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Clinical value of inflammatory indices in predicting poor prognosis and post-hemorrhagic hydrocephalus in patients with intraventricular hemorrhage

Haoxiang Wang[1†], Yuanyou Li[2†], Feng Ye[1†], Ziang Deng[1], Keru Huang[1], Gaowei Li[1], Yaxing Chen[1], Yi Liu[1] and Liangxue Zhou[1*]

Abstract

Background Hemorrhagic stroke has a high mortality and disability rate. Among them, intraventricular hemorrhage (IVH) is an important factor leading to adverse outcomes. IVH can induce acute obstructive hydrocephalus and chronic communicating hydrocephalus. However, there are currently no effective predictive factors for the early prediction of post-hemorrhage hydrocephalus (PHH).

Objectives To assess the role of inflammatory indicators in predicting PHH and poor prognostic outcomes in patients with ventricular hemorrhage.

Design Single center retrospective case-control study.

Methods We retrospectively examined IVH patients treated at our institution from April 2017 to March 2022. Patient characteristics, laboratory data, imaging findings, and 3-month follow-up results were recorded and analyzed.

Results Among the 145 patients included in the analysis, 102 eventually developed adverse outcomes. There were significant differences between patients with good and poor prognosis in terms of age at admission, GCS score, prevalence of hypertension, lymphocyte count, albumin level, red blood cell distribution width, neutrophil count, NLR, PLR, NAR, PIV, and SII; in addition, among the 110 surviving patients, 36 eventually developed posthemorrhagic hydrocephalus within 3 months. Multivariate logistic regression showed that age and NAR are independent predictors of poor prognosis in IVH patients, while albumin is an independent predictor of posthemorrhagic hydrocephalus within 3 months.

Conclusion The NLR and NAR are independent risk factors for poor prognosis in IVH patients. Additionally, albumin is an independent predictor of chronic hydrocephalus development within 3 months in IVH patients. The NLR, NAR and albumin level could provide prognostic information about IVH patients.

†Haoxiang Wang, Yuanyou Li and Feng Ye contributed equally to this work and should be considered co-first authors.

*Correspondence:
Liangxue Zhou
zhlxlll@163.com

Full list of author information is available at the end of the article

Keywords Neutrophil-lymphocyte ratio, Neutrophil-albumin ratio, Intraventricular hemorrhage, Post-hemorrhage hydrocephalus, Inflammatory markers

Introduction

Intracerebral hemorrhage (ICH) is the most devastating type of stroke with high morbidity and mortality rates [1]. Intraventricular hemorrhage (IVH) is a significant factor in the development of poor outcomes, such as coma, increased mortality, and long-term functional impairment after ICH, which occurs in approximately 40% of patients with ICH [2]. Post-hemorrhagic hydrocephalus (PHH) occurs in approximately 25–30% of newborns with high-level IVH and up to two thirds of adults [3, 4]. IVH can cause blood clots to block the flow of cerebrospinal fluid, potentially leading to acute obstructive hydrocephalus. In addition, long-term inflammation and fibrosis can lead to an imbalance in the production and drainage of cerebrospinal fluid, resulting in chronic hydrocephalus [5]. Hydrocephalus, as a serious complication after hemorrhagic stroke, could cause severe pain and health risks. However, the occurrence of chronic hydrocephalus in the distant stage of IVH is currently more often diagnosed from symptoms and imaging [6]. Actually, there is a lack of early, objective and easily accessible predictors of outcome for PHH.

Recently, preclinical study has identified multiple mechanisms of secondary injury after IVH, particularly the role of blood components such as hemoglobin, iron, and thrombin [7]. Moreover, inflammation plays a crucial role in the progression of intraventricular hemorrhage and PHH [5, 8]. Therefore, we aimed to investigate that whether blood markers of inflammation could predict the prognosis of IVH and the occurrence of PHH in IVH patients.

With a high level of neutrophil-to-lymphocyte ratio (NLR) indicating an imbalance between central and peripheral inflammation and serving as a risk factor, NLR is a potential predictor of ICH [9]. The platelet-to-lymphocyte ratio (PLR) reflects platelet aggregation and systemic inflammation levels, and has been validated as a predictor of inflammatory diseases of the central nervous system [10]. In addition, recent studies have highlighted the neutrophil/albumin ratio (NAR), systemic inflammatory index (SII) and pan-immuno-inflammatory value (PIV) as comprehensive inflammatory biomarkers that can be used for prognostic purposes in stroke and have been shown to provide valuable prognostic information in stroke patients [11–13]. Therefore, we hypothesized that these complex inflammatory markers may also predict IVH prognosis and the development of PHH.

In this study, we attempted to investigate the predictive role of NLR, NAR, PLR, SII, and PIV on the near-term prognosis and long-term chronic hydrocephalus formation in IVH patients. The study intends to identify predictive indicators that can effectively forecast the near-term prognosis and post-hemorrhagic hydrocephalus formation in IVH patients and provide theoretical support for clinical decision.

Methods

Patients

This was a retrospective case-control study of patients admitted to West China Hospital of Sichuan University's Intensive Care Unit and Neurosurgery Department from April 2017 to March 2022. To verify the diagnosis of IVH, these patients underwent CT or MRI upon admission, as well as routine laboratory blood sample testing within 24 h of admittance. The inclusion criteria consist of the following: the patient experiences their first, non-traumatic primary or secondary ventricular hemorrhage (i.e. spontaneous cerebral hemorrhage that extends into the ventricle). Exclusion criteria were listed as below: Previous head trauma; Immunomodulatory therapy prior to admission, including biologics, azathioprine, corticosteroids, and methotrexate; Arteriovenous malformations; Recent cardiovascular and cerebrovascular diseases; Autoimmune diseases; Severe compound damage; Severe organ damage (liver, spleen, heart, kidneys); Insufficient data from laboratory or imaging and patients whose follow-up data could not to be obtained. We established the following parameters: effect size ($h = 0.5$), significance level ($\alpha = 0.05$), statistical power ($1 - \beta = 0.8$), and calculated the required sample size ($n = 62.79$). We collected a total of 315 patients and ultimately enrolled 145 patients after applying exclusion criteria (Fig. 1). In addition, we captured baseline characteristics for full cohort as well as group characteristics based on survival (Table 1). The study had approval from the ethics committee of the West China Hospital, Sichuan University. Informed consent was waived due to the retrospective nature of this study (ethics committee of the West China Hospital, Sichuan University). All methods were performed in accordance with the relevant guidelines and regulations or declaration of Helsinki.

