ASSOCIATION BETWEEN LOWER PLATELET-TO-LYMPHOCYTE RATIO AND MORTALITY RISK IN MODERATE-TO-SEVERE TRAUMATIC BRAIN INJURY : A RETROSPECTIVE COHORT STUDY

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ABSTRAK

Penelitian ini menyelidiki hubungan antara rasio trombosit terhadap limfosit dan risiko kematian pada pasien dewasa dengan COT sedang hingga berat di rumah sakit tersier di Indonesia. Sistem registrasi rumah sakit dikaji secara retrospektif untuk mengumpulkan rekam medis dari 77 pasien dewasa yang menjalani rawat inap dari 1 Juni 2024 hingga 31 Desember 2024 dan didiagnosis dengan COT sedang hingga berat. Rasio neutrofil terhadap limfosit (NLR) serta rasio trombosit terhadap limfosit (PLR) dibandingkan antara kelompok pasien yang bertahan hidup (n=59) dan yang tidak bertahan hidup (n=18). Kemampuan prediktif NLR dan PLR dianalisis menggunakan area di bawah kurva karakteristik operasi penerima (AUC). Analisis tabel kontingensi dilakukan untuk menentukan sensitivitas, spesifisitas, nilai prediksi positif (PPV), nilai prediksi negatif (NPV), akurasi, serta rasio odds (OR) dari NLR dan PLR dalam kaitannya dengan tingkat kematian. Variasi kelangsungan hidup di antara subkelompok PLR dievaluasi melalui analisis kelangsungan hidup Kaplan-Meier. PLR pada pasien yang meninggal secara signifikan lebih rendah dibandingkan dengan kelompok yang bertahan hidup (nilai p = 0,026). Kurva ROC menunjukkan bahwa PLR merupakan prediktor terkuat dibandingkan dengan kedua rasio lainnya (area di bawah kurva ROC = 0,674, sensitivitas = 0,874, spesifisitas = 0,56, sesuai dengan nilai batas = 120,09). Ketika kelompok pasien dibagi berdasarkan kuartil PLR, analisis Kaplan-Meier menunjukkan kelangsungan hidup yang jauh lebih buruk pada kelompok dengan kuartil PLR terendah (< 120,09) dibandingkan dengan kelompok kuartil lainnya. Nilai PLR yang lebih rendah dikaitkan dengan tingkat kematian yang lebih tinggi pada pasien dewasa dengan COT sedang hingga berat, menunjukkan potensi penggunaan PLR dalam stratifikasi risiko yang memerlukan validasi lebih lanjut.

Kata kunci **:** cedera otak traumatic, limfosit, rasio trombosit terhadap limfosit, risiko kematian, trombosit

ABSTRACT

This study investigates the relationship between PLR, and mortality risk in moderate-to-severe adult TBI patients in an Indonesian tertiary hospital. The hospital registry system was retrospectively reviewed to gather medical records of 77 adult patients who were hospitalized from June 1, 2024 to December 31, 2024 and had moderate-to-severe TBI. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were compared between the survivor (n=59) and nonsurvivor (n=18). The predictive capabilities of NLR and PLR were assessed using the area under the receiver operating characteristic curve (AUC). The PLR of the deceased patients was considerably lower than that of the survivors (p value = 0.026). The receiver operating curve (ROC) established PLR as the strongest predictor among the three ratios (area under the ROC curve = 0.674, sensitivity = 0.874, specificity = 0.56, according to the cut-off value = 120.09). When the patient groups were divided by the PLR quartile, the Kaplan-Meier analysis showed significantly worse survival in the lowest PLR quartile group (< 120.09) compared with the other quartile groups. Lower PLR values were linked to higher mortality in adults with moderate-to-severe TBI, suggesting potential utility for PLR in risk stratification pending further validation.

