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Inflammatory composite indicators and clinical features for prognostic factor analysis and malignancy prediction model construction in patients with glioma

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SUMMARY

Introduction/Objective The objective was to evaluate inflammatory composite indicators and clinical features as prognostic factors and develop a predictive model for glioma malignancy grade.

Methods A retrospective analysis of 107 patients with glioma who underwent surgical resection was conducted. Clinical data, including age, sex, body mass index, Karnofsky Performance Status, tumor characteristics and complete blood count parameters, were collected preoperatively and postoperatively. Cox proportional hazards regression was performed to identify independent prognostic factors for progression-free survival (PFS). The receiver operating characteristic curve analysis was used to evaluate the diagnostic performance of inflammatory markers in predicting high-grade glioma.

Results The cohort included 107 patients (mean age: 54.3 ± 13.5 years, 53.3% men). High-grade gliomas (World Health Organization grade IV) accounted for 55.1% of cases. Perioperative neutrophil counts increased significantly, whereas lymphocyte counts remained stable. In multivariate Cox analysis, younger age (hazard ratio 0.93, 95% confidence interval: 0.89–0.98, p = 0.009) was independently associated with improved PFS. The receiver operating characteristic analysis demonstrated that age (area under the curve [AUC] = 0.632, p = 0.019) and preoperative neutrophil-to-lymphocyte ratio (NLR) (AUC = 0.606, p = 0.058) showed potential in predicting high-grade glioma. Spearman correlation analysis revealed a significant negative correlation between Karnofsky Performance Status and NLR.

Conclusions Age represents an independent prognostic factor for PFS in patients with glioma. Preoperative inflammatory markers, particularly NLR, combined with clinical parameters such as age, show promise in predicting glioma malignancy grade.

Keywords: glioma; neutrophils; prognosis; inflammation

INTRODUCTION

Gliomas are the most common primary malignant brain tumors in adults, accounting for approximately 75% of all malignant central nervous system neoplasms [1]. Glioblastoma (GBM) (World Health Organization [WHO] grade IV) is the most aggressive subtype, with median overall survival (OS) of only 12–15 months despite surgery, radiotherapy, and temozolomide [2]. Reliable prognostic biomarkers are urgently needed.

Traditional prognostic factors include age, Karnofsky Performance Status (KPS), extent of resection (EOR) and molecular markers (e.g. isocitrate dehydrogenase [IDH] mutation, O6-methylguanine-DNA methyltransferase [MGMT] promoter methylation) [3, 4]. However, they often require complex testing or subjective assessment.

Inflammation is a cancer hallmark [5]. In gliomas, the tumor microenvironment involves complex interactions between tumor cells and inflammatory infiltrates, including neutrophils and lymphocytes [6]. The neutrophil-to-lymphocyte ratio (NLR), calculated as absolute neutrophil count divided by absolute lymphocyte count, reflects the balance between protumor inflammation and antitumor immunity.

Multiple studies demonstrate NLR's prognostic value in glioma. Chung et al. [7] reported that elevated NLR (≥ 5) following the standard Stupp protocol was associated with worse OS in GBM, suggesting that dynamic NLR changes may track recurrence. A meta-analysis by Yang et al. [8] confirmed that elevated NLR predicted worse OS in GBM (hazard ratio [HR] = 1.63, 95% confidence interval [CI]: 1.23–2.15, p = 0.0007). Higher NLR also correlates with increased tumor grade [7].

Perioperative stress and treatments alter peripheral blood counts. Han et al. [9] found that pretreatment NLR was associated with neutrophil and T-cell infiltration and predicted clinical outcomes in GBM. The EOR remains a key modifiable factor: gross total resection (GTR) improves survival compared with subtotal resection (STR) or biopsy [10, 11].

Functional status, measured by KPS (0–100), is another crucial determinant. Postoperative KPS has superior predictive value over preoperative KPS [12]. Recent research has emphasized

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the importance of maintaining KPS ≥ 50%, which allows patients to live at home and maintain personal care activities, as a key quality-of-life endpoint [13].

Despite NLR's established value, significant gaps remain: perioperative inflammatory dynamics are poorly characterized, the relationship between systemic inflammation and KPS has not been systematically explored and the integrated utility of inflammatory markers for preoperative grade prediction is uncertain. Addressing these gaps could improve preoperative risk stratification and treatment planning.

This study aimed to evaluate the prognostic significance of inflammatory composite indicators and clinical features for progression-free survival (PFS); to analyze perioperative changes in inflammatory markers; to develop a predictive model distinguishing high- from low-grade gliomas using pre-treatment parameters; to explore correlations between inflammatory markers and clinical features to better understand systemic inflammation in glioma.

