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Platelet-to-Lymphocyte Ratio as a Prognostic Biomarker for Overall Survival in Glioma Patients: A Retrospective Cohort Study in Yogyakarta, Indonesia

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ABSTRACT

Background: Glioma is the most common primary brain tumor in adults, with a generally poor prognosis despite advances in treatment. Inflammation plays a role in tumor initiation, progression, and invasion. The platelet-to-lymphocyte ratio (PLR) is a minimally invasive, cost-effective biomarker that may predict overall survival (OS) in glioma patients. Objective: This Study aims to evaluate the association between pre-treatment PLR and overall survival in patients with glioma. Methods: This retrospective cohort study included glioma patients treated at Dr. Sardjito General Hospital and affiliated hospitals in Yogyakarta between 2017–2022. PLR was calculated from pre-treatment complete blood counts. The optimal cut-off value was determined via ROC curve analysis. Kaplan–Meier survival analysis and Cox proportional hazards regression were performed to evaluate associations between PLR and OS, adjusting for age, sex, tumor grade, size, location, surgery type, and Karnofsky Performance Status (KPS). Results: A total of 149 patients were included (median age: 48 years; 57.7% male; 69.1% high-grade glioma). The optimal PLR cut-off was 236.77 (AUC = 0.591; sensitivity = 42.9%; specificity = 77.8%). Median OS was 14.1 months for PLR < 236.77 versus 5.8 months for PLR ≥ 236.77. High PLR was associated with increased mortality risk (HR = 2.18; 95% CI: 1.37–3.45). Conclusion: Elevated pre-treatment PLR is independently associated with shorter OS in glioma patients. PLR may serve as a simple, inexpensive prognostic biomarker in clinical practice, particularly in resource-limited settings.

1. INTRODUCTION

Glioma is the most common primary brain tumor in adults (70-80%). Glioma can be benign or malignant. The tumors originate from non-neuronal normal glial cells that serve to maintain homeostasis, form myelin, and support and protect nerve cells (Louis et al., 2007). Every year, around 5-6 out of 100,000 people are diagnosed with primary malignant brain tumors, approximately 80% of which are malignant gliomas (Alifieris & Trafalis, 2015). In general, glioma sufferers have a short survival rate due to their high recurrence rate and resistance to therapy (Yang et al., 2022). The burden of primary brain tumors in Southeast Asia is considerable, with 15,193 cases reported in 2016. Indonesia contributed the largest proportion, with 6,337 cases, followed by Thailand (2,747) and the Philippines (2,297). Indonesia also recorded the highest mortality related to primary brain tumors in the region, with 5,405 deaths, and the greatest disease burden, with 214,521 disability-adjusted life years (DALYs). Although glioma-specific data remain limited, these figures underscore the significant contribution of glioma to the national burden of brain tumors, given that gliomas account for the majority of primary malignant brain tumors. This high incidence and mortality highlight the urgent need for research into prognostic markers and treatment strategies that are affordable, accessible, and applicable to the Indonesian healthcare context.

Research on the role of the platelet-lymphocyte ratio (PLR) as a prognostic biomarker in glioma remains very limited, particularly in Indonesia. To date, most evidence has originated from

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studies conducted in developed countries, where patient characteristics, healthcare resources, and access to medical services differ from those in Indonesia. Therefore, international findings may not be fully generalizable to the Indonesian population.

Yogyakarta was chosen as the study site because it is one of the major referral healthcare centers in Indonesia, particularly in Central Java, and is equipped with teaching hospitals that have well-established neurosurgical and oncology facilities. Moreover, Yogyakarta has a heterogeneous patient population, as patients come not only from the Special Region of Yogyakarta but also from surrounding areas, including southern Central Java. This diversity allows the data obtained to better reflect real-world clinical conditions.

