

ORIGINAL ARTICLE

Platelet-to-White Blood Cell Ratio as a Predictor for Thirty-Day Mortality in Patients with Spontaneous Supratentorial Intracerebral Hemorrhage

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SUMMARY

Background: Spontaneous intracerebral hemorrhage (ICH) presents a substantial public health challenge due to its high mortality rates. Although the platelet-to-white blood cell ratio (PWR) has been identified as an independent prognostic factor in various diseases, its association with ICH outcome remains unclear. This study aimed to investigate the relationship between PWR and the thirty-day mortality rate in patients with spontaneous supratentorial ICH.

Methods: A retrospective analysis of 296 adult patients was conducted, collecting data on demographics, Glasgow Coma Score (GCS), underlying conditions, and laboratory results. PWR was calculated as the absolute value of the platelet-to-white blood cell ratio. The primary outcome was the thirty-day mortality during hospitalization. Multivariable logistic regression analysis was performed to identify independent predictors of thirty-day mortality.

Results: The study revealed a significant inverse association between PWR and thirty-day mortality (odds ratio: 0.88, 95% CI: 0.79 - 0.98, $p = 0.02$). A 12% increase in mortality risk was observed for every unit decrease in PWR. Kaplan-Meier survival curves demonstrated a significantly lower survival rate within 30 days for patients with $PWR < 15.0$ (log-rank test: $p < 0.01$). Admission GCS and chronic kidney disease were also identified as independent predictors of thirty-day mortality ($p = 0.04$ and $p < 0.01$, respectively).

Conclusions: PWR is a significant predictor of thirty-day mortality in patients with spontaneous supratentorial ICH. Lower PWR values correspond to a higher mortality risk, highlighting the potential utility of PWR as a prognostic indicator for ICH patients.

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KEYWORDS

intracerebral hemorrhage, white blood cell, platelet, platelet-to-white blood cell ratio, mortality

INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) presents a major public health issue, as it often leads to high death rates in adults [1]. Many patients who endure the initial ICH event continue to experience functional dependence [2]. Recognizing prognostic factors early and accounting for individual variability is crucial for making well-informed clinical decisions after ICH. In particular,

inflammation plays a role in secondary brain injury following acute ICH and significantly impacts the overall outcome [3]. While white blood cell (WBC) count can serve as an indicator of systemic inflammation, its clinical connection to ICH prognosis remains debated [4,5]. Moreover, a low platelet count may contribute to bleeding complications; however, one study found that reduced platelet count does not influence functional outcome rates in ICH patients [6]. Interestingly, a combined index of platelet and WBC has been demonstrated as an independent prognostic factor in various diseases [7-9]. In studies examining the correlation between platelet-to-white blood cell ratio (PWR) and acute ischemic stroke outcomes, PWR has been shown to be a significant prognostic marker [10,11]. However, the direct link between PWR and ICH prognosis is still undetermined, highlighting the need for a comprehensive evaluation.

Consequently, this study sought to examine the connection between PWR and the thirty-day mortality rate by collecting clinical and laboratory data from patients experiencing spontaneous supratentorial ICH.

MATERIALS AND METHODS

Data collection

This research took place in the 20-bed neurosurgical intensive care unit at Kaohsiung Chang Gung Memorial Hospital in Taiwan and obtained approval from the institutional review board. From 2008 through 2011, 300 adult patients were initially identified with spontaneous supratentorial ICH as their primary diagnosis. Patients with incomplete medical records were excluded, resulting in a final sample of 296 patients. The study involved a retrospective review of patients' medical charts, collecting data on demographics and Glasgow Coma Score (GCS) at admission. Underlying conditions and pre-admission medication history included seizure, hypertension, diabetes mellitus, atrial fibrillation, stroke history, coronary artery disease, chronic kidney disease, smoking, alcoholism, anticoagulant therapy, antiplatelet therapy, and statin therapy. Venous blood samples were collected within 24 hours of admission, and WBC and platelet counts were determined in the hospital's clinical chemistry laboratory. The PWR was calculated as the absolute value of the platelet-to-WBC ratio. The primary clinical outcome was the thirty-day mortality during hospitalization.

