MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 4413-4420
DOI: 10.12659/MSM.910845

Received: 2018.04.27
Accepted: 2018.06.03
Published: 2018.06.27

Platelet-to-Lymphocyte Ratio as a New Predictive Index of Neurological Outcomes in Patients with Acute Intracranial Hemorrhage: A Retrospective Study

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Manuscript Preparation E
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Source of support: Departmental sources

Background: Systemic inflammation plays a critical role in the pathophysiological process of intracranial hemorrhage (ICH). Recently, the platelet-to-lymphocyte ratio (PLR) has become a research focus that indicates inflammation in various diseases. Thus, this study aimed to investigate the predictive value of PLR in patients with acute ICH.

Material/Methods: This study was performed in a single teaching hospital. Glasgow coma scale at hospital discharge (GCS_{dis}) and modified Rankin score (MRS) at 6 months were recorded as short-term and long-term neurological outcomes. Ordered and binary logistic regression methods were used to explore the associations.

Results: Finally, data on 183 ICH patients were included. A knot of PLR around 100 was detected and applied in the extended ordered logistic regression models. For PLR >100, PLR on ICU admission was significantly associated with worse GCS_{dis} (from Model 1: OR: 1.004, 95% CI 1.001–1.007 to Model 4: OR: 1.006, 95% CI 1.002–1.009) while the PLR on Emergency Department (ED) admission was insignificant. For PLR ≤100, neither the PLR on ICU or ED admission was associated with GCS_{dis} level. In the quartile grouping analysis, PLR Q2 was used as a reference level. Both Q3 and Q4 on ICU admission were significantly associated with lower GCS_{dis} level (OR, 3.30; 95%CI 1.38–7.88; and OR, 3.79; 95%CI 1.54–9.33, respectively), while Q1 was insignificant. All 4 quartiles of PLR on ED admission were not associated with GCS_{dis}.

Conclusions: Only higher PLR value on ICU admission but not on ED admission was associated with worse GCS_{dis}.

MeSH Keywords: Glasgow Coma Scale • Intracranial Hemorrhages • Lymphocyte Count • Platelet Count

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/910845

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Background

Intracranial hemorrhage (ICH) is a common subtype of stroke and is associated with extremely high morbidity and mortality. Efforts have been made to explore appropriate predictive factors for poor outcomes, including neurological outcomes and mortality, such as hyperglycemia [1], serum uric acid [2] and C-reactive protein level [3]. However, challenges remain. Studies have demonstrated that inflammatory system activation was one of the major pathological pathways contributing to ICH-induced secondary brain injury [4], such as brain edema formation [5] and hematoma enlargement [6]. Thus, identifying inflammatory indexes that can predict the prognosis of ICH patients has become a research focus.

Recently, the platelet-to-lymphocyte ratio (PLR) has emerged as a prognostic marker of inflammatory response in various conditions, such as acute pulmonary embolism [7], myocardial infarction [8] and various cancer [9]. However, the predictive value of PLR in patients with acute ICH has not been investigated. Thus, we performed this study to evaluate the prognostic value of PLR in predicting neurological outcomes in patients with acute ICH.

Material and Methods

Study population

This retrospective observational study was performed in a 20-bed Intensive Care Unit (ICU) of Dongyang People's Hospital, a tertiary teaching hospital of Wenzhou Medical University. Patients diagnosed with acute ICH who were admitted to the ICU after intracranial surgery from January 2016 to June 2017 were initially screened. Inclusion criteria were: 1) older than 18 years; 2) Glasgow coma scale (GCS) ≥4 and ≤12 on admission; and 3), emergency intracranial surgery was performed within 24 h after onset of ICH. Patients who were pregnant, lacked sufficient information for PLR calculation, or were diagnosed with aneurysmal subarachnoid hemorrhage were also excluded from this study. All patients received standard treatment according to management guidelines [10,11] and were followed up through telephone interview. Modified Rankin score (MRS) at 6 months after hospital discharge was recorded. The study was approved by the Ethics Committee of Dongyang People's Hospital and informed consent was waived due to the retrospective study design.