Data collection

We collected data on Demographic characteristics, anthropometric characteristics, medical history data, clinical characteristics, laboratory findings and imaging information, including Glasgow Coma Scale (GCS, with lower scores indicating poorer level of consciousness) scores, length of intensive care unit (ICU) stay, in-hospital mortality and 6-months modified rankin scale (mRS)

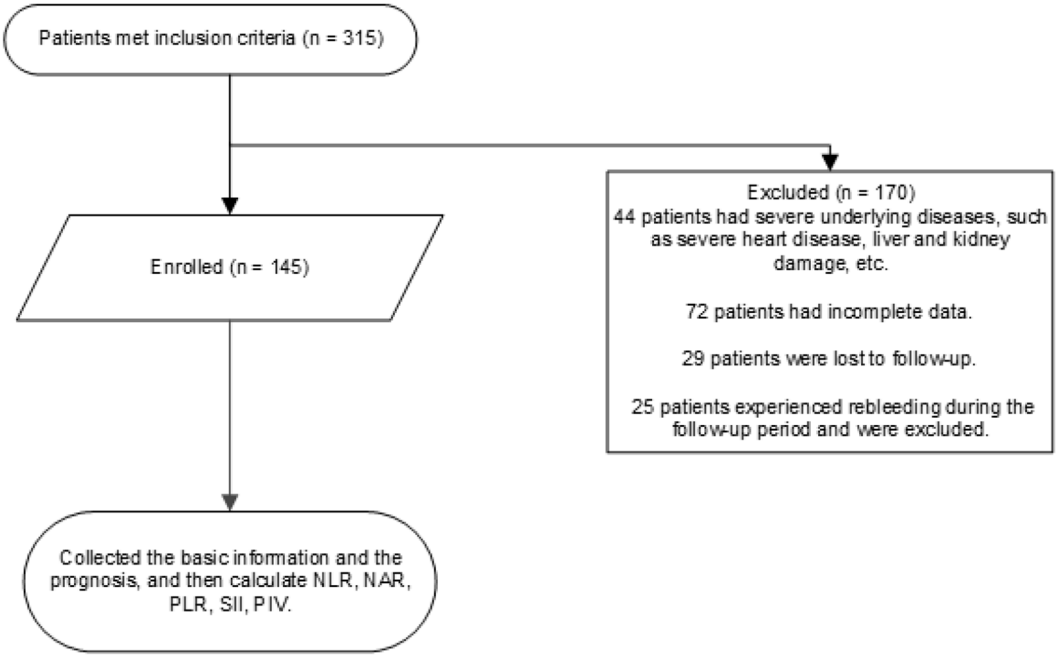

Fig. 1 The flow chart of excluded patients

prognostic scores. In addition, we also documented the location of the patient's primary hematoma (brain parenchyma or ventricle). We calculated NLR, PLR, NAR, SII and PIV according to the following formulae: NLR = neutrophil count/lymphocyte count; PLR = platelet count/lymphocyte count; NAR = neutrophil count/albumin count; SII = neutrophil count × platelet count/lymphocyte and PIV = neutrophil count × platelet count × monocyte count/lymphocyte. Patients were followed up by outpatient 3 months after discharge and MRI scan of the head was also conducted to check for enlarged ventricles and chronic hydrocephalus. Neurological function was assessed 3 months after IVH by using the mRS. Patients were divided into a poor outcome group with high mRS (≤ 2) and a good outcome group with a low mRS score (>2). We defined chronic hydrocephalus as ventricular enlargement (Evan's Index > 0.3) that occurs within three months and cannot be explained by other causes [8]. Furthermore, based on the occurrence of chronic hydrocephalus, the patients were categorized into another two groups, one with chronic hydrocephalus and the other with no chronic hydrocephalus.

Data analysis

Statistical analysis was performed using GraphPad Prism 9.0 and R version 4.2.0. Prior to statistical analysis, the data were analyzed for normality. Continuous variables that followed a normal distribution were expressed as means with standard deviations, and the remaining continuous variables were expressed as medians with interquartile ranges (IQR) and compared using non-parametric rank sum tests or independent samples t-tests as appropriate. Categorical variables are expressed as frequencies and percentages and compared using chi-squared or Fish exact tests where appropriate. Plot the receiver operating characteristic (ROC) curve of the predictor and evaluate the predicted value using the area under the curve (AUC). The correlation among SII, PIV, NLR, PLR, NAR was assessed by Spearman correlation. Determining independent predictors of prognosis and occurrence of chronic hydrocephalus in patients with IVH by using univariate and multivariate logistic regression. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. All P values are on both sides and the significance is set to $P < 0.05$.

Results

In summary, the study included 145 patients with a mean age of 51.76 years (range 1–89), 103 of whom were male and 42 were female. The mean Glasgow Coma Scale (GCS) score for all patients was 6 (range 3–15). 110 patients survived during their stay in hospital. Patients who died during hospitalization had significantly lower GCS scores ($p < 0.001$) and significantly higher levels of erythrocyte distribution width ($p = 0.004$), neutrophils ($p = 0.008$), monocytes ($p = 0.005$), procalcitonin ($p = 0.003$) and C-reactive protein ($p = 0.017$) as compared to those who survived. In a comparison of multiple novel inflammatory compliance indicators, it was found that patients who died during hospitalization had significantly higher levels of NAR ($p = 0.006$) and PIV ($p = 0.013$) compared to the patients who survived.