In addition, advanced molecular biomarker testing remains limited in most hospitals in Yogyakarta and its surrounding regions. This highlights the urgency of exploring alternative biomarkers such as PLR, which are simple, minimally invasive, and cost-effective, making them more feasible for widespread clinical use. Thus, this study is important not only to strengthen scientific evidence regarding the role of PLR in glioma but also to provide a practical solution tailored to the realities of healthcare services in Indonesia, particularly in Yogyakarta

The prognosis of glioma is closely malignant (Ostrom et al., 2014). In general, glioma is diagnosed and graded by histopathological examination of biopsy samples or tumor resection wich is needed operative surgery to get the sample with limited fascility in rural area this make operative surgery available just in big hospital. However, this histopathological determination of the degree often gives inconsistent results due to the variability between examiners. Therefore, in 2016 WHO published a new classification system that uses molecular parameters as well as histopathology to define a tumor and updated it in 2021. It accordingly formulated how central nervous system (CNS) tumors should be diagnosed in the molecular era (Louis et al., 2007).

Molecular markers are currently playing an increasingly important role in glioma cases. These markers have a role in assisting the diagnosis (diagnostic biomarkers), determining the success of certain therapies (predictive biomarkers), becoming therapeutic targets (targeted therapy), as well as determining the prognosis (prognostic biomarkers). Several identified molecular markers in glioma include IDH1/2 mutations, TP53 mutations, MGMT methylation status, EGFR mutations, and VEGF expression. However, the use of this molecular marker has a weakness because it must be examined on tumor tissue. Biopsy or tumor resection procedures are invasive and cannot be performed on patients with poor general conditions or patients who refuse surgery. In addition, the costs required are relatively expensive and not all health facilities have adequate technology. Therefore, it is necessary to develop other biomarkers that are relatively minimal invasive, easy to perform, and affordable.

Inflammatory processes play a role in the initiation, progression, and invasion of glioma tumor cells. Several studies have proven that inflammation-related hematological parameters such as C reactive protein (CRP) levels and neutrophil-lymphocyte ratio (NLR) have high prognostic value for glioma (Wang et al., 2018; Marini et al., 2020;). Another potential inflammatory marker in glioma cases is the platelet lymphocyte ratio (RPL) which is a minimal invasive, user-friendly, and inexpensive marker of systemic inflammation and has been shown to have prognostic value in various cases of solid tumors. Several studies have also stated the potential of RPL as a marker of glioma prognosis, where increased RPL is associated with shorter patient survival (Wang et al., 2018; Marini et al., 2020; Stoyanov et al., 2022;).

Pathophysiologically, an increase in platelet number will be beneficial in the growth and development of intracranial tumors. Platelets stimulate angiogenesis, facilitate tumor growth, and spread intracranial tumors. On the other hand, decreased lymphocyte numbers in glioma cases decrease the immune system which will worsen the patient's general condition and reduce the patient's survival (Cong et al., 2021).

Several studies like liu chang and marini have demonstrated that inflammation-related hematological parameters, such as C-reactive protein (CRP) levels and the neutrophil-to-lymphocyte ratio (NLR), have high prognostic value for glioma. Another study cong said inflammatory marker with potential relevance in glioma is the platelet-to-lymphocyte ratio (PLR). PLR is a minimally invasive, simple, and inexpensive marker of systemic inflammation that has been shown to possess prognostic value in various solid tumors. Wang, marini and syoyanov

studies have also reported the potential of PLR as a prognostic marker in glioma, where elevated PLR is associated with shorter patient survival. Pathophysiologically, an increase in platelet count favors the growth and development of intracranial tumors. Platelets play a role in stimulating angiogenesis, facilitating tumor growth, and promoting intracranial tumor dissemination. Conversely, a decrease in lymphocyte count in glioma cases contributes to impaired immune function, which worsens the patient's general condition and consequently reduces survival. Pathophysiologically, an increase in platelet count favors the growth and development of intracranial tumors. Platelets play a role in stimulating angiogenesis, facilitating tumor growth, and promoting intracranial tumor dissemination. Conversely, a decrease in lymphocyte count in glioma cases contributes to impaired immune function, which worsens the patient's general condition and consequently reduces survival. Therefore, the platelet lymphocyte ratio is a potential biomarker and prognostic indicator in glioma. On the other hand, research on the role of the platelet-lymphocyte ratio as a prognostic marker for glioma in the Indonesian population is absent. The platelet lymphocyte ratio can be a relatively inexpensive, minimal invasive, and user-friendly prognostic biomarker than the more commonly used molecular markers. In this study, researchers evaluated the association between the platelet lymphocyte ratio and the prognosis of glioma patients as assessed by overall survival (OS).