Keywords ***:*** *lymphocyte, mortality risk, platelet, platelet-to-lymphocyte ratio, traumatic brain injury*

INTRODUCTION

Traumatic brain injury (TBI) remains the leading cause of death and long-term disability among individuals under 40 years of age, with a global incidence estimated at 50 million cases annually (Khellaf et al., 2019). The burden is disproportionately higher in low- and middle-income countries (LMICs), where outcomes are often worse due to limited access to acute and rehabilitative care. Early identification of high-risk TBI patients is essential for timely intervention and effective resource allocation. Prognostic indicators such as initial Glasgow Coma Scale (GCS) score, age, presence of coagulopathy, and neuroimaging findings are well-established markers associated with increased mortality risk (Turner et al., 2021). Neuroinflammation following TBI involves activation of resident glial cells, including microglia and astrocytes, along with infiltration of peripheral immune cells. Microglia, the brain's primary immune effector cells, originate from yolk sac progenitors during early embryogenesis. Upon injury, microglia coordinate inflammatory and reparative responses by releasing cytokines, clearing debris, and promoting neurorestoration (Xiong et al., 2018).

A complete blood count (CBC) is a routinely available test in trauma settings and provides valuable information about immune and inflammatory responses. Several studies have identified white blood cell (WBC) subtypes, including neutrophils and lymphocytes, and derived ratios—such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR)—as promising prognostic markers in trauma and TBI (Ke et al., 2021; Emektar et al., 2017; Vijenthira et al., 2020). These findings reinforce the value of monitoring WBC subtypes as a noninvasive tool for assessing and managing inflammatory and immune responses in patients with trauma. The detection of CBC subtypes is useful in prognosticating the outcomes and predicting the complications of TBI (Arslan & Sahin, 2024). Elevated NLR has been associated with poorer outcomes in pediatric TBI patients, particularly when measured at 24 and 48 hours post-injury (Kimball et al., 2020). Additionally, increased NLR levels can serve as an early indicator of developing traumatic intracerebral hemorrhage (Zhuang et al., 2021).

In adult patients, a persistently elevated NLR one week after a brain contusion has been linked to unfavorable neurological outcomes at six months. A low PLR, especially when accompanied by elevated NLR and hyperglycemia, has been identified as a risk factor for trauma-induced coagulopathy and worse prognosis in TBI patients (Chen et al., 2021). These hematological markers reflect systemic inflammation and impaired hemostasis, which may contribute to secondary injury. Approximately half of patients with severe trauma present with platelet hypofunction upon admission (Kutcher et al., 2012). Reduced platelet counts have been associated with a higher risk of coagulopathy and disseminated intravascular coagulation (DIC), both of which significantly increase mortality (Gando, 2001). Trauma-induced coagulopathy may lead to secondary bleeding, characterized by diffuse microvascular hemorrhage beyond the initial site of brain injury (Savioli et al., 2021).

Moreover, a link was established between lymphocyte count and the incidence of multiple organ dysfunction syndrome in patients who have sustained severe trauma (Idowu et al., 2022). Neutrophils and monocytes can also serve as biomarkers of both immunological status and bone marrow hematopoietic activity, which may influence patient outcomes after trauma (van Helmond et al., 2016). Given the heterogeneity of trauma presentations and the limited tools for early prognostication, this retrospective study aimed to investigate the association between NLR, PLR, and in-hospital mortality among adult patients with moderate-to-severe TBI (defined as head AIS $\geq$ 3) (Natakusuma et al., 2021). This study investigates the relationship between PLR, and mortality risk in moderate-to-severe adult TBI patients in an Indonesian tertiary hospital.

METHOD

This retrospective study was approved by the Institutional Review Board of Prof. IGNG Ngoerah Hospital (approval number: 1324/UN14.2.2.VII.14/LT/2024), with informed consent waived due to its design. Conducted at a tertiary teaching hospital, the study analyzed adult trauma patients admitted to the Emergency Department between June 1 and December 31, 2024. Of the 146 registered patients, 77 met inclusion criteria—having a head AIS ≥ 3 and no polytrauma (ISS > 15) or diabetes—and were included in the final analysis. Patients were categorized as survivors (n = 59) and non-survivors (n = 18), then stratified into quartiles based on platelet-to-lymphocyte ratio (PLR). Demographic and clinical data—including age, sex, GCS, ISS, and outcomes—were collected, along with admission blood samples before any treatment. Complete blood counts were used to calculate neutrophil-to-lymphocyte ratio (NLR) and PLR. Instead of applying a fixed PLR cutoff, the study used quartiles to explore dose-response relationships and better evaluate prognostic value. Only patients with complete data were included, and data extraction was performed independently to reduce bias.