Table 1 Comparison of demographic, clinical and laboratory characteristics of patients

Demographic	Full cohort (*n* = 145)	Survivors (*n* = 110)	Non-survivors (*n* = 35)	t/x2/z	*p*-value
Demographic					
Age, years, Mean (SD)	51.76 ± 20.58	49.75 ± 20.66	54.32 ± 16.50	1.519	0.131[a]
Gender, male, n (%)	103 (71.0%)	76 (69.1%)	27 (77.1%)	0.837	0.360[b]
Primary cerebral hemorrhage region					
Thalamus, n (%)	23 (15.9%)	22 (20.0%)	1 (2.8%)	/	/
Basal ganglia, n (%)	38 (26.2%)	31 (28.2%)	7(20%)	/	/
Cerebellum, n (%)	8 (5.4%)	5 (4.5%)	3 (8.6%)	/	/
Ventricle, n (%)	53 (36.6%)	39 (35.5%)	14 (40%)	/	/
Others, n (%)	23 (15.9%)	13 (11.8%)	10 (28.6%)	/	/
Clinical characteristics					
Hypertension, n (%)	83 (57.2%)	65 (59.1%)	18 (51.4%)	0.637	0.425[b]
Diabetes, n (%)	18 (12.4%)	12 (10.9%)	6 (17.1%)	0.949	0.330[b]
Pulmonary infection, n (%)	101 (69.7%)	73 (66.4%)	28 (80%)	2.336	0.126[b]
GCS score, median (IQR)	6 [3–14]	8 [5–14]	3 [3–5]	5.057	**< 0.001[c]**
BMI, kg/m_2, median (IQR)	23.90 ± 3.86	23.77 [20.80–26.59]	23.66 [21.23–25.71]	0.508	0.611[c]
Temperature, ℃, median (IQR)	36.92 ± 0.79	36.7 [36.5–37.1]	36.8 [36.4–38]	0.438	0.661[c]
Laboratory examination					
Hemoglobin, 10^9/, Mean (SD)	131.68 ± 26.35	131.51 ± 2.33	132.23 ± 5.40	0.122	0.903[a]
RDW, fL, median (IQR)	43.2 [41.2–46.5]	42.65 [41.08–45.8]	45.6 [42.3–49.2]	2.913	**0.004[c]**
Leukocytes, 10^9/L, median (IQR)	11.39 [9.05–15.13]	11.05 [8.96–14.33]	14.77 [9.63–17.58]	1.887	0.059[c]
Platelets, 10^9/L, median (IQR)	188 [131–228.5]	189.5 [130.75–229]	176 [135–226]	0.457	0.647[c]
Neutrophils, 10^9/L, median (IQR)	10.2 [8.34–13.79]	9.76 [8.13–13.21]	12.38 [9.44–16.04]	2.645	**0.008[c]**
Lymphocyte, 10^9/L, median (IQR)	0.88 [0.63–1.39]	0.88 [0.62–1.32]	0.99 [0.64–1.44]	0.266	0.790[c]
Monocyte, 10^9/L, median (IQR)	0.58 [0.36–0.77]	0.52 [0.35–0.68]	0.73 [0.46–1.07]	2.948	**0.005[c]**
PCT, median (IQR)	0.33 [0.12–1.20]	0.28 [0.1–0.76]	0.71 [0.28–1.39]	2.926	**0.003[c]**
CRP, median (IQR)	32.8 [14.8–73.5]	31.7 [14.5–66.5]	56.4 [18.3–111]	2.393	**0.017[c]**
Albumin, g/L, Mean (SD)	38.7 [33.6–43.1]	38.49 ± 0.60	37.71 ± 1.25	0.612	0.542[a]
SII, median (IQR)	2126 [1266.90–3457.55]	2126.47 [1246.92–3467.35]	2421.69 [1333.38–3451.57]	0.832	0.406[c]
NLR, median (IQR)	12.36 [7.21–18.41]	11.82 [7.14–17.75]	13.92 [9.03–20.51]	1.308	0.191[c]
PLR, median (IQR)	193.08 [128.50–280.44]	194.09 [135.89–282.70]	193.8 [118.33–253.85]	0.571	0.568[c]
NAR, median (IQR)	0.28 [0.22–0.36]	0.27 [0.21–0.34]	0.34 [0.25–0.43]	2.758	**0.006[c]**
PIV, median (IQR)	1113.98 [576.48–2321.08]	951.54 [547.66–1912.91]	1637.55 [760.29–3757.63]	2.481	**0.013[c]**
Length of ICU stay (day)	4 [0–15]	4 [0–16]	4 [1–14]	0.602	0.547[c]
Length of hospital stay (day)	7 [3.5–19]	8 [4–20]	5 [3–13]	2.013	0.044[c]

SD: Standard deviation; GCS: Glasgow Coma Scale; BMI: Body Mass Index; IQR: Interquartile range; RDW: Red blood cell distribution width; PCT: Procalcitonin; CRP: C-reactive protein; SII: Systemic immune-inflammation index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NAR: Neutrophil-to-albumin ratio; PIV: Pan-immuno-inflammatory value; The bold values indicated was considered statistically significant

[a] Independent sample *t*-test; [b] χ2 test; [c] Mann–Whitney U-test

We assessed the correlation between various composite indicators of inflammation by using Spearman correlation analysis. The outcomes demonstrated that there was some correlation between the other indicators with the exception of the insignificant correlation between PLR and NAR (Fig. 2). Consequently, we will refrain from incorporating the indicators possessing strong correlation coefficients into the same regression model while conducting multivariate analyze subsequently. We proceeded to investigate the predictive efficacy of these metrics of IVH patients by using univariate and multivariate analyses.