Therefore, the problems formulated in this research are the association between the platelet-lymphocyte ratio and the survival of glioma patients. This study aims to prove the association between the platelet lymphocyte ratio and the survival of glioma patients. This research has theoretical benefits in determining the association between the platelet-lymphocyte ratio and the survival of glioma patients. Likewise, it can provide information regarding the potential of the platelet-lymphocyte ratio as a marker of glioma prognosis for clinicians. It will educate the patients and their families about the prognosis of glioma in a more comprehensive manner. Equally important, it provides an easy, inexpensive, and minimal invasive alternative examination in determining the prognosis of glioma patients. The hypothesis of this study is the existence of an association between a high platelet lymphocyte ratio and the overall survival (OS) of glioma patients. This study aims to demonstrate the association between the platelet-to-lymphocyte ratio (PLR) and the survival of glioma patients. The expected theoretical benefit of this research is to establish the relationship between PLR and glioma patient survival. For clinicians, the findings are anticipated to provide valuable information regarding the potential of PLR as a prognostic marker in glioma. For patients and their families, the study is expected to offer more comprehensive education about glioma prognosis, as well as provide an alternative prognostic assessment that is simple, inexpensive, and minimally invasive. The hypothesis of this study is that a higher platelet-to-lymphocyte ratio is associated with shorter survival/overall survival (OS) in glioma patients

2. METHOD

This was a retrospective cohort study conducted at Dr. Sardjito General Hospital, Yogyakarta, and its affiliated hospitals, including Dr. S. Hardjolukito Air Force Central Hospital, PKU Muhammadiyah Hospital Yogyakarta, and Jogjakarta International Hospital. Dr. Sardjito General Hospital was chosen as the study site because it is one of the major referral healthcare centers in Indonesia, particularly in Central Java, and is equipped with teaching hospitals that have well-established neurosurgical and oncology facilities. Moreover, Yogyakarta has a heterogeneous patient population, as patients come not only from the Special Region of Yogyakarta but also from surrounding areas, including southern Central Java. This diversity allows the data obtained to better reflect real-world clinical conditions. The study period covered January 2017 to October 2022. The target population was all patients diagnosed with glioma in Yogyakarta during the study period.

Consecutive sampling was employed to identify eligible cases from medical records. Inclusion criteria: 1. Diagnosis of glioma confirmed by neuroimaging and histopathology, 2. Availability of complete medical records, including pre-treatment hematological parameters. Exclusion criteria: 1. History of hematologic disorders, 2. History of autoimmune disease. Data

collection in this study was conducted using medical records as the research instrument. The medical records contain documents including patient identity, demographic data, examinations, treatments, procedures, and other healthcare services provided to the patients. This study also utilized electronic medical records accessible through the Integrated Hospital Management Information System (SIMETRIS) of Dr. Sardjito General Hospital, Yogyakarta, via the link. On the homepage, a supporting services feature is available, which includes patient data such as laboratory results, radiological images, as well as radiology and anatomical pathology reports. Relevant data required for the study were extracted from these medical records for subsequent analysis The sample size required minimum sample size was 108, calculated using survival analysis parameters. The final analysis included 149 patients.