METHODS

Study design and patient population

This retrospective study included consecutive patients who underwent surgical resection for histologically confirmed glioma at a tertiary center (from January 2017 until December 2025). The institutional ethics committee approved the protocol; informed consent was waived.

The inclusion criteria included age ≥ 18 years, histopathologically confirmed glioma (WHO classification), complete blood count data within seven days preoperatively and postoperatively and complete clinical and follow-up data. The exclusion criteria included prior brain surgery/radiotherapy, active infection/inflammatory disease at surgery, the use of immunosuppressants or corticosteroids (> 8 mg/day dexamethasone equivalent) for > 7 days preoperatively, hematologic disorders and incomplete data.

Data collection and variable definition

Clinical data from electronic medical records included age, sex, body mass index (BMI) (kg/m²), smoking status and preoperative KPS (assessed within 24 hours; scale 0–100, ≥ 80 = normal activity with minor symptoms, < 70 = requires assistance). Additional variables included neurological symptoms, symptom duration and antiepileptic use.

Tumor characteristics on preoperative magnetic resonance imaging (MRI) included maximum diameter (contrast-enhanced T1 or T2-FLAIR), location (lobe, hemisphere), eloquent area involvement (motor/sensory/language/visual cortex, deep grey matter), multifocality and contrast enhancement. Histopathology, as per WHO specification, was low-grade (II), intermediate (III) and high-grade (IV).

Surgical variables included EOR – GTR (≥ 95% removal on postoperative MRI within 48 hours) or STR (75–94% removal) – determined via volumetric analysis (three-dimensional reconstruction).

Laboratory parameters (within seven days pre/postoperatively) included absolute neutrophil, lymphocyte and monocyte counts ($\times 10^9$/L); platelet count ($\times 10^9$/L); NLR; and platelet/lymphocyte ratio (PLR).

Treatment and follow-up

Treatment included maximal safe resection guided by neuronavigation and neurophysiological monitoring. Postoperative treatment was performed by a multidisciplinary board, including adjuvant radiotherapy (60 Gy/30 fractions for high grade, 50.4–54 Gy for intermediate grade) and chemotherapy (temozolomide or other).

The follow-up was every three months for two years, then every six months, and included clinical examination, KPS and MRI. Disease progression was defined in accordance with Response Assessment in Neuro-Oncology criteria. Progression-free survival was defined as time from surgery to progression or death; OS was defined as time from surgery to death or last follow-up.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) based on normality (Shapiro–Wilk test). Categorical variables were expressed as frequencies/percentages. A paired t-test or Wilcoxon's signed-rank test was used to compare preoperative and postoperative blood parameters. An independent t-test or the Mann–Whitney U test was used for two-group comparisons; a χ^2 test or Fisher's exact test was used for categorical variables.

Univariate Cox proportional hazards regression identified potential prognostic factors for PFS. Variables with $p < 0.20$ in univariate analysis, plus clinically recognized prognostic factors, entered the multivariate Cox (backward elimination) regression analysis. Hazard ratios with 95% CIs were calculated (HR > 1: increased risk; HR < 1: protective effect). The proportional hazards assumption was verified using Schoenfeld residuals.

Kaplan–Meier curves visualized PFS; log-rank tests were used to compare survival distributions. Optimal cut-offs for continuous variables were determined via maximally selected rank statistics or receiver operating characteristic (ROC) curve analysis. The ROC analysis evaluated the diagnostic performance of inflammatory markers and clinical variables for predicting high-grade gliomas (WHO grade IV) versus low- or intermediate-grade gliomas. Area under the curve (AUC) values with 95% CIs were calculated; the optimal cut-off was determined using Youden's index (sensitivity+specificity−1). Sensitivity, specificity, positive predictive value and negative predictive value were calculated for each significant predictor.

Spearman's rank correlation coefficients were used to assess relationships between inflammatory markers and clinical features. Correlation strength was weak ($r < 0.3$), moderate ($0.3 \leq r < 0.7$) or strong ($r \geq 0.7$). Correlation matrices with heatmaps were generated.