Computed tomography (CT) studies and measurements Upon arrival at the emergency room, all patients received brain CT scans. Follow-up CT scans were performed for cases with acute onset of focal neurological deficits, progressively deteriorating consciousness, or no neurological improvement. Chun-Wei Ting, one of the authors, reviewed all brain images and radiological data for each patient. The initial CT scans were interpreted to identify individual features, including ICH location, which involved the cerebral lobe, thalamus, basal gan-

gia, and pure ventricles. The volume of intraparenchymal hematoma was calculated using the formula $(A \times B \times C/2)$ [12]. Midline shift was measured in millimeters. Additionally, the presence of hematoma extension into the ventricles and instances of hydrocephalus were documented.

Surgical indications and procedures

Conservative treatment was offered to patients in good neurological condition or those unable to tolerate surgery due to age or comorbidities. Craniotomy evacuation of the hematoma was deemed necessary if the intraparenchymal hematoma volume exceeded 30 mL or the patient's consciousness progressively deteriorated. Decompressive craniectomy was performed on patients with severe brain swelling after hematoma removal. If the hematoma extended into the ventricles, causing hydrocephalus, unilateral or bilateral ventricles were drained simultaneously. In cases where patients experienced ongoing hydrocephalus or persistent neurological symptoms such as headaches, cognitive impairment, or gait disturbances, a permanent cerebrospinal fluid (CSF) shunt was required to divert excess fluid. Tracheostomy was considered for patients who needed reintubation or experienced weaning failure following ICH.

Statistical analysis

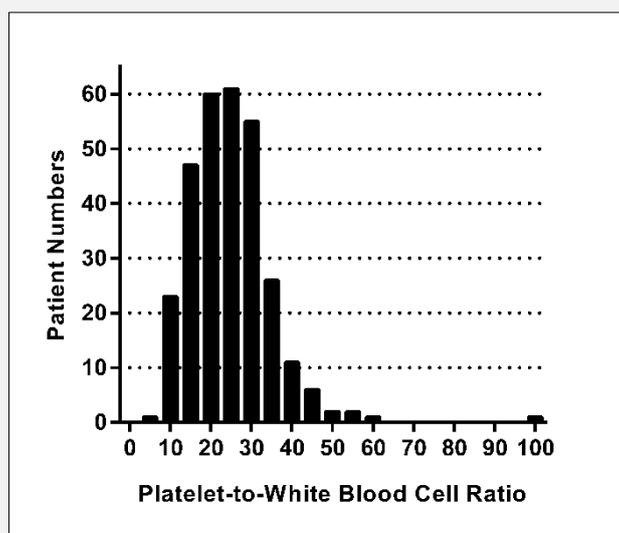
Data analysis was performed using IBM SPSS Statistics software (version 22). Data were presented as either numbers (percentages) or mean \pm standard deviation (SD). To assess intergroup differences, the chi-squared test or Fisher's exact test was utilized for categorical variables, and Student's *t*-test was applied for continuous variables. All parameters with a *p*-value < 0.05 were incorporated into a multivariable logistic regression analysis to adjust for independent predicting factors of thirty-day mortality after ICH. Receiver operating characteristic (ROC) curves were created for the predictors of thirty-day mortality, and the area under the curve (AUC) was calculated. Kaplan-Meier survival curves were generated and compared using the log-rank test. Statistical significance was established at a *p*-value < 0.05 .

RESULTS

Supplementary Table S1 shows the demographic and clinical characteristics of the 296 patients included in the study, grouped by thirty-day mortality (270 patients with no mortality and 26 patients with mortality). The average age of the patients was significantly higher in the mortality group (68.6 years with SD 13.1) compared to the non-mortality group (60.9 years with SD 13.6) ($p < 0.01$). Admission GCS was also significantly different between the groups ($p < 0.01$). There was no significant difference in ICH location ($p = 0.15$). Intraventricular extension was significantly more common in the mortality group (80.8%) compared to the non-mortality

Table 1. Multivariate logistic regression analysis of factors linked to thirty-day mortality.

Variables	Thirty-day mortality				
	OR	95% CI		p	
Age	1.04	0.99	-	1.09	0.13
Admission GCS					
9 - 15	1.00				
6 - 8	0.63	0.05	-	7.28	0.71
3 - 5	7.49	1.10	-	50.74	0.04
Intraventricular extension	0.83	0.17	-	3.90	0.81
Intraparenchymal hematoma volume	1.00	0.99	-	1.01	0.80
Midline shift	1.07	0.96	-	1.19	0.23
White blood cell	1.02	0.87	-	1.19	0.85
Platelet-to-white blood cell ratio	0.88	0.79	-	0.98	0.02
Seizure	2.90	0.43	-	19.59	0.27
Chronic kidney disease	25.19	5.83	-	108.80	< 0.01
Antiplatelet therapy	2.89	0.81	-	10.33	0.10

**Figure 1. Distribution of ICH patients according to platelet-to-white blood cell ratio.**

group (34.4%) ($p < 0.01$). There was no significant difference in the presence of hydrocephalus ($p = 0.15$). The average intraparenchymal hematoma volume and midline shift were significantly higher in the mortality group ($p < 0.01$ for both). WBC count was also significantly higher in the mortality group ($p < 0.01$), while PWR was significantly lower ($p < 0.01$). Chronic kid-

ney disease and antiplatelet therapy were significantly more prevalent in the mortality group ($p < 0.01$ for both).

