuscript, and all authors contributed substantially to its revision. T.T. takes responsibility for the paper as a whole.

Funding

None.

Conflict of Interest

The authors declare that there were no conflicts of interest concerning the work contained herein.

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