Variables Primary outcome: overall survival (OS). Main predictor: platelet-to-lymphocyte ratio (PLR). The platelet-to-lymphocyte ratio (PLR) was obtained from blood samples analyzed in the hospital laboratory. The values were then categorized into two groups, namely high expression and low expression, using the Receiver Operating Characteristic (ROC) curve. Confounders: age, sex, WHO grade, tumor size, tumor location, extent of surgery, Karnofsky Performance Status (KPS). KPS is scoring using objective examination an independent prognostic factor for glioma in both univariate and bivariate analyses, where a KPS score of <70 is associated with shorter survival in glioma patients. Data Collection Data were extracted from medical records and hospital databases, Tumor grading was classified into WHO grades I, II, III, and IV based on histopathological findings in accordance with the 2016 WHO criteria. Tumor size was categorized into two groups: ≥ 6 cm and < 6 cm. Tumor location was classified as either supratentorial or infratentorial. including pre-treatment blood counts, imaging, and pathology reports. Data that was uncomplete or missing was excluded from study. The categorization of PLR values into high and low groups was determined using ROC curve analysis, with the optimal cut-off defined as the value yielding the highest sensitivity and specificity. The corresponding Area Under the Curve (AUC) was calculated to evaluate the accuracy of the selected cut-off. Overall survival was analyzed using Kaplan–Meier survival analysis in relation to PLR and other confounding variables. Cox regression identified independent predictors. Analyses were performed using SPSS v23, with significance at $p < 0.05$, Multivariate analysis was further conducted using Cox regression to assess the relationship between significant variables..

3. RESULT AND DISCUSSION

Result

A total of 149 patients met the inclusion criteria. The median age was 48 years (range: 5–73), with 82.6% aged <60 years. Males comprised 57.7% of the cohort. Most patients (69.1%) had high-grade gliomas (WHO grade III–IV), with glioblastoma (grade IV) being the most frequent histology. The majority of tumors were located in the supratentorial region (91.3%) and measured <6 cm in diameter (51.0%). At admission, 65.8% of patients had a Karnofsky Performance Status (KPS) <70.

The median pre-treatment platelet count was 286 $\times 10^3/\mu L$ (range: 4.7–782), median lymphocyte count was 1.54 $\times 10^3/\mu L$ (range: 0.06–10.82), and median PLR was 190.38 (range: 4.91–6347.15). At the end of follow-up, 77 patients (51.7%) had died.

Tabel *1. Patient* Characteristics (n=149)

	n (%)	Median (min-max)
Demografik Characteristics		
Age		48 (5-73)
Age		
a. <60 Years old	123 (82.6%)	
b. ≥ 60 Years old	26 (17.4%)	
Sexs		
a. Woman	63 (42.3%)	
b. Man	86 (57.7%)	

Clinical Characteristics	
WHO Grade Glioma	
a. I	8 (5.4%)
b. II	38 (25.5%)
c. III	27 (18.1%)
d. IV	76 (51.0%)
WHO Grade Categorik	
a. Low Grade (*grade* I dan II)	46 (30.9%)
b. High Grade (*grade* III dan IV)	103 (69.1%)
Location	
a. Supratentorial	136 (91.3%)
b. Infratentorial	7 (4.7%)
Tumor Size	
a. <6cm	76 (51.0%)
b. ≥ 6 cm	49 (32.9%)
KPS	
a. <70	98 (65.8%)
b. ≥ 70	45 (30.2%)
Last *follow up*	
a. Survive	72 (48.3%)
b. Passed Away	77 (51.7%)
Laboratory Finding	
Platelet (10^3/µL)	286 (4.7-782)
Limfosit (10^3/µL)	1.54 (0.06-10.82)
Platelet to Limfosit	190.38 (4.91-6347.15)

WHO: *World Health Organization*; KPS: *Karnofsky Performace scale*

ROC curve analysis for PLR in predicting mortality yielded an AUC of 0.591 (p = 0.054), indicating weak but measurable discriminative ability. The optimal cut-off value was 236.77, with sensitivity of 42.9% and specificity of 77.8% (Figure 1). Patients were categorized into low PLR (<236.77) and high PLR (≥236.77) groups.