Parameters with a p -value < 0.05 were included in the multivariable regression analysis based on the evaluation of the patients' clinical characteristics. Table 1 illustrates the logistic regression analysis results for thir-

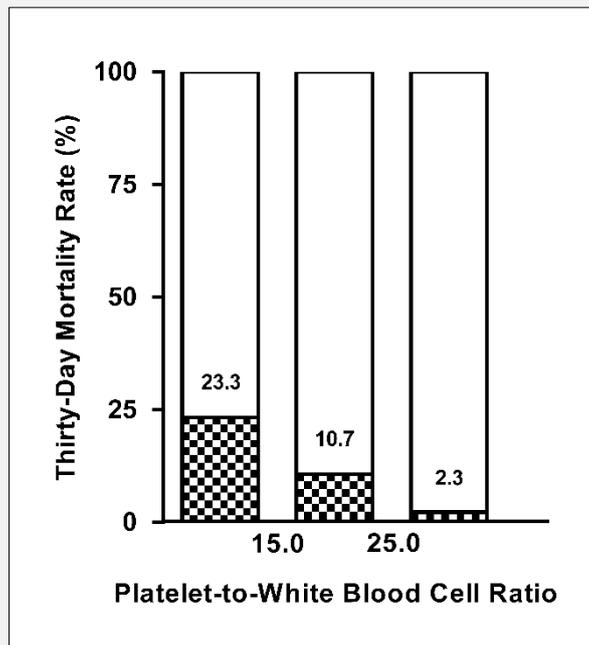


Figure 2. Stratified thirty-day mortality rates in ICH patients based on platelet-to-white blood cell ratio.

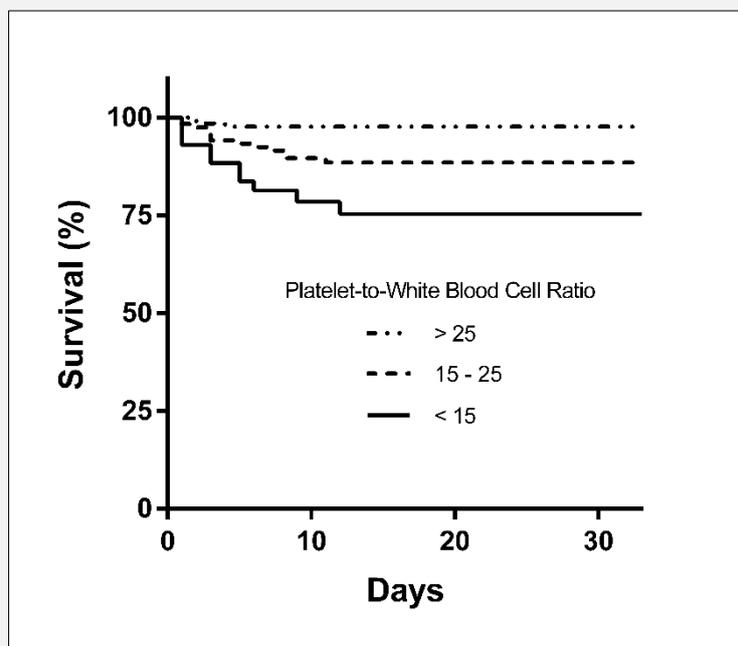


Figure 3. Kaplan-Meier survival analysis of ICH patients stratified by platelet-to-white blood cell ratio (log-rank test: $p < 0.01$).