Table 1. Baseline characteristics of the study population (n = 107)

Variable	Value
Demographics	
Age (years), mean ± SD	54.3 ± 13.5
Age (years), median (range)	55 (21–82)
Sex, male, n (%)	57 (53.3)
Sex, female, n (%)	50 (46.7)
Body mass index (kg/m²), mean ± SD	24.7 ± 3.2
Clinical features	
Preoperative KPS, mean ± SD	79.2 ± 29.7
Preoperative KPS, median (interquartile range)	95 (80–95)
KPS ≥ 80, n (%)	72 (67.3)
KPS < 80, n (%)	35 (32.7)
Tumor characteristics	
Tumor size (cm), mean ± SD	5.45 ± 2.08
Tumor location	
- Frontal lobe, n (%)	41 (38.3)
- Temporal lobe, n (%)	35 (32.7)
- Parietal lobe, n (%)	18 (16.8)
- Other locations, n (%)	13 (12.2)
Eloquent location, n (%)	48 (44.9)
Pathology	
Low grade (II), n (%)	26 (24.3)
Mid grade (III), n (%)	22 (20.6)
High grade (IV), n (%)	59 (55.1)
Surgical Details	
Extent of resection	
- gross total resection (≥ 95%), n (%)	69 (64.5)
- subtotal resection (75–94%), n (%)	38 (35.5)
Preoperative laboratory values	
Neutrophils (× 10⁹/L), mean ± SD	4.81 ± 2.54
Lymphocytes (× 10⁹/L), mean ± SD	1.66 ± 0.68
Platelets (× 10⁹/L), mean ± SD	223 ± 71.4
Neutrophil-to-lymphocyte ratio, mean ± SD	4.21 ± 8.05
Neutrophil-to-lymphocyte ratio, median (interquartile range)	2.85 (1.98–4.52)
Platelet-to-lymphocyte ratio, mean ± SD	162.11 ± 102.02
Adjuvant therapy	
Radiotherapy, n (%)	28 (26.2)
Chemotherapy, n (%)	26 (24.3)

SD – standard deviation; KPS – Karnofsky performance status

All tests were two tailed, with $p < 0.05$ indicating statistical significance. Analyses were conducted using R version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria) with the survival, survminer, pROC and corrplot packages.

RESULTS

Baseline characteristics

A total of 107 patients were included in the final analysis (Table 1). The mean age at diagnosis was 54.3 ± 13.5 years, with 57 male patients (53.3%) and 50 female patients (46.7%). The mean BMI was 24.7 ± 3.2 kg/m²; the mean preoperative KPS was 79.2 ± 29.7 (median: 95). Tumor pathology results were as follows: high-grade (WHO IV) 55.1% (n = 59), intermediate (III) 20.6% (n = 22) and low-grade (II) 24.3% (n = 26). The mean tumor diameter was 5.45 ± 2.08 cm. Frontal lobe tumors were the most common type (38.3%), followed by temporal tumors (32.7%). The eloquent location percentage was 44.9%; GTR was identified in 64.5% of cases and STR in 35.5%.

Preoperative neutrophil count was 4.81 ± 2.54 × 10⁹/L, lymphocyte count was 1.66 ± 0.68 × 10⁹/L and platelet count was 223 ± 71.4 × 10⁹/L. The mean NLR was 4.21 ± 8.05 (median: 2.85, IQR: 1.98–4.52), and the mean PLR was 162.11 ± 102.02. Adjuvant radiotherapy was performed in 28 (26.2%) cases, and chemotherapy in 26 (24.3%), typically for high-grade or incompletely resected tumors.

Perioperative changes in inflammatory markers

Paired analysis (Table 2, Figure 1) showed a significant postoperative neutrophil increase from 4.81 ± 2.54 to 6.57 ± 3.21 × 10⁹/L (mean difference: +1.76, $p < 0.001$). Lymphocytes decreased non-significantly from 1.66 ± 0.68 to 1.6 ± 0.71 × 10⁹/L ($p = 0.391$). Platelets increased from 223 ± 71.4 to 229 ± 88.2 × 10⁹/L ($p = 0.418$), and NLR