Data extraction

Demographic data of the included patients were extracted from the electronic medical records system. Clinical data were recorded within 24 h after ICU admission, including routine blood tests, serum biochemical indexes, comorbidities, bleeding sites, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score, were recorded on ICU admission. Clinical outcomes, including GCS at hospital discharge, MRS at 6 months after hospital discharge, ICU length of stay, and ventilation duration, were also recorded.

Outcome definition

The primary endpoint was GCS at hospital discharge (GCS_{dis}) and was divided into 3 levels: level 1: 3~8, level 2: 9~12, and level 3: 13~15. MRS at 6 months was also divided into 2 levels: favorable (0~2) and unfavorable (3~6). If a patient died within 6 months, the MRS at 6 months was recorded as 6.

Grouping methods for PLR in logistic models.

As a knot of PLR (around 100) was detected using Lowess smoother technique, linear spline function (PLR ≤100 and PLR >100) was initially applied in ordered logistic regression models. For better interpretation, quartile grouping method of PLR was also used in multivariate logistic regression models, using PLR quartile 2 as the reference level.

Missing data management

The percentages of most missing variables were less than 3% and were simply replaced by the mean value. More than 20% of C-reactive protein was missing and was not imputed.

Statistical analysis

Continuous data were expressed as mean ±SD or median (interquartile range). The variance analysis or Kruskal–Wallis test was used as appropriate. Categorical data were expressed as percent and compared using the χ^2 test. GCS_{dis} was divided into 3 levels (level 1: 3~8, level 2: 9~12, and level 3: 13~15) and ordered logistic regression method was applied. MRS was divided into 2 levels (favorable (0~2) and unfavorable (3~6)), and ordinary logistic regression was applied. Grouping methods of PLR were described in the method section. As we aimed at adjusting for potential confounding factors, either clinically important or statistically significant variables were including in the logistic models. In order to achieve a robust conclusion, an extended model approach was used and is presented in Table 1: Model 2=Model 1+age, diabetes mellitus, hypertension. Model 3=Model 2+(bleeding sites). Model 4=Model 3+(serum sodium, hospital acquired pneumonia, APACHE II score on ICU admission). Multi-collinearity was tested using variance inflation factor (VIF) method, with VIF ≥5 indicating multi-collinearity existence. The two-tailed test was used, and $p<0.05$ was considered statistically significant. All statistical analyses were performed using STATA 11.2 software (College Station, TX, USA).

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Table 1. Extended ordered logistic regressions of PLRs on ER/ICU admission using linear spline function.

ER admission	PLR (≤100)		PLR (>100)		ICU admission	PLR (≤100)		PLR (>100)	
	OR (95% CI)	p	OR (95% CI)	p		OR (95% CI)	p	OR (95% CI)	p
Model 1	1.007 (0.99–1.02)	0.306	0.99 (0.98–1.00)	0.429	Model 1	0.986 (0.96–1.00)	0.145	1.004 (1.001–1.007)	0.002
Model 2	1.005 (0.99–1.02)	0.448	0.99 (0.99–1.00)	0.490	Model 2	0.989 (0.97–1.00)	0.253	1.005 (1.001–1.008)	0.002
Model 3	1.001 (0.99–1.02)	0.417	0.99 (0.99–1.00)	0.583	Model 3	0.989 (0.97–1.00)	0.270	1.005 (1.002–1.008)	0.001
Model 4	1.005 (0.99–1.02)	0.450	0.99 (0.99–1.00)	0.879	Model 4	0.994 (0.97–1.01)	0.575	1.006 (1.002–1.009)	0.001

Ordered GCS scores (level one: 3–8, level two: 9–12, level three: 13–15) at hospital discharge was used as the dependent variable in all logistic models. Different associations between GCS score and PLR on ER/ICU admission were explored. Crude odds ratio was listed in model 1. Adjusted covariates: Model 2= age, diabetes mellitus, hypertension. Model 3= Model 2 + (bleeding sites). Model4= Model 3 + (serum sodium, hospital acquired pneumonia, APACHE II score on ICU admission). GCS – Glasgow Coma Scale; PLR – platelet to lymphocyte ratio; ER – Rmergency Room; ICU – Intensive Care Unit; OR – odds ratio; CI – confidence interval.