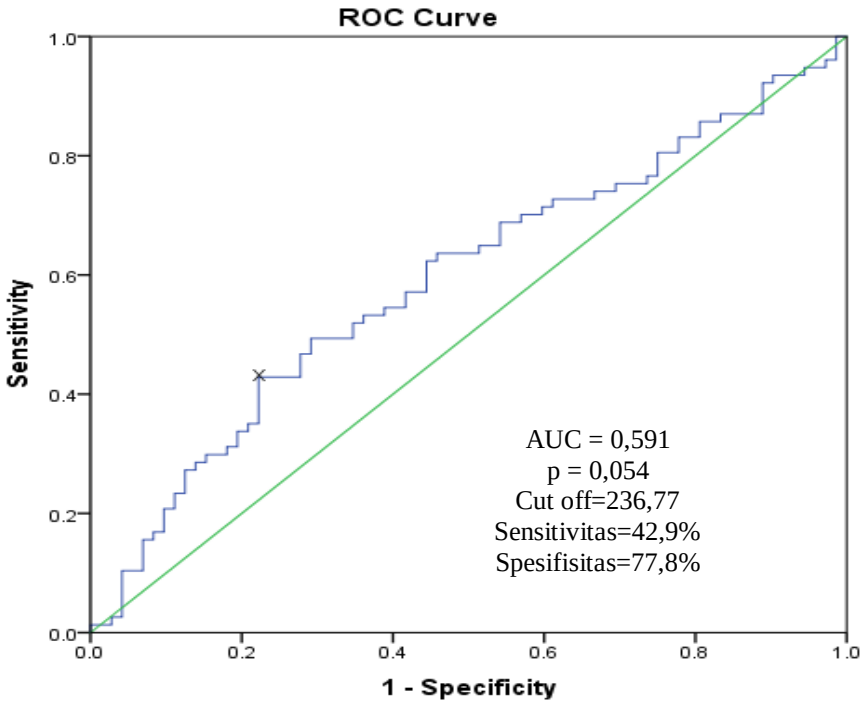

Figure 1 determination of the cut-off point of the Lymphocyte Platelet Ratio (LPR) based on the ROC curve

Kaplan–Meier analysis demonstrated significantly shorter overall survival in the high PLR group compared with the low PLR group (*log-rank p* < 0.001). Median OS was 14.1 months for patients with low PLR and 5.8 months for those with high PLR. These findings are consistent with previous studies, in which elevated PLR was associated with increased mortality risk in glioma patients; for instance, Wang et al. (2018) reported that patients with PLR >200 had significantly shorter OS. The survival curves in our study diverged early and remained clearly separated throughout the follow-up period (Figure 2).

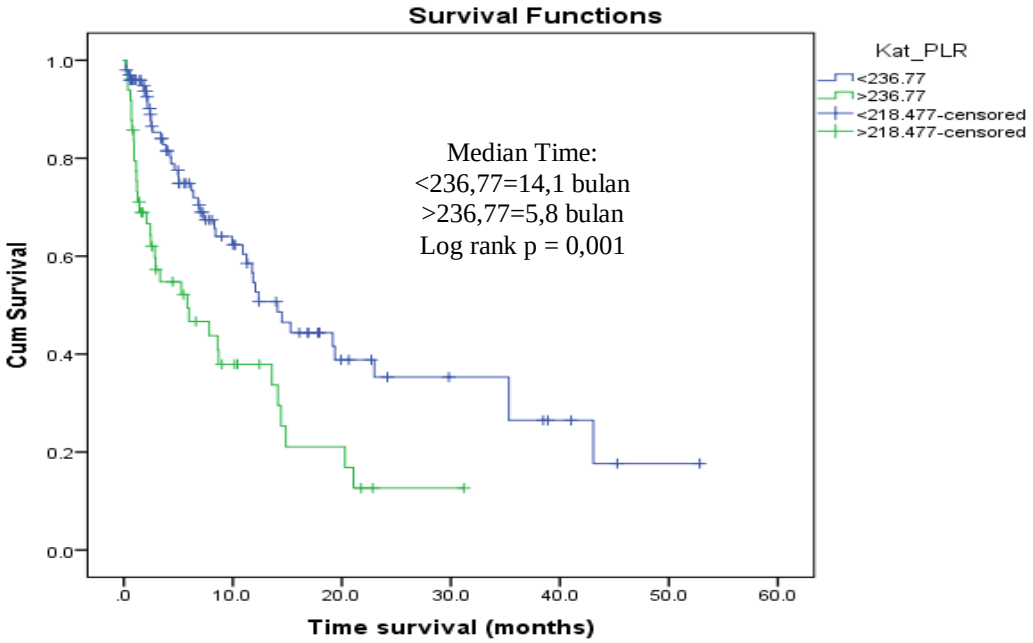

Figure 2. Kaplan Meier graph of the Lymphocyte Platelet Ratio (LPR) against survival