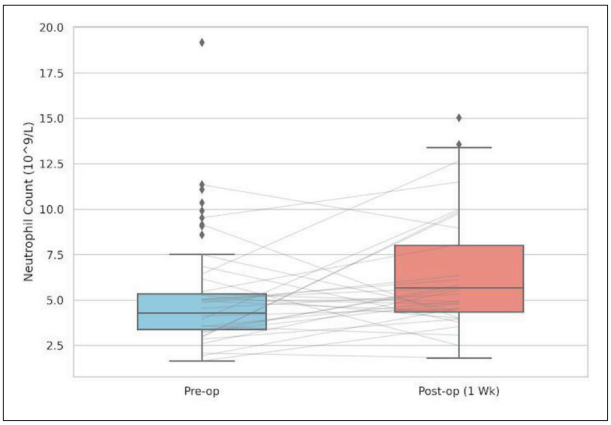


Figure 1. Paired comparison of perioperative neutrophil counts

Table 2. Comparison of preoperative and postoperative blood indices

Indicator	Pre-op mean ± SD	Post-op mean ± SD	Mean difference	95% CI	p	Interpretation
Neutrophils (× 10⁹/L)	4.81 ± 2.54	6.57 ± 3.21	+1.76	1.02–2.50	< 0.001*	Significant increase
Lymphocytes (× 10⁹/L)	1.66 ± 0.68	1.6 ± 0.71	-0.06	-0.18–0.06	0.391	No significant change
Platelets (× 10⁹/L)	223 ± 71.4	229 ± 88.2	+6	-7.2–19.2	0.418	No significant change
Neutrophil-to-lymphocyte ratio	4.21 ± 8.05	4.77 ± 3.94	+0.57	-0.91–2.05	0.466	No significant change
Platelet-to-lymphocyte ratio	162.11 ± 102.02	169.34 ± 115.28	+7.23	-12.45–26.91	0.512	No significant change

SD – standard deviation; CI – confidence interval; *statistically significant at $p < 0.05$

increased from 4.21 to 4.77 (p = 0.466). These findings reflect surgical stress and highlight timing considerations for inflammatory marker assessment.

Univariate analysis of prognostic factors for progression-free survival

Univariate Cox regression (Table 3) identified trends towards better PFS with younger age (HR = 0.97 per year, 95% CI: 0.93–1.01, p = 0.151) and GTR versus STR (HR = 0.49, p = 0.302), and worse prognosis with high-grade pathology (HR = 2.34, p = 0.166). However, none reached statistical significance. Male sex (HR = 0.69, p = 0.508), BMI (HR = 0.97, p = 0.763), preoperative KPS (HR = 1, p = 0.589), tumor size (HR = 1.07, p = 0.637), neutrophil count (HR = 1.12, p = 0.188), NLR (HR = 1, p = 0.924) and PLR (HR = 1, p = 0.782) showed no significant associations. Adjuvant radiotherapy (HR = 6.42, 95% CI: 1.76–23.40, p = 0.005) and chemotherapy (HR = 7.69, 95% CI: 2.09–28.33, p = 0.002) were paradoxically associated with worse PFS, reflecting selection bias (these therapies were preferentially given to patients at higher risk).

Table 3. Univariate Cox regression analysis for progression-free survival

Variable	Hazard ratio	95% CI	p
Age (per year)	0.97	0.93–1.01	0.151
Sex (male *vs.* female)	0.69	0.23–2.05	0.508
Body mass index (per kg/m^2)	0.97	0.79–1.18	0.763
Preoperative Karnofsky performance status (per point)	1.00	0.98–1.01	0.589
Tumor size (per cm)	1.07	0.80–1.45	0.637
Resection (GTR *vs.* STR)	0.49	0.13–1.91	0.302
Pathology (high *vs.* low/mid)	2.34	0.70–7.80	0.166
Eloquent location (yes *vs.* no)	1.12	0.38–3.28	0.838
Preoperative neutrophils	1.12	0.95–1.32	0.188
Preoperative lymphocytes	0.88	0.45–1.73	0.715
Preoperative NLR	1.00	0.94–1.07	0.924
Preoperative PLR	1.00	0.99–1.01	0.782
Radiotherapy (yes *vs.* no)	6.42	1.76–23.40	0.005*
Chemotherapy (yes *vs.* no)	7.69	2.09–28.33	0.002*

CI – confidence interval; GTR – gross total resection; STR – subtotal resection; NLR – neutrophil-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio; *statistically significant at p < 0.05

Table 4. Multivariate Cox proportional hazards model for progression-free survival

Variable	Hazard ratio	95% CI	p
Age (per year)	0.93	0.89–0.98	0.009*
Pathology (high *vs.* low/mid)	4.67	0.48–45.41	0.185
Resection (gross total resection *vs.* subtotal resection)	0.97	0.06–15.12	0.980
Preoperative Karnofsky performance status (per point)	0.99	0.97–1.01	0.252
Preoperative neutrophil-to-lymphocyte ratio	0.99	0.92–1.08	0.902

*statistically significant at p < 0.05

Multivariate Cox regression analysis

Variables with p < 0.20 (age, pathology grade, resection extent, preoperative KPS and neutrophil count / NLR) were entered into multivariate Cox analysis with backward elimination. The final model retained age as the only independent prognostic factor (Table 4). Younger age independently predicted better PFS (HR = 0.93 per year, 95% CI: 0.89–0.98, p = 0.009); each additional year increased the progression hazard by approximately 7%. Pathology grade (p = 0.185), EOR (p = 0.980), KPS (p = 0.252) and NLR (p = 0.902) were not independently significant.