Statistical analysis was conducted using SPSS version 25. Categorical variables were compared using the chi-square test, and continuous variables were analyzed based on distribution using either parametric or non-parametric tests. Predictive performance of NLR and PLR for in-hospital mortality was assessed via ROC curves and AUC values, with optimal cutoffs determined by Youden's index. Sensitivity, specificity, PPV, NPV, accuracy, and OR were calculated. Kaplan-Meier survival curves were also used to evaluate 60-day survival across PLR quartiles, with significance set at $p < 0.05$.

RESULT

Patient and Injury Characteristic

Table 1. General and Injury Characteristics of Survivors and Non-Survivors

Variables	Non-survive (n= 18)	Survive (n= 59)	p
Age (years)	46.5 (26.5–61.75)	28 (21–53)	0.042*
Sex			0.419
Male, n (%)	11 (61.1%)	42 (71.2%)	
Female, n (%)	7 (38.9%)	17 (28.8%)	
GCS, median (IQR)	8.5 (4.75–12)	12 (10–15)	0.002*
ISS, median (IQR)	13.5 (9–17.75)	9 (5–13)	0.026*
Neutrophil (10^3/ml)	12.25±4.12	13.59±4.60	0.273
Lymphocyte (10^3/ml)	1.41 (0.67–5.36)	1.21 (0.72–1.89)	0.243
Monocyte (10^3/ml)	0.84 (0.59–1.03)	0.91 (0.69–1.36)	0.159
Platelet (10^3/ml)	199.5 (162.75–283.5)	259 (203–312)	0.023*
NLR	6.83 (2.58–13.45)	10.61 (7.58–17.39)	0.102
PLR	110.89 (51.03-293.39)	219.33 (162.43–292.17)	0.026*
Hospital stay (days)	5.5 (3.75–19.5)	6 (5–11)	0.875

Table 1 summarizes baseline characteristics. There was no significant association between sex and mortality. However, patients in the non-survivor group were significantly older than survivors (median age: 46.5 [IQR: 26.5–61.75] vs. 28 [21–53] years, $p = 0.042$). Compared to survivors, deceased patients presented with more severe neurological impairment, evidenced by lower median GCS scores (8.5 [4.75–12] vs. 12 [10–15], $p = 0.002$), and higher injury severity scores (ISS: 13.5 [9–17.75] vs. 9 [5–13], $p = 0.026$). Non-survivors had significantly lower platelet counts (199.5 [162.75–283.5] vs. 259 [203–312] $\times 10^3/\mu L$, $p = 0.023$), though no significant differences were observed in neutrophil, monocyte,

or lymphocyte counts. Notably, the PLR was significantly lower in the mortality group (110.89 [51.03–293.39] vs. 219.33 [162.43–292.17], p = 0.026), whereas NLR values did not differ significantly (p = 0.102). There was also no significant difference in hospital length of stay between the two groups (5.5 [3.75–19.5] vs. 6 [5–11] days, p = 0.875).

PLR Subgroup Analysis

Patients were divided into quartiles based on PLR values: <120.09, 120.09–203.85, 203.85–291.17, and ≥291.17 (Table 2). The lowest PLR quartile (<120.09) had the highest lymphocyte counts and the highest mortality rate (52.6%). A clear trend was observed, with lymphocyte counts decreasing as PLR increased (p < 0.001). While platelet counts did not significantly differ across quartiles (p = 0.662), these findings suggest that a lower PLR may reflect more pronounced systemic inflammation or immune dysregulation in patients with poor outcomes.