Results

Baseline characteristics

Finally, data on 183 patients with acute ICH were included in this study after screening (Figure 1), and the demographic characteristics within 3 GCS_{dis} levels are compared in Table 2. Patients with high GCS_{dis} were significantly younger than those with low GCS_{dis} (59.9±15.1 *vs.* 51.0±14.8 *vs.* 48.5±13.7, p<0.001). Compared to patients with low GCS_{dis}, the PLR on ICU admission (291.0±363.9 *vs.* 177.3±103.5 *vs.* 165.5±83.4, p=0.002) but not the PLR on ED admission (137.5±91.3 *vs.* 154.2±140.3 *vs.* 147.3±144.1, p=0.794) was significantly lower in patients with high GCS_{dis} level. However, the crude comparisons of platelet count and lymphocyte count on ED or ICU admission were insignificant.

Crude comparisons within 4 PLR quartiles

Platelet count was significantly increased (from Q1 128.7±50.7 to Q4 190.0±51.7, p<0.001) while lymphocyte count was decreased stepwise (from Q1 1.97±1.07 to Q4 0.56±0.21, p<0.001) with increasing quartiles of PLR in Table 3. In this crude comparison, PLR Q2 was associated with highest GCS_{dis} (13 (10–15)) and lowest percent (n=21 (45.6%)) of patients with MRS ≥3.

Association between PLR and short-term GCS_{dis}

A knot around 100 of PLR on ICU admission was detected in the Lowess smoother curve between PLR and GCS_{dis} in Figure 2. Thus, in the extended ordered logistic models (Table 1), linear spline function was applied using the cut-off value of 100. We found that for PLR >100, only PLR value on ICU admission was

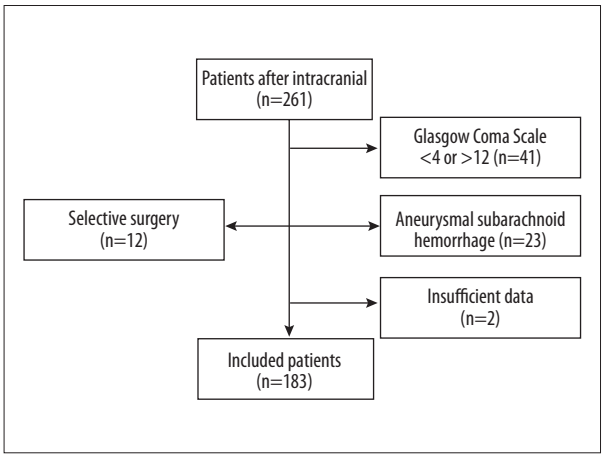

Figure 1. Flow chart of patient selection.

significantly associated with worse GCS_{dis} level (from Model 1: OR: 1.004, 95% CI 1.001–1.007 to Model 4: OR: 1.006, 95% CI 1.002–1.009) while the PLR value on ED admission was insignificant in all 4 extended logistic models. For PLR ≤100, neither the PLR on ICU admission nor the PLR on ED admission were associated with GCS_{dis} level. For better interpretation, quartile method was also applied for PLR and Q2 was used as the reference level (Table 4). The conclusion was similar. High PLR (Q3 and Q4) level on ICU admission was significantly associated with lower GCS_{dis} level (OR, 3.30; 95%CI 1.38–7.88; and OR, 3.79; 95%CI 1.54–9.33, respectively) while low PLR (Q1) was insignificant. None of the 4 quartiles of PLR on ED admission were associated with GCS_{dis} level.

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Table 2. Baseline characteristic comparisons within three GCS categories at hospital discharge.