Survival analysis by clinical and pathological factors

Kaplan–Meier curves (Figures 2 and 3) demonstrated clear PFS stratification by pathology grade (log-rank p < 0.001).

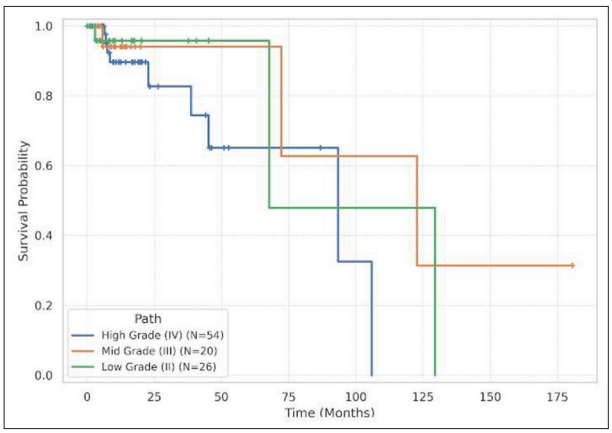


Figure 2. Kaplan-Meier survival analysis by pathology grade; the survival curves demonstrate significant differences in progression-free survival across glioma grades; high-grade [World Health Organization (WHO) grade IV] gliomas (blue line) show the most rapid decline in survival probability, with median progression-free survival of approximately eight months; mid-grade (WHO grade III, brown line) and low-grade (WHO grade II, green line) gliomas demonstrate considerably better survival outcomes; the "+" symbols indicate censored observations; log-rank test p < 0.001

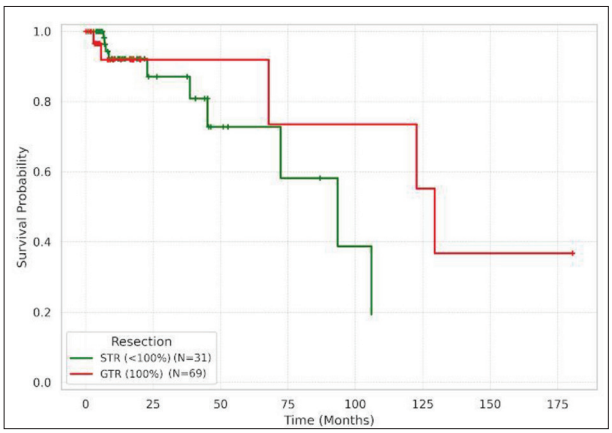


Figure 3. Impact of resection extent on progression-free survival; Kaplan–Meier curves comparing patients who underwent gross total resection [(GTR), red line] *vs.* subtotal resection [(STR), green line]; GTR patients demonstrate consistently higher survival probabilities throughout follow-up, with approximately 70% progression-free at 12 months compared to 55% for STR; log-rank test p = 0.089

Table 5. Diagnostic performance of inflammatory markers and clinical features for predicting high-grade glioma

Variable	AUC	95% CI	p	Cutoff	Sensitivity	Specificity
Age (years)	0.632	0.527–0.737	0.019*	> 58	56.5%	77.3%
Preoperative NLR	0.606	0.499–0.713	0.058	> 1.76	85.5%	34.1%
Preoperative PLR	0.542	0.433–0.651	0.456	> 124.55	68.1%	47.7%
Tumor size (cm)	0.526	0.417–0.635	0.641	> 4	82.6%	22.7%
Preoperative KPS	0.476	0.366–0.586	0.667	≤ 90	62.7%	47.9%

AUC – area under the curve; CI – confidence interval;
NLR – neutrophil-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio;
KPS – Karnofsky performance status;
*statistically significant at p < 0.05