Table 2. Comparison Among Various PLR Subgroups Divided by Quartile

Variables	PLR subgroup				P
	<120.09 n = 19	**120.09–203.85 n = 19**	**203.85–291.17 n = 20**	**≥291.17 n = 19**	
Age (years)	35 (22–50)	27 (18–55)	35 (21.25–56)	45 (23–61)	0.354
Sex					0.407
Male, n (%)	14 (73.7%)	15 (78.9%)	11 (55%)	13 (68.4%)	
Female, n (%)	5 (26.3%)	4 (21.1%)	9 (45%)	6 (31.6%)	
GCS, median (IQR)	11 (8–14)	12 (9–15)	10.5 (8–14.25)	10 (9–13)	0.483
ISS, median (IQR)	9 (5–17)	9 (8–14)	9.5 (4.25–17)	9 (5–12)	0.967
Lymphocyte (10^3/ml)	3.38 (2.49–6.59)*	1.51 (1.16–1.95)*	1.08 (0.72–1.52)*	0.66 (0.46–0.72)*	<0.001
Platelet (10^3/ml)	232 (161–316)	275 (198–317)	260 (190.5–353.25)	241 (201–283)	0.662
Hospital stay (days)	6 (4–11)	6 (5–8)	5.5 (4.25–11.5)	8 (3–14)	0.910
Mortality, n (%)	10 (52.6%)	2 (10.5%)	2 (10%)	4 (21.1%)	0.007

Prediction Performance of NLR and PLR for Mortality

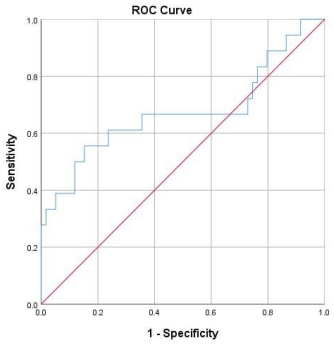

Figure 1. Performance of PLR in Predicting Mortality determined by the Area Under The Receiver Operating Characteristic Curve

Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive utility of PLR (Figure 2) and NLR (Figure 3). PLR demonstrated modest discriminatory ability with an AUC of 0.674 (95% CI: [exact CI needed], p < 0.05). The optimal PLR cutoff of 120.09, determined by Youden's index, yielded a sensitivity of 55.56% and specificity of 84.75%. Although the AUC is not high, the strong specificity suggests PLR may be more useful in ruling in high-risk cases rather than screening broadly. NLR also demonstrated modest discriminatory ability with an AUC of 0.678 with

insignificant p value result (95% CI: [exact CI needed], p = 0.102). The optimal NLR cutoff of 5.8, determined by Youden's index, yielded a sensitivity of 50.00% and specificity of 81.00%. Although the AUC is low, the strong specificity suggests NLR may be more useful in ruling in high-risk cases rather than screening broadly.

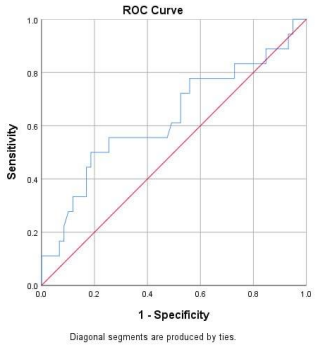

Figure 2. Performance of NLR in Predicting Mortality determined by the Area Under The Receiver Operating Characteristic Curve

Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Accuracy, and Odds Ratio

As shown in table 3, patients with PLR <120.09 had a significantly increased risk of mortality. The calculated odds ratio was 6.94 (95% CI: 2.16–22.37, p = 0.001), indicating a strong association. Despite low sensitivity (55.56%), the high specificity (84.75%) and negative predictive value (86.21%) suggest that a higher PLR may help identify patients with lower mortality risk.

Table 3. Contingency Table of PLR Categorized by Cutoff Value for Mortality

		Outcome	
		Survive	**Death**
PLR cut-off	<120.09	9 (15.3%)	10 (55.6%)
	≥120.09	50 (84.7%)	8 (44.4%)
Total		59 (100%)	18 (100%)

Sensitivity = 55.56%; Specificity = 84.75%; PPV = 52.63%; NPV = 86.21%; Accuracy = 77.92%; OR = 6.94 (95% CI: 2.16–22.37; p = 0.001)