Variables	3≤ GCS ≤8 (n=48)	9≤ GCS ≤12 (n=69)	13≤ GCS ≤15 (n=66)	p
Age (years)	59.9±15.1	51.0±14.8	48.5±13.7	< 0.001
Gender (male) [n (%)]	28 (58.3)	44 (63.7)	45 (68.1)	0.557
Alcohol drinking [n (%)]	4 (8.3)	14 (29.1)	18 (26.1)	0.042
Smoking [n (%)]	12 (25.0)	18 (26.1)	19 (27.5)	0.891
Comorbidities				
Hypertension [n (%)]	29 (50.0)	34 (49.2)	27 (39.1)	0.121
Diabetes mellitus [n (%)]	2 (4.1)	3 (4.3)	3 (4.5)	0.995
Cardiac disease [n (%)]	3 (6.2)	3 (4.3)	4 (6.1)	0.874
Kidney disease [n (%)]	6 (12.5)	5 (7.2)	3 (4.5)	0.284
Liver disease [n (%)]	1 (2.1)	11 (15.9)	8 (12.1)	0.057
Bleeding sites				
Basalganglia [n (%)]	11 (22.9)	21 (30.4)	16 (24.2)	0.595
Frontal lobe [n (%)]	15 (31.2)	22 (31.8)	16 (24.2)	0.570
Parietal lobe [n (%)]	9 (18.7)	9 (13.0)	8 (12.1)	0.570
Temperal lobe [n (%)]	20 (41.6)	25 (36.2)	19 (28.7)	0.349
Epidural hemorrhage [n (%)]	3 (6.2)	8 (11.6)	11 (16.7)	0.238
Subdural hemorrhage [n (%)]	15 (31.2)	14 (20.2)	9 (13.6)	0.072
Trauma [n (%)]	25 (52.1)	36 (52.1)	32 (48.5)	0.893
Blood loss during surgery (ml)	230.4±201.8	211.9±147.3	202.9±202.7	0.730
Fluid input/output				
Fluid intake (ml/24 hr)	4527±2750	3873±1783	3935±1712	0.195
Fluid balance (ml/24 hr)	715±2298	518±1780	310±1736	0.533
Disease severity scores				
APACHE II on ICU admission [median (IQR)]	23 (20–27)	18 (16–21)	16 (12–19)	< 0.001
GCS on admission [median (IQR)]	5 (4–7)	7 (6–9)	10 (8–12)	< 0.001
Outcomes on ER admission				
Onset duration on ER admission (hour)	2.2±2.9	3.2±4.2	3.1±4.1	0.366
Platelet count (*10^9/L)	208.7±84.8	207.2±72.9	240.0±21.4	0.334
Lymphocyte count (*10^9/L)	2.36±2.05	2.15±1.60	2.46±1.69	0.529
PLR	137.5±91.3	154.2±140.3	147.3±144.1	0.794
C-reactive protein (mg/L)	9.1±22.5 (n=27)	18.9±43.7 (n=48)	18.1±33.7 (n=36)	0.499
Outcomes on ICU admission				
Platelet count (*10^9/L)	153.9±61.8	161.2±52.9	167.3±56.7	0.461
Lymphocyte count (*10^9/L)	0.91±0.91	1.24±0.84	1.20±0.59	0.064
PLR	291.0±363.9	177.3±103.5	165.5±83.4	0.002
C-reactive protein (mg/L)	84.9±50.9 (n=34)	105.0±53.1 (n=44)	76.1±52.2 (n=47)	0.030

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Table 2 continued. Baseline characteristic comparisons within three GCS categories at hospital discharge.