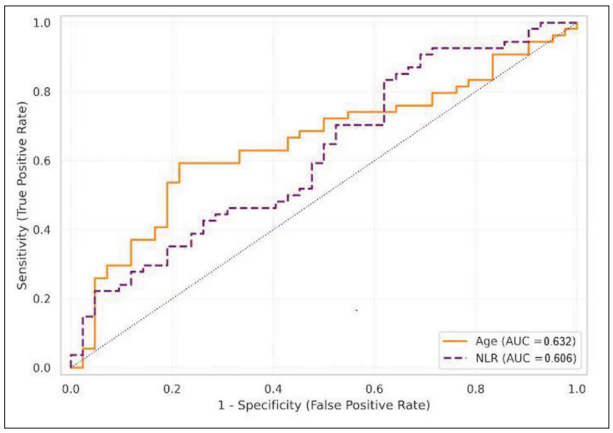


Figure 4. Diagnostic ROC curve analysis for predicting high-grade glioma; the stepped ROC curves display the diagnostic performance of age (orange solid line, AUC = 0.632) and preoperative neutrophil-to-lymphocyte ratio (purple dashed line, AUC = 0.606) in distinguishing high-grade (World Health Organization grade IV) from lower-grade gliomas; the characteristic stepped appearance reflects the finite sample size typical of real-world clinical datasets; the diagonal reference line represents random chance (AUC = 0.5); both markers showed modest but statistically significant or near-significant predictive value

High-grade (WHO IV) gliomas had a median PFS of approximately eight months, whereas lower-grade tumors showed substantially longer survival. Regarding EOR, patients with GTR had higher survival probabilities at all time points than those with STR (12-month PFS: approx. 70% *vs.* 55%), but the log-rank test was not significant (p = 0.089).

Table 6. Spearman correlation matrix of clinical features

Variables	Correlation coefficient (r)	p	Interpretation
KPS *vs.* NLR	-0.453	< 0.001*	Moderate negative correlation
Age *vs.* KPS	-0.387	< 0.001*	Moderate negative correlation
NLR *vs.* PLR	+0.632	< 0.001*	Strong positive correlation
Tumor size *vs.* NLR	-0.110	0.259	No significant correlation
Tumor size *vs.* KPS	+0.088	0.368	No significant correlation
Age *vs.* NLR	+0.156	0.109	Weak positive correlation

NLR – neutrophil-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio;
KPS – Karnofsky performance status;
*statistically significant at p < 0.05

Table 7. Impact of adjuvant therapy on progression-free survival (subgroup analysis)

Treatment	N yes/no	Hazard ratio	95% CI	p	Interpretation
Radiotherapy	28/79	6.42	1.76–23.40	0.005*	Selection bias effect
Chemotherapy	26/81	7.69	2.09–28.33	0.002*	Selection bias effect

CI – confidence interval;
*statistically significant (reflects selection bias rather than treatment harm)

Diagnostic performance of inflammatory markers for predicting high-grade glioma

The ROC analysis (Table 5, Figure 4) evaluated preoperative markers for predicting high-grade (WHO IV) glioma. Age showed moderate discriminative ability (AUC = 0.632, 95% CI: 0.527–0.737, p = 0.019); an optimal cut-off > 58 years yielded a sensitivity of 56.5% and a specificity of 77.3%. Preoperative NLR showed borderline significance (AUC = 0.606, 95% CI: 0.499–0.713, p = 0.058); a cut-off > 1.76 yielded high sensitivity (85.5%) but low specificity (34.1%); PLR (AUC = 0.542, p = 0.456), tumor size (AUC = 0.526, p = 0.641) and preoperative KPS (AUC = 0.476, p = 0.667) showed no significant discriminative ability.

Correlation analysis of clinical features

Spearman correlation analysis (Table 6) revealed a significant negative correlation between preoperative KPS and NLR (r = -0.453, p < 0.001). Age also correlated negatively with KPS (r = -0.387, p < 0.001); NLR and PLR showed a strong positive correlation (r = 0.632, p < 0.001). Tumor size correlated with neither NLR (r = -0.110, p = 0.259) nor KPS (r = 0.088, p = 0.368).

Impact of adjuvant therapy

As shown in Table 7, adjuvant radiotherapy (HR = 6.42, 95% CI: 1.76–23.40, p = 0.005) and chemotherapy (HR = 7.69, 95% CI: 2.09–28.33, p = 0.002) were paradoxically associated with worse PFS, reflecting confounding by indication. Among radiotherapy recipients, 89.3% had high-grade gliomas compared with 42% of non-recipients (p < 0.001). Chemotherapy recipients had larger tumors (6.2 ± 2.3 *vs.* 5.1 ± 1.9 cm, p = 0.012) and lower GTR rates (46.2% *vs.* 72.8%, p = 0.009).