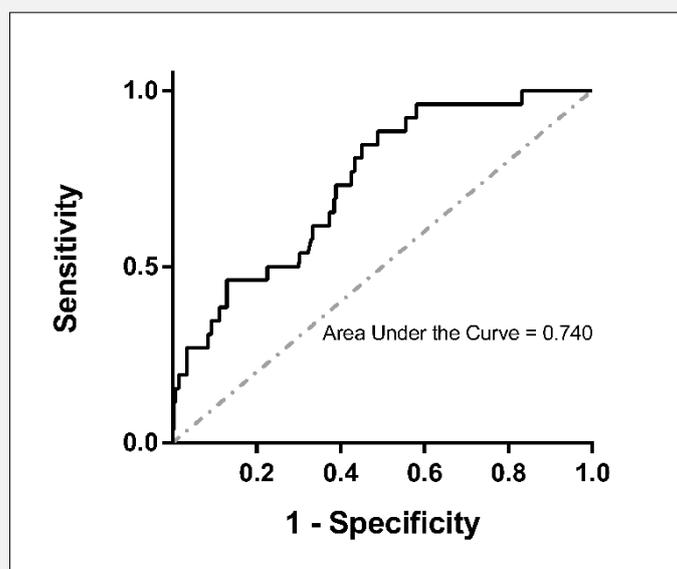


Figure 4. Receiver operating characteristic curve demonstrating the predictive accuracy for thirty-day mortality: area under the curve of 0.740 for platelet-to-white blood cell ratio ($p < 0.01$).

ty-day mortality. Variables such as age, intraventricular extension, intraparenchymal hematoma volume, midline shift, WBC, and seizure did not exhibit significant relationships with thirty-day mortality. The odds ratio (OR) for having a GCS of 3 - 5 relative to 9 - 15 was 7.49 (95% CI: 1.10 - 50.74, $p = 0.04$), indicating an increased mortality risk. Chronic kidney disease was also associated with a higher mortality risk (OR: 25.19, 95% CI: 5.83 - 108.80, $p < 0.01$). PWR showed a significant inverse association with mortality (OR: 0.88, 95% CI: 0.79 - 0.98, $p = 0.02$). This indicates that for every unit decrease in PWR, the odds of mortality increase by 12%, highlighting the crucial role of PWR in predicting patient outcomes.

Out of the 296 patients in the study, twenty-six experienced mortality within 30 days after ICH, resulting in an 8.8% mortality rate. Figure 1 illustrates the distribution of patients based on their admission PWR. In order to explore the relationship between PWR and thirty-day mortality more closely, patients were divided into three subgroups based on their PWR values, using cutoff points of 15.0 and 25.0. Figure 2 shows the mortality rates for ICH patients according to their PWR group. The data revealed that 23.3% (10 out of 43) of patients with $PWR < 15$, 10.7% (13 out of 121) of patients with PWR between 15.0 - 25.0, and 2.3% (3 out of 132) of patients with $PWR > 25.0$ had died. The Kaplan-Meier survival curves for these three groups indicated a significantly lower survival rate within 30 days after ICH for patients with $PWR < 15.0$ (log-rank test: $p < 0.01$). Fig-

ure 3 depicts these survival curves. Furthermore, we conducted an ROC curve analysis to assess the predictive power of PWR, as shown in Figure 4. The AUC for the PWR was 0.740 ($p < 0.01$), indicating its effectiveness in differentiating between patients who did or did not experience thirty-day mortality following an ICH.

DISCUSSION

This investigation aimed to examine the link between PWR and thirty-day mortality in patients with spontaneous supratentorial ICH. Importantly, this is the first study to uncover a significant association between PWR values and thirty-day mortality rates post-ICH. Additionally, the study identified an inverse connection between PWR and mortality, with each unit decrease in PWR contributing to a 12% rise in the odds of mortality. These findings highlight the potential importance of PWR as a prognostic indicator for ICH patients.

The diverse prognosis for ICH patients highlights the importance of having quantitative prognostic estimates that cater to the heterogeneous nature of ICH in clinical settings. These estimates can guide clinical decision-making and evaluate the necessity for aggressive interventions. Although the GCS remains the primary tool for assessing ICH severity and its association with patient outcomes [13,14], obtaining an accurate GCS in acute settings can prove difficult. In real-life situations, many hospitalized patients are sedated and intubated,

complicating neurological assessments. The endotracheal tube hinders verbal responses, and interpreting motor responses becomes challenging due to either discomfort incorporation or the effects of myorelaxants. In the context of ICH, utilizing individual or combined laboratory variables offers an alternative approach for prognostic purposes.