Analysis of the Kaplan-Meier Survival Curves

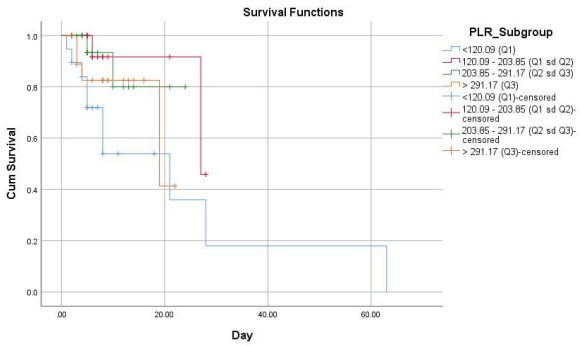

Figure 3. Analysis of the Kaplan-Meier Survival Curves by Patient Subgroups according to PLR Quartile

Kaplan–Meier curves stratified by PLR quartiles (Figure 4) revealed significant differences in 60-day survival among the groups. The lowest PLR quartile (<120.09) exhibited significantly poorer survival compared to the second quartiles (log-rank p < 0.05)

and the third quartiles (log-rank $p < 0.05$). However, the difference between the lowest and highest quartiles (≥291.17) was not statistically significant ($p = 0.279$), suggesting a potential U-shaped relationship or other confounding influences. The log-rank test was used for survival comparison. However, no multivariable adjustment or test of proportional hazards assumption was performed in this analysis.

DISCUSSION

This study identified a significant association between lower platelet-to-lymphocyte ratio (PLR) values and increased in-hospital mortality among adults presenting with moderate-to-severe traumatic brain injury (TBI). Among the hematologic markers evaluated, PLR demonstrated the highest discriminative ability for predicting mortality, as evidenced by receiver operating characteristic (ROC) curve analysis. PLR outperformed the neutrophil-to-lymphocyte ratio (NLR), which did not significantly differ between survivors and non-survivors. A contingency table analysis reinforced the association between low PLR values and fatal outcomes (Arslan & Sahin, 2024). Survival analysis using Kaplan-Meier curves revealed that individuals in the lowest PLR quartile had significantly poorer survival compared to those in the second and third quartiles. Interestingly, survival in the highest PLR quartile was not significantly different from that in the lowest quartile, suggesting a possible non-linear or U-shaped relationship between PLR and mortality risk. This finding may reflect the complex and opposing roles of platelets and lymphocytes in the inflammatory and coagulative responses following TBI (Zhang & Shen, 2018; Yun et al., 2021).

Patients who did not survive were generally older and presented with more severe neurological impairment, as indicated by lower Glasgow Coma Scale (GCS) scores and higher trauma severity scores. Additionally, they exhibited lower platelet counts on admission, further supporting the association between reduced PLR and adverse outcomes (Chen et al., 2021; Kutcher et al., 2012). PLR is a composite biomarker derived from two hematologic components—platelets and lymphocytes—which are both dynamically altered in response to trauma. Platelet depletion in the acute phase of TBI may result from activation of the coagulation cascade, triggered by the release of tissue factor from damaged brain tissue, leading to consumption coagulopathy and thrombocytopenia (Gando, 2001; Savioli et al., 2021). Simultaneously, the inflammatory response following TBI can enhance thrombopoiesis through neuroinflammatory cytokines that stimulate megakaryocyte proliferation (Kutcher et al., 2012).

Lymphocytosis, which contributes to a lower PLR, has also been linked to systemic hypovolemia and the acute stress response in trauma patients. During central hypovolemia, leukocytosis—especially an elevation in lymphocyte count—has been observed as part of the hemodynamic and immune response (van Helmond et al., 2016). In the context of TBI, hypovolemia may exacerbate cerebral hypoperfusion and secondary brain injury, mechanisms known to increase mortality risk (Robertson et al., 1992). Nevertheless, the functional significance of increased lymphocyte counts is complex. While lymphocytes may modulate and downregulate inflammatory responses (Xiong et al., 2018), an acute rise in lymphocyte count may also reflect the severity of injury and correlate with poor outcomes (Pinkerton et al., 1989).