DISCUSSION

The present study evaluated clinical, pathological, treatment-related and systemic inflammatory factors in relation to PFS and the preoperative identification of high-grade glioma. Age was the only variable retained as an independent factor in the multivariable Cox model (HR = 0.93, 95% CI: 0.89–0.98, p = 0.009), confirming the importance of age in prognostic assessment [14]. Pathological grade clearly stratified PFS in the Kaplan–Meier analysis, whereas GTR showed

a favorable but statistically nonsignificant survival trend. Preoperative NLR demonstrated limited, borderline discriminatory ability for high-grade glioma and was significantly associated with functional status. Taken together, these findings suggest that prognosis is not determined by a single marker but by the interaction of tumor aggressiveness, host functional reserve, systemic inflammation, surgical treatment and subsequent treatment selection.

Age, KPS and systemic inflammatory indices should therefore be interpreted as related rather than isolated prognostic domains. Age was moderately and negatively correlated with preoperative KPS (r = -0.387, $p < 0.001$), indicating that older patients tend to have poorer functional status. In parallel, NLR was moderately and negatively correlated with KPS (r = -0.453, $p < 0.001$), suggesting that a greater systemic inflammatory burden was associated with reduced functional capacity. However, the direct correlation between age and NLR was weak and not statistically significant (r = 0.156, $p = 0.109$). This pattern is compatible with, but does not prove, a clinical pathway in which age-related loss of physiological reserve and systemic inflammation jointly contribute to poorer performance status. Because these associations were cross-sectional, KPS cannot be considered a mediator between age, inflammation and PFS on the basis of the present data alone. Moreover, NLR and PLR were strongly correlated (r = 0.632, $p < 0.001$), which is biologically plausible because both indices reflect systemic inflammation and share lymphocyte count as their denominator. Their correlation also indicates that they should not automatically be treated as independent sources of prognostic information. By contrast, tumor size was not correlated with either NLR or KPS, suggesting that systemic inflammation and functional impairment were not simply proxies for radiological tumor size.

The perioperative findings further emphasize the importance of measurement timing. Neutrophil counts increased significantly after surgery, whereas lymphocyte and platelet counts did not change significantly. Although the mean NLR increased numerically from 4.21 to 4.77, this change was not statistically significant ($p = 0.466$). Therefore, the present results support a postoperative neutrophil response to surgical stress but do not establish a significant perioperative increase in NLR. Previous evidence suggests that a marked rise in NLR following tumor resection may be associated with poorer outcomes in GBM [15]. Prospective studies using standardized sampling intervals are needed to determine whether perioperative NLR trajectories provide information beyond baseline inflammatory status and established clinical factors.

In our ROC analysis, preoperative NLR showed moderate predictive value for high-grade glioma (AUC = 0.606), consistent with prior reports. A systematic review confirmed that elevated NLR is consistently associated with high-grade gliomas, although optimal cut-offs varied across studies [16]. Our identified cut-off of 1.76 is lower than many published thresholds, possibly due to differences in study populations, grade distributions or laboratory methods. At this cut-off, NLR demonstrated high sensitivity (85.5%) but low specificity (34.1%), suggesting it may be more useful as a negative predictive marker than a definitive diagnostic tool.

NLR was negatively correlated with preoperative KPS (r = -0.453, $p < 0.001$), suggesting that systemic inflammation contributes to functional decline. Prior research has also reported inverse correlations between KPS and inflammatory markers and has shown that baseline functional status predicts postoperative improvement [17]. Understanding this relationship may enable clinicians to identify patients at risk for poor functional outcomes and potentially implement prehabilitation strategies, although such interventions remain investigational.

EOR showed a favorable but nonsignificant survival trend ($p = 0.089$), contrasting with literature supporting maximal safe resection [18]. Several explanations may account for this discrepancy. First, our relatively modest sample size may have limited statistical power to detect significant differences. Second, the dichotomization of EOR into GTR compared with STR may oversimplify a more nuanced relationship. Third, the prognostic benefit of extensive resection may be most pronounced in specific molecular subtypes, and our study did not stratify by IDH mutation status or other molecular markers due to incomplete data availability.

Despite promising univariate trends, preoperative NLR was not independently prognostic in our multivariate Cox model, diverging from meta-analyses showing that elevated NLR predicts worse OS in GBM [8]. Possible explanations are that our heterogeneous cohort included all glioma grades, whereas supportive literature focuses on GBM; NLR's prognostic value may be grade dependent [19]; and post-treatment or dynamic NLR changes may be more informative than static preoperative values [20].

The paradoxical association of adjuvant radiotherapy/chemotherapy with worse PFS reflects confounding by indication, as these therapies were preferentially given to patients at higher risk. This well-documented phenomenon underscores the need for appropriate statistical adjustment and cautious interpretation. Future studies using propensity score matching may help address such selection bias.