Variables	3≤ GCS ≤8 (n=48)	9≤ GCS ≤12 (n=69)	13≤ GCS ≤15 (n=66)	p
White blood cell (*10⁹/L)	13.1±5.1	12.3±4.3	11.8±3.6	0.268
Hemoglobin (g/L)	106.9±24.3	106.8±25.8	112.7±20.4	0.275
Serum creatinine (mmol/L)	49.8±75.8	36.4±33.8	44.9±89.9	0.478
Serum albumin (g/L)	39.2±46.2	33.2±31.8	38.7±35.6	0.506
Serum sodium (mmol/L)	139.1±4.31	135.8±16.7	137.7±3.39	0.255
Clinical outcomes				
Hospital acquired pneumonia [n (%)]	27 (56.2)	36 (52.1)	25 (37.8)	0.106
Other infection [n (%)]	4 (8.3)	3 (4.3)	4 (6.1)	0.672
ICU length of stay (days)	15.3±11.1	11.0±9.8	5.9±4.3	< 0.001
Ventilation duration (days)	13.0±11.4	3.9±3.0	2.5±2.8	< 0.001
Tracheoctomy [n (%)]	13 (27.1)	11 (15.9)	1 (1.5)	< 0.001

GCS – Glasgow Coma Scale; ER – Emergency Room; ICU – Intensive Care Unit; APACHE II– acute physiology and chronic health evaluation II; PLR – platelet to lymphocyte ratio; IQR – interquartile range.

Table 3. Comparisons of clinical outcomes within four PLR quartiles on ICU admission.

Variables	PLR Q1 (n=46)	PLR Q2 (n=46)	PLR Q3 (n=46)	PLR Q4 (n=45)	p
Platelet count (*10⁹/L)	128.7±50.7	154.5±50.8	173.5±55.7	190.0±51.7	<0.001
Lymphocyte count (*10⁹/L)	1.97±1.07	1.14±0.16	0.88±0.31	0.56±0.21	<0.001
GCS at hospital discharge [median (IQR)]	12 (9–13)	13 (10–15)	11 (8–13)	10 (7–13)	0.016
MRS ≥3 [n (%)]	25 (54.3)	21 (45.6)	25 (54.3)	26 (57.54)	0.688
ICU length of stay (days)	10.1±9.4	9.7±8.6	9.5±8.5	11.0±10.5	0.860

PLR – platelet to lymphocyte ratio; ICU – Intensive Care Unit; GCS – Glasgow Coma Scale; MRS – Modified Rankin Scale; IQR, –interquartile range.

Association between 4 PLR quartiles and long-term MRS

We found a similar but insignificant pattern between PLR quartiles on ICU admission and MRS, shown in Supplementary Table 1.

Discussion

The major findings of our study are that in patients with ICH, only high PLR value (>100) on ICU admission was significantly associated with worse GCS_{dis} while low PLR (≤100) was insignificant. A similar but insignificant pattern between PLR on ICU admission and MRS at 6 months after discharge was also found. However, the high and low PLR values on ED admission were not associated with GCS_{dis} or MRS. Further studies are needed to validate this relationship.

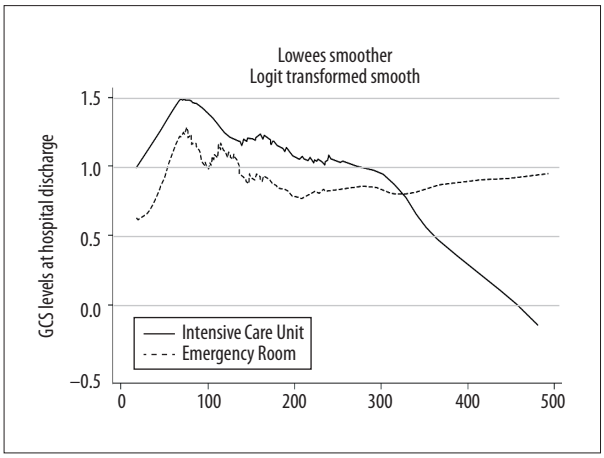

Figure 2. Crude relationship between PLRs on ED/ICU admission and GCS at hospital discharge. GCS was used as a dichotomous variable in Figure 1 (GCS ≤8 and GCS >8).

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Table 4. Ordered logistic regressions of PLR on ER/ICU admission using quartile method.