In the present study, we did not observe significant differences in monocyte, neutrophil, or absolute lymphocyte counts between survivors and non-survivors, nor did the NLR differ significantly. This suggests that PLR may better capture the integrated balance between thrombosis and immune response than its individual components (Arslan & Sahin, 2024; Ke et al., 2021). The prognostic value of PLR in neurotrauma remains a subject of debate. Prior studies have reported contradictory findings. For example, one retrospective study involving

183 patients with cerebral hemorrhage found that a high PLR on admission was associated with lower GCS scores and worse neurologic outcomes (Zhang & Shen, 2018). This may be due to the pro-inflammatory and pro-thrombotic state indicated by elevated PLR, reflecting heightened platelet activation and systemic inflammation (Erdal & İnanir, 2019).

These seemingly divergent findings may be reconciled by considering the possibility of a U-shaped association between PLR and mortality, where both very low and very high values reflect different but deleterious pathophysiological processes. Variability in study designs, patient populations, timing of blood sampling, and control for confounders such as comorbidities or interventions may also contribute to inconsistent results across studies (Natakusuma et al., 2021). This study has several important limitations. First, as a retrospective analysis, it is subject to inherent biases, including selection bias and residual confounding. Key variables, such as pre-existing comorbidities and ongoing medications, could not be fully controlled. Importantly, patients who died before arriving at the emergency department were excluded, potentially underestimating the true early mortality burden in this population (Turner et al., 2021).

The sample size was modest, which may limit the generalizability and statistical power of subgroup analyses. Additionally, hematologic parameters were assessed only at the time of admission, preventing evaluation of dynamic changes in PLR during hospitalization. Although the likelihood of blood transfusion before sampling was low, the lack of standardized fluid resuscitation protocols and undocumented fluid volumes may have introduced variability in the measured parameters. Finally, the study was conducted at a single tertiary referral center. While this enhances internal validity through consistent care protocols, it may limit external validity when applied to other settings with differing patient populations, resource availability, or clinical practices.

CONCLUSION

This study found that lower PLRs were associated with higher mortality rates in adult patients with moderate-to-severe TBI. As a readily accessible inflammatory marker, PLR may offer additional value in risk stratification, though further validation is needed to confirm its prognostic utility.

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REFERENCES

Arslan, K., & Sahin, A. S. (2024). *Prognostic value of systemic immune-inflammation index, neutrophil-lymphocyte ratio, and thrombocyte-lymphocyte ratio in critically ill patients with moderate to severe traumatic brain injury*. *Medicine (Baltimore), 103*(29), e39007. https://doi.org/10.1097/md.0000000000039007

Chen, Y., Tian, J., Chi, B., Zhang, S., Wei, L., & Wang, S. (2021). *Factors associated with the development of coagulopathy after open traumatic brain injury*. *Journal of Clinical Medicine, 11*(1), 185.

Erdal, E., & İnanir, M. (2019). *Platelet-to-lymphocyte ratio (PLR) and Plateletcrit (PCT) in young patients with morbid obesity*. *Revista da Associação Médica Brasileira, 65*(9), 1182–1187.

Figueroa, J. M., Semonche, A., Magoon, S., et al. (2020). *The role of neutrophil-to-lymphocyte ratio in predicting overall survival in patients undergoing laser interstitial thermal therapy for glioblastoma. Journal of Clinical Neuroscience, 72*, 108–113. https://doi.org/10.1016/j.jocn.2019.12.057

Gando, S. (2001). *Disseminated intravascular coagulation in trauma patients*. *Seminars in Thrombosis and Hemostasis, 27*(6), 585–592. https://doi.org/10.1055/s-2001-18864

Idowu, O. E., Oyeleke, S. O., & Vitowanu, J. M. (2022*). Impact of inflammatory cell ratio, biomarkers, activated partial thromboplastin time and prothrombin time on chronic subdural haematoma severity and outcome*. *European Journal of Trauma and Emergency Surgery, 48*(2), 1085–1092. https://doi.org/10.1007/s00068-021-01665-5

Ke, R. T., Rau, C. S., Hsieh, T. M., et al. (2021). *Association of platelets and white blood cells subtypes with trauma patients' mortality outcome in the intensive care unit. Healthcare, 9*(8), 942. https://doi.org/10.3390/healthcare9080942

Khellaf, A., Khan, D. Z., & Helmy, A. (2019). *Recent advances in traumatic brain injury. Journal of Neurology, 266*(11), 2878–2889.