First of all, the patients were classified into two groups based on their mRS scores: those with good outcome ($n = 43$) and those with poor outcome ($n = 102$) (Table 2). Patients in the poor outcome group were older on average ($p < 0.001$) and had notably lower GCS scores at admission ($p < 0.001$). Furthermore, the poor outcome group showed a significantly higher prevalence of hypertension ($p = 0.039$). The poor outcome group had a lower lymphocyte count ($p = 0.012$) and albumin level ($p = 0.001$) in comparison to the good outcome group, whereas the proportion of patients who contracted pneumonia during their hospitalization was significantly higher ($p < 0.001$). Additionally, the poor outcome group exhibited significantly higher red blood cell distribution width (RDW) ($p = 0.003$) and neutrophil count ($p = 0.002$). In this study, we focused on several inflammatory composite

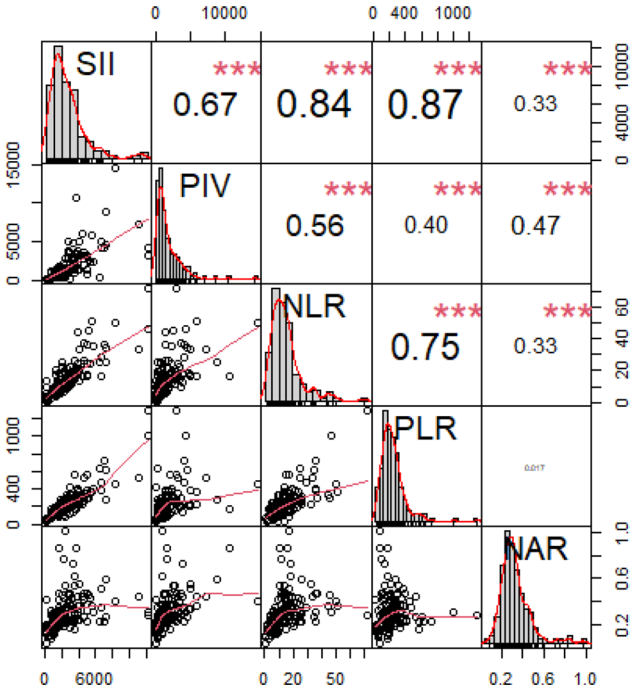

Fig. 2 The schematic diagram of correlation coefficient. SII: Systemic immune-inflammation index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NAR: Neutrophil-to-albumin ratio; PIV: Pan-immuno-inflammatory value

indicators. Patients categorized in the group with a poor outcome exhibited a significantly higher SII ($p = 0.004$), NLR ($p < 0.001$), PLR ($p = 0.035$), NAR ($p < 0.001$), and PIV ($p = 0,027$) in comparison to their counterparts in the group with a good outcome. Furthermore, we investigated the diagnostic efficacy of five composite markers for adverse outcomes in IVH patients by employing ROC curve analysis. Our findings demonstrate that while all five composites were proved in diagnosing unfavorable outcomes in IVH patients, NAR (AUC = 0.713) demonstrated more superior diagnostic potential (Fig. 3).

Next, to eliminate confounding factors from the analysis, we incorporated variables with a significance level of $p < 0.1$ in a multifactorial logistic regression model while including baseline factors like age, gender, and BMI. Moreover, the composite indicators of inflammation were included separately in the same regression model to evaluate their capacity to predict an adverse prognosis (Supplementary Table 1). Due to the small fluctuations in NAR, the use of NAR as a continuous variable in multifactor logistic regression analyses may result in unusually significant ORs (Supplementary Table 1). Therefore, we categorized patients into high and low NAR groups based on the cut-off values (0.235) obtained from the ROC curves and included NAR as a categorical variable in the model. The results showed that age (OR = 1.027, 95% CI, 1.001–1.054, $P = 0.040$) and NAR (OR = 3.653, 95% CI, 1.418–9.408, $P = 0.007$) are independent predictors of poor prognosis in IVH patients following the exclusion of confounding factors (Table 3).

Chronic hydrocephalus is a frequent and crucial complication in patients experiencing intraventricular hemorrhage [5, 7]. Therefore, we investigate the risk factors that predict the emergence of chronic hydrocephalus in surviving IVH patients. We divided the surviving patients ($n = 110$) into chronic hydrocephalus group ($n = 36$) and non-chronic hydrocephalus group ($n = 74$) based on the 6-month follow-up results. Patients in the non-chronic hydrocephalus group had a higher prevalence of diabetes mellitus ($P = 0.020$), lower RDW ($P = 0.021$) and higher albumin levels ($P < 0.001$). In a comparison of several composite inflammatory indices, patients in the chronic hydrocephalus group demonstrated significantly higher NAR ($P = 0.003$) levels compared to the non-chronic hydrocephalus group, while there were no significant differences in SII, PIV, NLR, and PLR indices (Table 4). Similarly, we analyzed the diagnostic performance of five composite markers and albumin levels for chronic hydrocephalus in IVH patients by ROC curves. The results showed that albumin and NAR had good diagnostic performance in diagnosing the development of chronic hydrocephalus in IVH patients while albumin had more superior diagnostic potential (Fig. 4).

Similarly, we integrated variables that reached a significance level of $p < 0.1$ into a multifactorial logistic regression model, in conjunction with baseline factors such as age, gender, and BMI. We converted NAR into a categorical variable using cut-off values (0.249) from the ROC curve. Subsequently, we separately included NAR and albumin in the same regression model (Supplementary Table 2). Our results suggest that albumin (OR = 0.829, 95% CI, 0.757–0.907, $P < 0.001$) is an independent predictor of chronic hydrocephalus in IVH patients after elimination of confounding factors (Table 5).

Discussion

Our study discovered that age, GCS score on admission, RDW, SII, NLR, PLR, NAR, PIV, albumin, leukocyte, neutrophil and lymphocyte counts were significantly associated with poor prognosis in patients with IVH. The prevalence of hypertension and pulmonary infections was significantly higher in the poor prognosis group than that in the good prognosis group. Among the significantly higher factors, age and NAR were independent risk factors for poor prognosis in the multifactorial analysis. Furthermore, our findings indicate that age, RDW, NAR, and albumin count are significantly associated with the occurrence of PHH in IVH patients. Notably, albumin was identified as an independent risk factor for the development of PHH in multifactorial analysis.