ER admission				ICU admission			
Variables	**Adjusted odds ratio**	**95% CI**	**p**	**Variables**	**Adjusted odds ratio**	**95% CI**	**p**
PLR Q1	0.72	0.31–1.67	0.459	PLR Q1	1.21	0.51–2.28	0.657
PLR Q2	Ref.	–	–	PLR Q2	Ref.	–	–
PLR Q3	1.37	0.59–3.15	0.457	PLR Q3	3.30	1.38–7.88	0.001
PLR Q4	0.77	0.33–1.77	0.541	PLR Q4	3.79	1.54–9.33	0.004
Age (>65)	1.56	0.69–3.53	0.282	Age (>65)	1.76	0.78–4.00	0.171
Diabetes mellitus	0.71	0.16–3.16	0.656	Diabetes mellitus	0.65	0.14–2.93	0.583
Hypertension	0.99	0.52–1.88	0.977	Hypertension	0.99	0.52–1.88	0.977
Extradural hemorrhage	0.47	0.17–1.27	0.141	Extradural hemorrhage	0.42	0.15–1.16	0.097
Subdural hemorrhage	2.31	1.05–5.12	0.037	Subdural hemorrhage	2.38	1.07–5.27	0.032
Serum sodium >140 mmol/L	1.78	0.90–3.51	0.096	Serum sodium >140 mmol/L	2.02	1.00–4.05	0.047
Hospital acquired pneumonia	1.73	0.96–3.14	0.067	Hospital acquired pneumonia	1.98	1.08–3.62	0.027
APACHE II score	1.19	1.11–1.27	<0.001	APACHE II score	1.21	1.13–1.29	<0.001

Ordered GCS scores (level one: 3–8, level two: 9–12, level three: 13–15) at hospital discharge was used as the dependent variable in two logistic models. PLRs on ER/ICU admission were divided into four quartiles, and the second quartile was used as the reference level. PLR – platelet to lymphocyte ratio; ER – Emergency Room; ICU – Intensive Care Unit; CI – confidence interval; APACHE – acute physiology and chronic health evaluation.

Experimental researchers have indicated that inflammatory response plays a pivotal role in the pathophysiological process of ICH. A series of complex inflammatory responses are activated after the onset of hemorrhage, such as activation of microglia [12], increased secretion of cytokine, and infiltration of neutrophils and macrophages in the injury sites [13,14], which lead to edema progression, cell death, and permanent neurological damage. A clinical study also found that in ICH patients, inflammatory response was trigged and was associated with poor outcomes such as hematoma enlargement [6]. Thus, identifying new inflammatory indexes that predict the prognosis of ICH patients has become a research focus.

Increased evidence shows that PLR is a novel inflammatory indicator in many disorders, such as atherosclerosis [15], acute kidney injury [16], and cancers [17,18]. Yang et al. reported that high PLR level (>260 *vs.* <260) was an independent predictor of venous thromboembolism in patients with cancer, and Cetin et al. found that high PLR (>151 *vs.* <151) was associated with increased long-term major adverse cardiovascular events in patients with myocardial infarction. Another study [7] included 646 patients with acute pulmonary embolism, and reported that high PLR level (>149 *vs.* <149) was significantly associated with high simplified pulmonary embolism severity index score, which was directly related with high hospital mortality. However, due to the heterogeneity within different cohorts, the cut-off values were largely different in all these studies, which limit their application in other cohorts. Furthermore, in most studies the PLR was converted into a dichotomous variable using the respective cut-off value, which to a certain degree weakened the statistical efficiency. As different correlation trends were detected on the 2 sides of the cut-off value in the present study (Figure 1), simply using the low PLR as the reference level decreased the power to detect the true association between low PLR and clinical outcomes. To address this limitation, PLR value was used as a continuous variable by applying linear spline function in logistic models. A "converse-U"-shaped relationship was initially detected; however, only high PLR level was significantly associated with low GCS_{dis}, while low PLR was insignificant after adjusting for confounding factors. Although the predictive value of PLR is widely reported in various diseases, the mechanism is largely unknown. We noticed that platelet counts increased stepwise and the lymphocyte counts decreased with increasing PLR quartiles. Studies have confirmed that platelets play a critical role in immunomodulatory and inflammatory processes [19,20] by inducing the release of inflammatory