Univariate Cox regression showed that high PLR was significantly associated with increased mortality risk (HR = 2.18; 95% CI: 1.37–3.45; p = 0.001). Other factors significantly associated with OS included age ≥60 years, high WHO grade, KPS <70, tumor size ≥6 cm, and subtotal resection. Similar findings have been reported in previous studies: Yan et al. (2021) found that glioma patients with PLR >134.4 had significantly lower survival (HR = 1.71; 95% CI: 1.14–2.56; p < 0.05), while Wang et al. (2018) reported that PLR ≥200 was associated with shorter survival (HR = 1.915; 95% CI: 1.17–3.13; p = 0.010). Collectively, these studies—including our own—demonstrate that higher PLR is consistently associated with increased mortality risk in glioma patients (Wang et al., 2018; Yan et al., 2021).

Table 2. Multiviariat Analysis

Variable	p	HR (95% IK)
RPL		
a. <236.77	0,021*	1,79 (1,09-2,93)
b. >236.77		
Age		
a. <60 Years Old	0,039*	1,79 (1,03-3,13)
b. ≥ 60 Years Old		
WHO Grades		
a. I		
b. II	0,622	1,46 (0,32-6,59)
c. III	0,155	3,07 (0,65-14,46)
d. IV	0,090	3,53 (0,82-1514)

Cox Proportional Hazards Regression Analysis (Enter Method) of Platelet-to-Lymphocyte Ratio (PLR) and Overall Survival was used In the multivariate Cox regression model, which adjusted for age, sex, WHO grade, tumor size, tumor location, extent of resection, and KPS, high PLR remained an independent predictor of poorer OS (adjusted HR = 2.18; 95% CI: 1.37–3.45; p = 0.001). WHO grade and KPS were also significant independent predictors of OS (Table 3). Variables with $p < 0.25$ in univariate analysis were included in the multivariate model, while only those with $p < 0.025$ proceeded to the final analysis—specifically, PLR, age, and WHO grade. The final multivariate analysis identified both PLR and age as statistically significant predictors of mortality in glioma patients: PLR (HR = 1.79; 95% CI: 1.09–2.93; p = 0.021) and age (HR = 1.79; 95% CI: 1.03–3.13; p = 0.039) (Table 10).

Age has long been recognized as a prognostic factor in adult glioma, with younger patients generally experiencing better outcomes (Dahlrot, 2014). Stark et al. (2012) proposed 60 years as the prognostic age threshold, a finding supported by Wang et al. (2018) and Jia et al. (2022), who reported that patients aged ≥60 years had worse survival—consistent with our results. In addition to age, our findings confirm PLR as a prognostic factor for glioma survival. While some prior studies reported that PLR was not an independent risk factor for glioma outcomes (Wang et al., 2018; Cong et al., 2021; Yan et al., 2021; Marini et al., 2020; Stoyanov et al., 2022), other studies have found significant associations. For example, Yan et al. (2021) observed that glioma patients with PLR >134.4 had a higher mortality risk (HR = 1.71; 95% CI: 1.14–2.56; $p < 0.05$), while Wang et al. (2018) reported shorter survival for those with PLR ≥200 (HR = 1.915; 95% CI: 1.17–3.13; p = 0.010).

Our findings strengthen the evidence for PLR as a readily obtainable, cost-effective prognostic biomarker in glioma. Given its simplicity and accessibility, PLR measurement could be incorporated into routine pre-treatment evaluation, particularly in resource-limited settings, to help guide prognosis estimation and therapeutic decision-making.