Studies have shown that ICH or IVH induce an inflammatory response in the local brain tissue, which includes

Table 2 Comparison of demographic, clinical, and laboratory characteristics between patients with and without poor outcome

Demographic	Poor outcome($n=102$)	Good outcome($n=43$)	t/x2/z	*p*-value
Demographic				
Age, years, Mean (SD)	56.27 ± 17.01	41.08 ± 24.30	3.731	**< 0.001**[a]
Gender, male, n (%)	77 (75.5%)	26 (60.5%)	3.319	0.068[b]
Clinical characteristics				
Hypertension, n (%)	64 (62.7%)	19 (44.2%)	4.257	**0.039**[b]
Diabetes, n (%)	16 (15.7%)	2 (4.7%)	3.388	0.066[b]
Pulmonary infection, n (%)	81 (79.4%)	20 (46.5%)	15.490	**< 0.001**[b]
GCS score, median (IQR)	5 [3–11]	13 [5–15]	4.130	**< 0.001**[c]
BMI, kg/m_2, Mean (SD)	24.23 ± 3.63	23.11 ± 4.29	1.751	0.080[a]
Temperature, ℃, median (IQR)	36.8 [36.5–37.33]	36.6 [36.4–36.9]	1.463	0.143[c]
Laboratory examination				
Hemoglobin, 10^9/, Mean (SD)	132.63 ± 27.79	129.44 ± 22.70	0.664	0.508[a]
RDW, fL, median (IQR)	43.8 [41.48–46.75]	42.1 [39.1–45.5]	3.013	**0.003**[c]
Leukocytes, 10^9/L, median (IQR)	11.41 [8.86–15.54]	11.04 [9.12–14.66]	0.719	0.472[c]
Platelets, 10^9/L, Mean (SD)	181.44 ± 66.03	196.16 ± 86.84	0.957	0.339[a]
Neutrophils, 10^9/L, median (IQR)	11.21 [8.78–14.71]	8.78 [6.53–12.67]	3.080	**0.002**[c]
Lymphocyte, 10^9/L, median (IQR)	0.85 [0.60–1.26]	1.08 [0.78–1.94]	2.520	**0.012**[c]
Monocyte, 10^9/L, median (IQR)	0.57 [0.35–0.79]	0.58 [0.41–0.71]	0.024	0.981[c]
PCT, median (IQR)	0.34 [0.12–1.24]	0.31 [0.09–0.83]	0.652	0.515[c]
CRP, median (IQR)	34.75 [16.08–74.4]	27.8 [11.80–66.90]	1.082	0.279[c]
Albumin, g/L, Mean (SD)	37.17 ± 6.73	40.99 ± 5.30	3.309	**0.001**[a]
SII, median (IQR)	2327.30 [1501.30–3742.46]	1362.48 [803.30–3140.66]	3.017	**0.004**[c]
NLR, median (IQR)	14.25 [9.57–19.23]	7.13 [5.31–15.13]	3.857	**< 0.001**[c]
PLR, median (IQR)	206.86 [138.97–283.52]	149.49 [101.35–263.75]	2.110	**0.035**[c]
NAR, median (IQR)	0.29 [0.24–0.41]	0.23 [0.17–0.31]	4.048	**< 0.001**[c]
PIV, median (IQR)	1233.83 [587.59–2711.95]	856.59 [450.58–1453.95]	2.212	0.027[c]

SD: Standard deviation; GCS: Glasgow Coma Scale; BMI: Body Mass Index; IQR: Interquartile range; RDW: Red blood cell distribution width; PCT: Procalcitonin; CRP: C-reactive protein; SII: Systemic immune-inflammation index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NAR: Neutrophil-to-albumin ratio; PIV: Pan-immuno-inflammatory value; The bold values indicated was considered statistically significant

[a] independent sample *t*-test; [b] χ2 test; [c] nonparametric rank-sum test

the release of cytokines, chemokines, and inflammatory mediators, as well as leukocyte infiltration [14, 15]. The inflammatory response disrupts the blood-brain barrier, exacerbating neuronal damage. ICH and IVH can also activate the immune system, leading to a systemic inflammatory response [16]. Immune cells, such as neutrophils, monocytes, macrophages and microglia, are mobilized to the brain and enter brain tissue by crossing the damaged blood-brain barrier [8]. These cells release large amounts of oxygen free radicals and enzymes, causing damage to neurons and glial cells [17]. Moreover, cerebral and ventricular hemorrhages may trigger an autoimmune response [5]. The inflammatory and immune response following cerebral and ventricular hemorrhage is a complex pathophysiological process involving multiple cellular and molecular interactions. Our study examined whether indicators of compound inflammation can be used to predict the prognosis of patients with IVH.

Neutrophils are widely recognized as a vital line of defense for the body's immune system, and they play a crucial role in stimulating angiogenesis, cytogenesis, antiviral defense, and regulating the immune response [18]. In recent years, composite indicators of inflammatory based on neutrophil have garnered increasing attention for its predictive value in the prognosis of various diseases [19, 20]. Neutrophils, as the primary effectors in acute inflammation, typically increase in number in response to injury or infection. In contrast, lymphocytes play a critical role in immune regulation and exert anti-inflammatory effects. Consequently, an elevated NLR reflects a relative increase in neutrophils accompanied by a decrease in lymphocytes, suggesting an imbalanced and persistent inflammatory state. This imbalance may contribute to additional neuronal injury, thereby exacerbating both local and systemic inflammatory responses and impairing neural recovery [21]. Moreover, the release of inflammatory mediators, such as cytokines and chemokines, can compromise the integrity of the blood-brain barrier, permitting harmful substances to infiltrate brain tissue [22]. Such processes may trigger or aggravate brain edema, promote neuronal apoptosis, and lead to secondary damage, ultimately detrimentally affecting patient prognosis [23]. The NLR is a simple and easily accessible biomarker that has been widely used to evaluate