The significant association between PWR and ICH mortality identified in this study is likely due to the platelet-leukocyte immune response. Inflammation following ICH occurs rapidly, involving the activation of both regional and general immune systems [15]. Hematoma-induced microglial activation and complement formation result in an upregulation of membrane attack complexes and the release of cytokines, matrix metalloproteinases, or adhesion molecules. This cascade causes blood-brain barrier disruption, and along with the heightened local proinflammatory environment, promotes peripheral leukocyte infiltration, which has been linked to secondary brain injury [16,17]. Pathological analyses of ICH patients' brains show that perihematomal inflammation can develop as early as 5 hours post-bleeding, with neutrophils among the first inflammatory cells to arrive at the brain [18,19]. Additionally, platelets have been demonstrated to interact with various leukocyte subsets physically during inflammatory processes, which has significant implications for leukocyte recruitment into peripheral tissues and the regulation of leukocyte cell autonomous functions [20]. Platelets, by releasing chemokines and membrane ligands, are shown to influence WBC and act as a bridge in leukocyte-platelet aggregates, with a particular focus on neutrophils. These aggregates upregulate leukocyte pro-inflammatory functions [21], which may affect the disease's progression. Consequently, PWR can represent the degree of inflammation, displaying a significant association with ICH outcomes.

Interestingly, while PWR stands out as a powerful predictor for thirty-day mortality, neither individual WBC nor platelet count is statistically significant in multivariate logistic regression models. There are several reasons for this observation. WBC count functions as a general inflammation indicator; however, the peripheral total WBC count at the time of ICH admission may not precisely represent the specific neuroinflammatory response, which predominantly occurs in the perihematomal region [17,22]. Additionally, thrombocytopenia often coincides with systemic inflammation, potentially arising from the immune response in blood circulation [20]; however, the admission platelet count may not reveal this immediate response. The reasoning behind using blood cell ratios is based on the general insensitivity of basic blood counts for prognostic prediction purposes. To detect more nuanced changes in peripheral blood, the analysis of specific composite parameters is recommended. By combining platelets and WBC, the sensitivity and specificity of ICH outcomes may be enhanced.

Previous research has underscored a significant correlation between PWR and acute ischemic stroke outcomes, establishing PWR as a valuable prognostic marker [10, 11]. In line with our results, Cao et al. similarly observed an inverse relationship between PWR and 90-day mortality in ischemic stroke patients, reporting mortality rates of 0.9% among those with $PWR \geq 20.62$ and 5.9% among those with $PWR < 20.62$ [11]. The current study broadens these findings to encompass spontaneous supratentorial ICH, suggesting that PWR could play a crucial role in predicting prognosis across a variety of cerebrovascular disorders. To further explore the association between PWR and stroke prognosis, it is recommended to conduct a larger multi-center study, which includes a more diverse patient population and utilizes standardized outcome definitions.

In addition to PWR, the multivariable logistic regression analysis identified admission GCS and chronic kidney disease as independent predictors of thirty-day mortality. GCS has long been acknowledged as a reliable indicator of neurological function, and its connection with ICH prognosis is well-documented [13,14]. Furthermore, this study included 26 patients with chronic kidney disease, out of which 15 had undergone maintenance hemodialysis before admission. It is noteworthy that patients with end-stage renal disease have a higher risk of atherosclerotic cardiovascular disease compared to the general population [24]. Hemodialysis may also contribute to life-threatening brain injuries due to factors such as heparin administration, excessive ultrafiltration, or intracranial pressure fluctuations [25,26]. The association between chronic kidney disease and increased mortality risk emphasizes the potential impact of comorbidities on ICH prognosis.

It is essential to recognize the limitations of our study. The retrospective approach inherently restricts the conclusions that can be drawn from the findings. The study's single-center design and relatively small sample size may also influence the generalizability of the results. Furthermore, we focused solely on short-term outcomes, neglecting to evaluate long-term outcomes that could provide a more comprehensive understanding. Additionally, since the study only considered spontaneous supratentorial ICH, the findings might not be applicable to other types of ICH. Despite the limitations, our study provides valuable insights by highlighting the relationship between PWR and ICH mortality. In the end, a deeper understanding of these connections will assist clinicians in making well-informed decisions, ultimately leading to enhanced patient outcomes.

In conclusion, PWR is a significant predictor of thirty-day mortality in patients with spontaneous supratentorial ICH. Lower PWR values were associated with a higher risk of mortality, underscoring the potential utility of this composite index in guiding clinical decision-making and risk stratification. Further research is needed to confirm our results and to determine the optimal cutoff points for PWR in predicting ICH outcomes.

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No funding was received for this study.

Declaration of Interest:

The authors declare that they have no conflicts of interest.

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