Discussion

This study evaluated the association between platelet-lymphocyte ratio (PLR) and overall survival (OS) in glioma patients. The results demonstrated that a high PLR was significantly associated with poorer survival outcomes. Patients with PLR above the determined cut-off (218.477) had higher mortality compared to those with lower PLR, and multivariate Cox regression confirmed PLR as an independent prognostic factor alongside age and WHO grade.

Our findings are consistent with previous reports showing that systemic inflammatory markers, including PLR, neutrophil-lymphocyte ratio (NLR), and lymphocyte-monocyte ratio (LMR), are correlated with prognosis in gliomas and other malignancie. Yan et al. (2021) reported that a PLR cut-off of 134.4 with an AUC of 0.575 could predict survival in diffuse glioma patients, whereas our study found a higher cut-off with slightly better discriminatory power (AUC 0.591). Although the discriminatory quality remains modest, the consistency of findings across studies highlights the biological plausibility of PLR as a surrogate marker of tumor–host interaction.

The prognostic role of PLR may be explained by the dual involvement of platelets and lymphocytes in tumor biology. Platelets promote tumor angiogenesis, invasion, and protection of tumor cells from immune surveillance, while lymphocytes are central to antitumor immune responses. An elevated PLR therefore reflects a pro-tumor systemic environment characterized by enhanced platelet activity and suppressed adaptive immunity.

In our cohort, most patients were male, <60 years, and had high-grade gliomas, aligning with known epidemiological patterns. Age and WHO grade remained strong independent predictors of survival, in line with established literatures. Interestingly, Karnofsky Performance Status (KPS) and tumor size were not independent predictors in the multivariate model, possibly due to interaction with grade and systemic inflammatory status.

This study has several strengths, including a relatively large cohort (149 patients) and the use of objective hematological parameters derived from routine tests. However, some limitations must be noted. First, as a retrospective single-center study, selection bias and missing data cannot be excluded. Second, the AUC value indicates only weak discriminatory ability, suggesting that PLR should not be used as a standalone marker. Third, molecular markers such as IDH mutation

and MGMT methylation, which are important in glioma prognosis, were not available for correlation in this dataset.

Despite these limitations, PLR offers potential clinical utility. It is inexpensive, minimally invasive, and widely available, making it particularly valuable in settings where molecular profiling is not accessible. Future prospective studies with integration of molecular markers and multi-center cohorts are warranted to validate the prognostic role of PLR in gliomas and to explore its utility in guiding individualized therapy.

4. CONCLUSION

This study demonstrates that a high pre-treatment platelet-to-lymphocyte ratio (PLR) is an independent predictor of shorter overall survival in glioma patients. PLR offers several practical advantages as a prognostic biomarker-it is derived from routine blood tests, inexpensive, widely available, and minimally invasive. In resource-limited settings where molecular profiling is not readily accessible, PLR could complement existing prognostic models to guide risk stratification, patient counseling, and treatment planning. Patients with high PLR may warrant closer clinical surveillance, earlier initiation of adjuvant therapy, or inclusion in clinical trials exploring novel immunomodulatory approaches.

The strengths of this study include a relatively large sample size for a single-center cohort, comprehensive adjustment for potential confounding variables, and use of standardized laboratory and imaging data. However, certain limitations should be acknowledged. First, the retrospective design carries the potential for selection and information bias. Second, PLR was measured only at baseline; changes during the course of treatment were not evaluated, which may provide additional prognostic insight. Third, inflammatory markers may be influenced by comorbidities or medications, which were not fully accounted for in our dataset. Finally, molecular tumor markers such as IDH mutation status and MGMT promoter methylation were not included, limiting direct comparison with integrated molecular–histological models.

Future research should include prospective studies with serial PLR measurements, larger multi-center cohorts, and integration of molecular and radiological biomarkers to enhance prognostic accuracy. Moreover, investigating whether targeted modulation of systemic inflammation can improve outcomes in high-PLR glioma patients could provide valuable clinical insights.

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