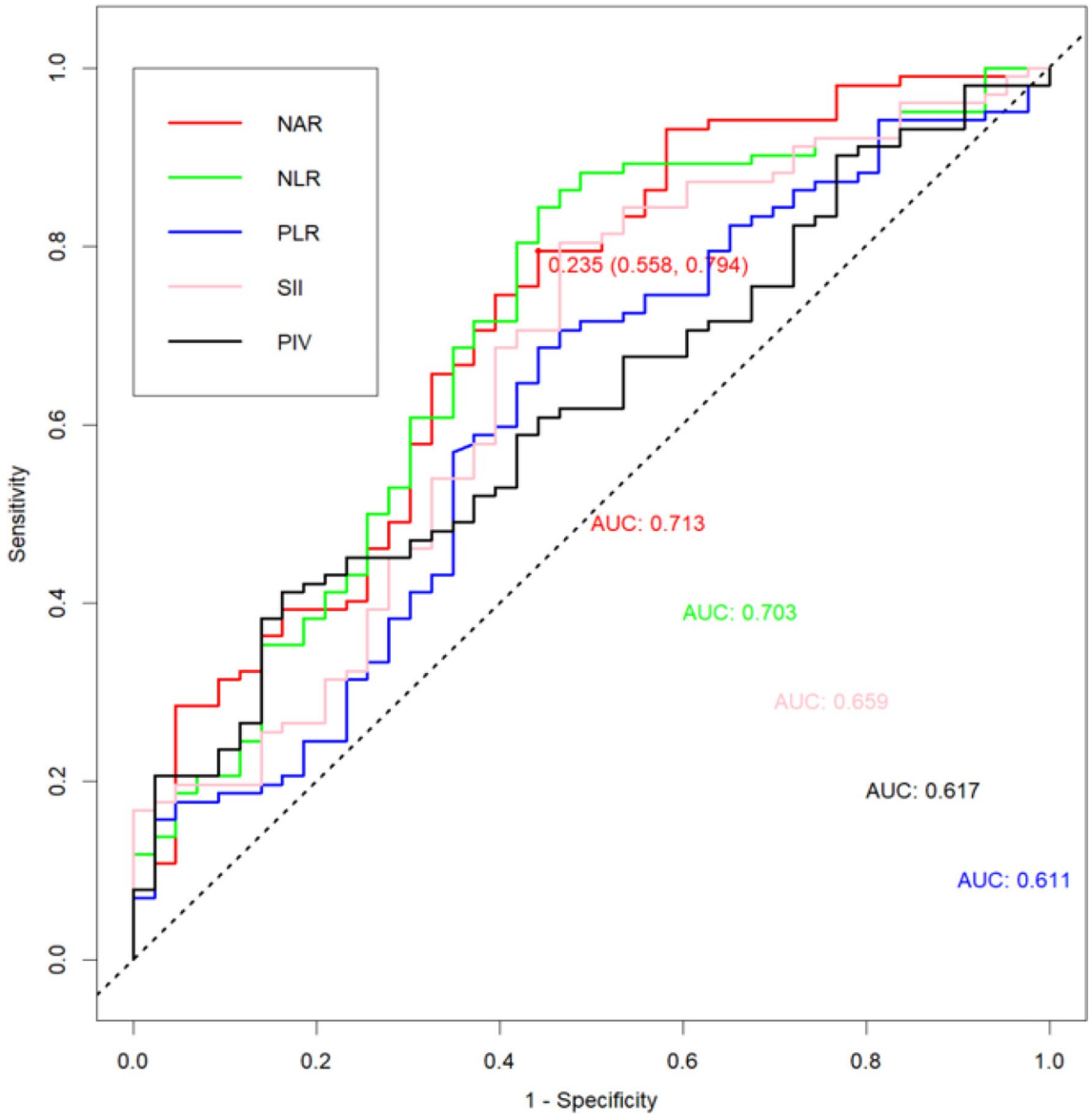

Fig. 3 ROC curve of NAR, NLR, PLR, SII and PIV diagnosis of poor prognosis at IVH patient admission. NAR, neutrophil-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte; SII, systemic immune-inflammation index; PIV: pan-immuno-inflammatory value; AUC: area under curve

inflammation and immune responses in various diseases. Studies have shown that NLR may be a useful predictor of disease severity, outcome, and prognosis in patients with stroke, including both ischemic and hemorrhagic strokes [24–26]. PLR reflects coagulation and inflammatory pathways [27]. It has been shown to be an independent risk factor for a hyperinflammatory process [28]. Some studies have reported a correlation between PLR and the prognosis of patients with cerebral hemorrhage [29–31]. The SII and PIV can assess the level of systemic inflammation, autoimmune diseases and cancer [32, 33]. For example, high levels of SII or PIV may indicate a more severe inflammatory response in patients with advanced melanoma, which could provide information about prognosis or response to therapy [34]. NAR is a biomarker that has been found to be associated with the severity and outcomes of hemorrhagic stroke [35, 36]. NAR integrates neutrophil count and albumin levels, serving as an indicator of both the degree of inflammation and the patient's nutritional status and protein reserves [37]. It can be easily obtained from routine blood tests, making it a convenient and cost-effective tool for risk stratification in these patients. However, more research is needed to confirm its clinical utility and establish optimal cut-off values. These studies emphasize the significance of inflammatory markers in predicting the prognosis of patients with intraventricular hemorrhage. In this study, we assessed the capacity of these metrics to

Table 3 Multivariable logistic regression models of IVH for predicting poor outcome

Variable	Odds Ratio	95% Confidence Interval [25%, 75%]	*p*-value
Gender	1.562	[0.602–4.054]	0.359
Age	1.027	[1.001–1.054]	**0.040**
BMI	0.962	[0.851–1.087]	0.536
Hypertension	0.914	[0.335–2.496]	0.860
Diabetes	0.414	[0.076–2.251]	0.307
Pulmonary infection	0.593	[0.234–1.499]	0.269
RDW	1.112	[0.988–1.251]	0.079
GCS score	0.933	[0.849–1.025]	0.150
Lymphocyte	1.187	[0.775–1.819]	0.430
NAR	3.653	[1.418–9.408]	0.007

BMI: Body Mass Index; RDW: Red blood cell Distribution Width; GCS: Glasgow Coma Scale; NAR: Neutrophil-to-Albumin Ratio; The bold values indicated was considered statistically significant

track the prognosis of IVH patients and found that NAR is an independent risk factor for poor outcomes in IVH patients. Furthermore, we present a validated threshold for NAR that enables effective prognosis prediction for patients with IVH. These findings align broadly with previous research [20].