Kimball, R., Shachar, E., Eyerly-Webb, S., Patel, D. M., & Spader, H. (2020). *Using the neutrophil-to-lymphocyte ratio to predict outcomes in pediatric patients with traumatic brain injury. Clinical Neurology and Neurosurgery, 193*, 105772. https://doi.org/10.1016/j.clineuro.2020.105772

Kutcher, M. E., Redick, B. J., McCreery, R. C., et al. (2012). *Characterization of platelet dysfunction after trauma. Journal of Trauma and Acute Care Surgery, 73*(1), 13–19. https://doi.org/10.1097/TA.0b013e318256deab

Natakusuma, T. I. S. D., Mahadewa, T. G. B., Mardhika, P. E., Maliawan, S., Senapathi, T. G. A., & Ryalino, C. (2021). *Role of monocyte-to-lymphocyte ratio, mean platelet volume-to-platelet count ratio, C-reactive protein and erythrocyte sedimentation rate as predictor of severity in secondary traumatic brain injury: A literature review*. *Open Access Macedonian Journal of Medical Sciences, 9*, 574–583. https://doi.org/10.3889/oamjms.2021.6985

Pinkerton, P. H., McLellan, B. A., Quantz, M. C., & Robinson, J. B. (1989). *Acute lymphocytosis after trauma—Early recognition of the high-risk patient*? *The Journal of Trauma, 29*(6), 749–751. https://doi.org/10.1097/00005373-198906000-00009

Robertson, C. S., Contant, C. F., Gokaslan, Z. L., Narayan, R. K., & Grossman, R. G. (1992). *Cerebral blood flow, arteriovenous oxygen difference, and outcome in head injured patients*. *Journal of Neurology, Neurosurgery & Psychiatry, 55*(7), 594–603. https://doi.org/10.1136/jnnp.55.7.594

Tekin, Y. K. (2019). *Are neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios associated with mortality in pediatric trauma patients? A retrospective study*. *Rambam Maimonides Medical Journal, 10*(4), e022. https://doi.org/10.5041/RMMJ.10376

Turner, G. M., McMullan, C., Aiyegbusi, O. L., et al. (2021). *Stroke risk following traumatic brain injury: Systematic review and meta-analysis. International Journal of Stroke, 16*(4), 370–384. https://doi.org/10.1177/17474930211004277

Van Helmond, N., Johnson, B. D., Curry, T. B., Cap, A. P., Convertino, V. A., & Joyner, M. J. (2016). *White blood cell concentrations during lower body negative pressure and blood loss in humans*. *Experimental Physiology, 101*(10), 1265–1275. https://doi.org/10.1113/EP085952

Vijenthira, A., Chiu, N., Jacobson, D., et al. (2020). *Predictors of intensive care unit admission in patients with hematologic malignancy*. *Scientific Reports, 10*(1). https://doi.org/10.1038/s41598-020-78114-7

Xiong, Y., Mahmood, A., & Chopp, M. (2018). *Current understanding of neuroinflammation after traumatic brain injury and cell-based therapeutic opportunities*. *Chinese Journal of Traumatology, 21*(3), 137–151.

Yun, S., Yi, H. J., Lee, D. H., & Sung, J. H. (2021). *Clinical significance of platelet to neutrophil ratio and platelet to lymphocyte ratio in patients with aneurysmal subarachnoid hemorrhage*. *Journal of Clinical Neuroscience, 92*, 49–54. https://doi.org/10.1016/j.jocn.2021.07.036

Zhang, W., & Shen, Y. (2018). *Platelet-to-lymphocyte ratio as a new predictive index of neurological outcomes in patients with acute intracranial hemorrhage: A retrospective study*. *Medical Science Monitor*, *24*, 4413–4420. https://doi.org/10.12659/msm.910845

Zhuang, D., Sheng, J., Peng, G., et al. (2021). *Neutrophil to lymphocyte ratio predicts early growth of traumatic intracerebral haemorrhage*. *Annals of Clinical and Translational Neurology, 8*, 1601–1609. https://doi.org/10.1002/acn3.51409