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cytokines [21] and interacting with various cells, including neutrophils, T lymphocytes, and macrophage, which contribute to the initiation or exacerbation of the inflammatory process [22]. Thus, high PLT may reflect the aggravated release of cytokines and increased thrombocyte activation, which lead to devastating inflammatory response. It was also reported that in patients with ICH, high PLT can predict elevated perihematomal edema and is associated with poor discharge outcome [23]. Furthermore, results published by Lattanzi et al. demonstrated that low lymphocyte count predicted worse 3-month outcome after ICH [24]. On the other hand, although PLT and lymphocyte were reported as predictive indexes in previous studies, we did not detect any statistical significance in the crude comparisons of platelet count and lymphocyte count within 3 GCS_{dis} levels. Thus, we speculated that PLR was superior to PLT or lymphocyte count alone in the prediction of neurological outcomes and may more accurately indicate a high level of inflammatory reaction [25] in ICH patients.

We also noticed that PLR on ED admission was not associated GCS_{dis} or MRS at 6 months. Unlike other reported diseases such as hepatocellular carcinoma, acute kidney injury, and pneumonia [16,26,27], ICH is an acute severe disease and we noticed that the time interval between symptom onset and ED admission was quite short (2~3 h, Table 2). Thus, it was reasonable that both the PLR and the C-reactive protein (a common inflammation indicator) on ED admission were not significantly increased, as the inflammatory response may not be aggravated.

Based on these findings, PLR on ICU admission can be used as a prognostic indicator to identify patients who are at higher risk of poor neurological outcomes. In patients with high PLR, more intensive monitoring and rigorous prognosis evaluation may be arranged. On the other hand, as high PLR indicated strong inflammatory response, it is unclear if anti-inflammatory strategies would be beneficial or if this index could be used as an indicator of the efficacy of therapies.

Several limitations to our study should be noticed. First, this study was performed in a single teaching hospital, and the sample size was relatively small, which may limit the statistical power to detect a significant difference in long-term MRS. Second, as the PLR value was used as a continuous variable in the logistic regression model using linear spline function, the OR was small (1.004 to 1.006). However, this only represents the odds ratio based on 1 unit change of PLR (95% interval: 58~390). For better interpretation, quartile grouping method was also used and is shown in Table 4. However, as the prognosis of patients with ICH was affected by many confounding factors, it is difficult to predict clinical outcomes based on a single index. We hope that our findings will add to the prognostic tools for ICH in future studies.

Conclusions

In patients with ICH, high PLR value on ICU admission but not the value on ED admission was significantly associated with short-term neurological outcome. However, this prediction for the long-term outcome was insignificant. Prospective studies are needed to comprehensively explore the impact of inflammatory response on ICH.

Conflict of interest

None.

Supplementary Table

Supplementary Table 1. Associations between PLRs on ER/ICU admission and modified Rankin score using quartile method.

ER admission				ICU admission			
Variables	Adjusted odds ratio	95% CI	p	Variables	Adjusted odds ratio	95% CI	p
Q1	0.70	0.25–1.94	0.495	Q1	1.40	0.51–3.85	0.508
Q2	Ref.	–	–	Q2	Ref.	–	–
Q3	1.57	0.57–4.32	0.381	Q3	2.16	0.79–5.89	0.129
Q4	0.95	0.35–2.57	0.926	Q4	2.50	0.88–7.09	0.085

Modified Rankin score (level one: 0–2, level two: 3–6) was used as a dichotomous variable. PLRs on ER/ICU admission were divided into four quartiles, and the second quartile was used as the reference level. Both the two models were adjusted for age, diabetes mellitus, hypertension, bleeding sites, serum sodium, hospital acquired pneumonia and APACHE II score on ICU admission.
PLR – platelet to lymphocyte ratio; ER – Emergency Room; ICU – Intensive Care Unit; CI – confidence interval; APACHE – acute physiology and chronic health evaluation.

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