PHH is a frequent complication following subarachnoid hemorrhage or IVH. It was previously believed that the hematoma caused by the hemorrhage obstructed the normal circulation and absorption of cerebrospinal fluid (CSF), leading to the accumulation of CSF inside the ventricles and the development of hydrocephalus [3, 4]. However, recent studies have demonstrated that inflammation plays a crucial role in the development of hydrocephalus following hemorrhage [38, 39]. To our knowledge, there has been insufficient investigation into the relationship between inflammatory markers and concomitant PHH in IVH patients. Albumin not only serves as a nutritional marker but also functions as an antioxidant, anti-inflammatory agent, and a key factor in maintaining vascular endothelial integrity [40]. A reduction in albumin levels may impair its ability to neutralize inflammatory mediators, thereby contributing to prolonged blood-brain barrier disruption and inflammatory damage to neural tissue. Additionally, low albumin concentrations

Table 4 Comparison of demographic, clinical, and laboratory characteristics between survival patients with and without chronic hydrocephalus

Demographic	Chronic hydrocephalus (*n* = 36)	Non-chronic hydrocephalus (*n* = 74)	|t|/|x2|/|z|	*p*-value
Demographic				
Age, years, Mean (SD)	52.11 ± 15.26	49.42 ± 24.00	0.712	0.478[a]
Gender, male, n (%)	26 (72.2%)	50 (67.6%)	0.246	0.620[b]
Clinical characteristics				
Hypertension, n (%)	24 (66.7%)	41 (55.4%)	1.271	0.260[b]
Diabetes, n (%)	2 (5.6%)	10 (13.5%)	21.09	**0.020[b]**
Pulmonary infection, n (%)	23 (63.9%)	43 (58.1%)	0.337	0.561[b]
GCS score, median (IQR)	7 [4–13.75]	9 [5–15]	1.586	0.113[c]
BMI, kg/m_2, Mean (SD)	24.61 ± 3.80	23.73 ± 4.27	1.051	0.296[a]
Temperature, ℃, median (IQR)	36.8 [36.5–37.08]	36.7 [36.5–37.03]	0.409	0.683[c]
Laboratory examination				
Hemoglobin, 10^9/, Mean (SD)	128.28 ± 27.80	133.08 ± 22.73	0.965	0.337[a]
RDW, fL, median (IQR)	44.4 [41.9–47.85]	42.5 [40.1–44.93]	2.313	**0.021[c]**
Leukocytes, 10^9/L, median (IQR)	11.71 [9.22–18.28]	10.80 [8.78–13.32]	1.207	0.227[c]
Platelets, 10^9/L, Mean (SD)	178.22 ± 64.61	192.39 ± 79.67	0.928	0.355[a]
Neutrophils, 10^9/L, median (IQR)	10.25 [8.08–15.21]	9.74 [7.94–12.48]	0.997	0.319[c]
Lymphocyte, 10^9/L, median (IQR)	0.9 [0.68–1.45]	0.85 [0.61–1.32]	0.522	0.601[c]
Monocyte, 10^9/L, median (IQR)	0.55 [0.35–0.80]	0.5 [0.35–0.65]	0.841	0.400[c]
PCT, median (IQR)	0.2 [0.08–0.41]	0.27 [0.09–0.75]	0.653	0.514[c]
CRP, median (IQR)	34.65 [14.4–72.68]	29.75 [13.48–59.87]	0.376	0.707[c]
Albumin, g/L, Mean (SD)	34.24 ± 5.39	40.55 ± 5.66	5.574	**< 0.001[a]**
SII, median (IQR)	2177.93 [1520.06–3209.83]	1828.28 [1210.99–3650.16]	0.261	0.794[c]
NLR, median (IQR)	12.63 [8.38–19.00]	11.30 [6.63–17.49]	0.675	0.500[c]
PLR, median (IQR)	213.89 [119.06–273.00]	190.23 [135.89–321.25]	0.268	0.789[c]
NAR, median (IQR)	0.30 [0.24–0.42]	0.24 [0.19–0.31]	2.994	**0.003[c]**
PIV, median (IQR)	1153.26 [567.93–1916.60]	920.21 [493.10–1910.25]	0.541	0.588[c]

SD: Standard deviation; GCS: Glasgow Coma Scale; BMI: Body Mass Index; IQR: Interquartile range; RDW: Red blood cell distribution width; PCT: Procalcitonin; CRP: C-reactive protein; SII: Systemic immune-inflammation index; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; NAR: Neutrophil-to-albumin ratio; PIV: Pan-immuno-inflammatory value; The bold values indicated was considered statistically significant

a independent sample t-test; b χ2 test; c nonparametric rank-sum test

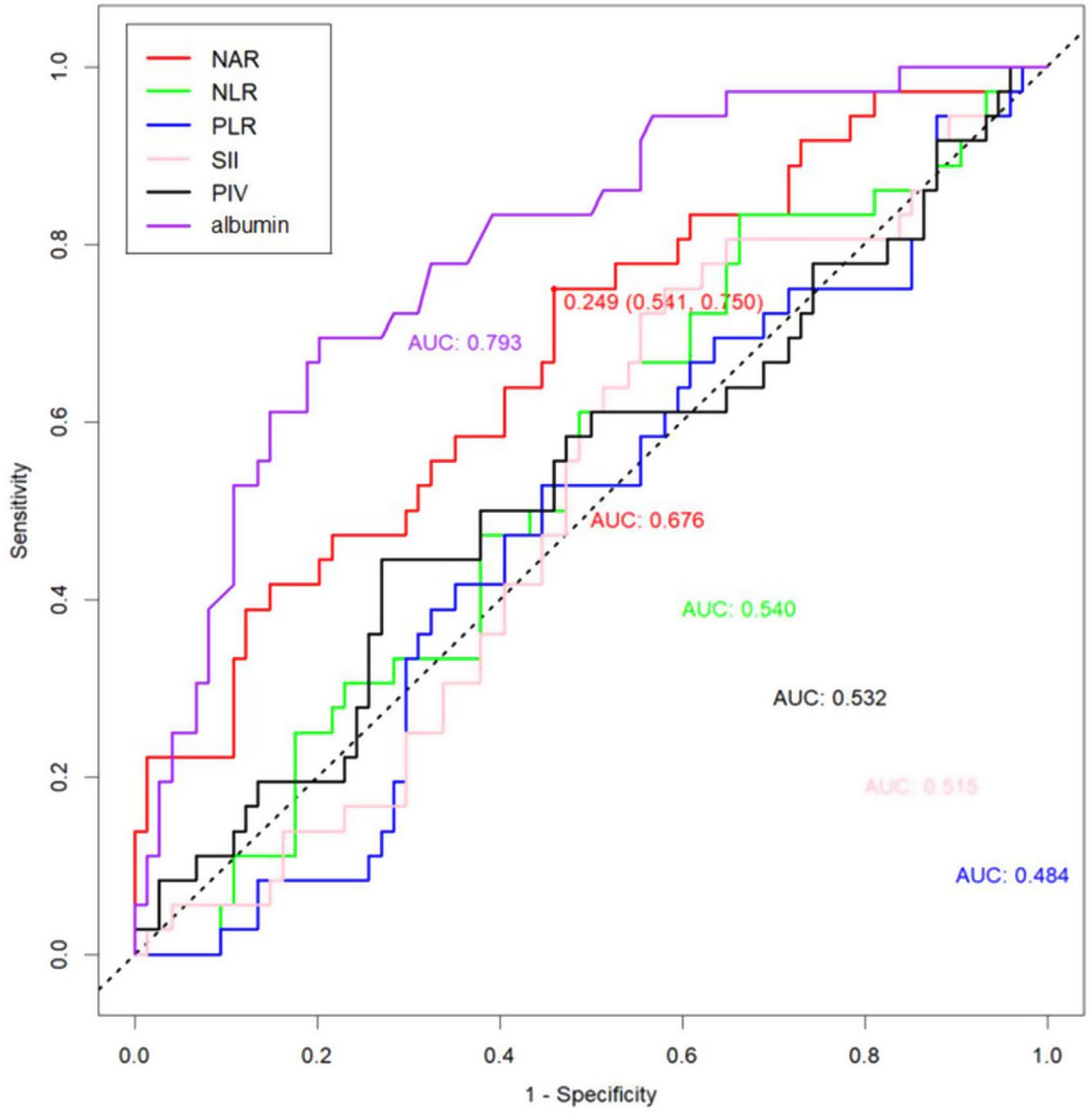

Fig. 4 ROC curve of NAR, NLR, PLR, SII, PIV and albumin diagnosis of PHH at IVH patient admission. NAR, neutrophil-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte; SII, systemic immune-inflammation index; PIV: pan-immuno-inflammatory value; AUC: area under curve

Table 5 Multivariable logistic regression models of IVH for predicting chronic hydrocephalus in survival patients

Variable	Odds Ratio	95% Confidence Interval [25%, 75%]	*p*-value
Gender	0.905	[0.309–2.650]	0.855
Age	0.995	[0.970–1.020]	0.690
BMI	1.027	[0.905–1.166]	0.680
RDW	1.051	[0.944–1.169]	0.363
Albumin	0.829	[0.757–0.907]	< 0.001

BMI: Body Mass Index; RDW: Red blood cell Distribution Width; The bold values indicated was considered statistically significant

can reflect an insufficient capacity to counteract inflammation and repair the blood-brain barrier, which may lead to a more persistent inflammatory response and further neuronal injury. Moreover, decreased albumin levels can increase vascular permeability, exacerbating local edema and potentially promoting ventricular fibrosis and cerebrospinal fluid circulation disorders through various pathways after IVH, ultimately raising the risk of PHH [41–43]. Notably, our study is the first to demonstrate that albumin acts not only as a nutritional indicator but also as an independent predictor of PHH development in IVH patients. This finding provides new insights into the role of the post-IVH inflammatory response in the injury and repair processes of the ventricular system. Furthermore, NAR, as a composite marker, may more accurately reflect the overall inflammatory and nutritional status of patients, offering a novel approach for risk assessment of secondary hydrocephalus in IVH. Early evaluation based on albumin levels and NAR could help clinicians identify

high-risk patients with poor prognoses and implement more proactive monitoring and intervention strategies. Our study has several limitations. Firstly, its design as a single-center may have introduced unwanted bias and data deficiencies. Potential biases could arise from: The demographic characteristics (e.g., ethnicity, socioeconomic status) and local healthcare practices at our center may differ from other regions; Management strategies for intraventricular hemorrhage (e.g., surgical intervention timing, laboratory testing protocols) at our institution might not reflect practices in other centers; Retrospective data collection may miss eligible patients with incomplete records. Secondly, data were partially lost during follow-up. Future large-scale prospective studies are warranted as well as more rigorous clinical follow-up. We are collaborating with other neurosurgical centers to conduct a prospective multicenter study, enrolling patients from diverse geographic and socioeconomic backgrounds; We will further validate the predictive value of NLR, NAR, and albumin, along with emerging biomarkers such as IL-6, in a larger, independent cohort; Furthermore, in future studies, we will perform stratified analyses by patient characteristics (e.g., age, hemorrhage volume, treatment modalities) to refine the clinical utility of these markers.

Conclusion

NLR and NAR are independent risk factors for poor prognosis in IVH patients. Additionally, albumin is an independent predictor of chronic hydrocephalus development within 3 months in IVH patients.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions
H-Wang: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – reviewing and editing. Y-Li: Data curation, Formal analysis, Investigation, Resources, Software, Writing – Original Draft Preparation. F-Ye: Data curation, Formal analysis, Software, Writing – Original Draft Preparation. Z-Deng: Data curation, Formal analysis, Investigation, Validation, Writing – reviewing and editing. K-Huang: Investigation, Methodology, Validation, Writing – reviewing and editing. G-Li: Conceptualization, Supervision, Writing – Original Draft Preparation. Y-Chen: Investigation, Methodology, Supervision, Writing – Original Draft Preparation. Y-Liu: Conceptualization, Supervision, Writing – reviewing and editing. L-Zhou: Investigation, Methodology, Validation, Writing – reviewing and editing.

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Data availability
This study strictly follows the terms of the Ethics Committee of West China Hospital of Sichuan University and respects patient privacy. The dataset used and analyzed during this study is available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Biomedical Ethics Committee of West China Hospital of Sichuan University (No.2023442). Informed consent was waived due to the retrospective nature of this study (the Ethics Committee of the Biomedical Ethics Committee of West China Hospital of Sichuan University). The study was conducted in accordance with the declaration of Helsink.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Neurosurgery, West China Medical School, West China Hospital, Sichuan University, Chengdu, China
[2]Department of Pediatric Neurosurgery, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China

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