Inflammatory markers could serve as surrogate biomarkers for treatment response and surveillance. Unlike imaging, peripheral blood markers offer objective, non-invasive and cost-effective monitoring [21]. Serial NLR measurements may detect early progression before radiological changes.

Mechanistically, neutrophils promote tumor progression via matrix metalloproteinases and vascular endothelial growth factor and suppress antitumor immunity [22]. Lymphocytes mediate antitumor responses, and lymphopenia reflects impaired immunity [23]. Thus, NLR represents a clinically measurable proxy for tumor-immune equilibrium.

Immunotherapies (e.g., immune checkpoint inhibitors, CAR T-cell therapy) have limited success [24]. Baseline inflammation may predict response, and elevated NLR might indicate poor benefit. Inflammatory markers could become companion biomarkers.

The clinical translation of inflammatory markers as prognostic tools requires careful consideration of cut-off values, measurement standardization and integration into decision-making frameworks. Unlike molecular markers, which typically have biologically defined thresholds, inflammatory markers are continuous variables subject to laboratory variation and influenced by numerous confounding factors, including infection, stress, medications and comorbidities [25]. Efforts to standardize collection protocols, define universal cut-offs through large prospective studies and develop validated algorithms will be essential for clinical implementation.

This study has several limitations. First, the retrospective single-center design may have introduced selection bias and limit generalizability. Second, the modest sample size lacked sufficient statistical power for subgroup analyses, and the heterogeneous follow-up durations further limited comprehensive survival assessment. Notably, molecular marker data (IDH mutation, MGMT promoter methylation) were unavailable, despite the 2021 WHO classification emphasizing their fundamental role in glioma diagnosis and prognostication [26]; IDH mutation and MGMT methylation strongly influence survival and treatment response [27]. Additionally, we did not evaluate post-treatment inflammatory marker dynamics or their association with disease recurrence, which warrant future investigation.

Despite these limitations, our study provides valuable insights into the interplay between systemic inflammation, clinical features and glioma prognosis. The demonstration of a significant correlation between NLR and functional status provides biological plausibility for the use of inflammatory markers as prognostic tools. The independent prognostic value of age reinforces its importance in contemporary glioma management. The modest but significant predictive value of age and NLR for high-grade pathology suggests potential utility in preoperative risk stratification and surgical planning.

CONCLUSION

In conclusion, the present findings support a multidimensional interpretation of prognosis in glioma. Age provided independent prognostic information in the multivariable model, pathological grade reflected tumor aggressiveness, EOR represented a potentially modifiable treatment factor and KPS reflected the patients' functional reserve. Furthermore, NLR and PLR characterized systemic inflammatory status but were closely related to each other and should not be regarded as independent predictors. The association between higher NLR and lower KPS suggests a clinically relevant connection between systemic inflammation and functional impairment, whereas the absence of correlations with tumor size indicates that these measures capture information not provided by tumor dimensions alone. Given the limited discrimination of individual markers, future models should integrate clinical, pathological, molecular, treatment-related and longitudinal inflammatory variables and should undergo external validation before being used for individual patient counselling or treatment selection.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Hebei YanDa Hospital. Due to the nature of retrospective study and anonymized patient information, informed consent is waived with the approval of Ethics Committee of Hebei YanDa Hospital.

Availability of data and materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Authors' contributions

Wang BH and He YC conceived of the study, and Wang BH and He YC participated in its design and data analysis and statistics and Wang BH and He YC helped to draft the manuscript. All authors read and approved the final manuscript.

Conflict of interest: None declared.

REFERENCES

1. Park YW, Vollmuth P, Foltyn-Dumitru M, Sahm F, Ahn SS, Chang JH, et al. The 2021 WHO Classification for Gliomas and Implications on Imaging Diagnosis: Part 1-Key Points of the Fifth Edition and Summary of Imaging Findings on Adult-Type Diffuse Gliomas. J Magn Reson Imaging. 2023;58(3):677–89. [DOI: 10.1002/jmri.28743] [PMID: 37069792]
2. Wang LM, Englander ZK, Miller ML, Bruce JN. Malignant Glioma. Adv Exp Med Biol. 2023;1405:1–30. [DOI: 10.1007/978-3-031-23705-8_1] [PMID: 37452933]
3. Xu H, Fan Z, Jiang S, Sun M, Chai H, Zhu R, et al. Integrating Multiplex Immunohistochemistry and Machine Learning for Glioma Subtyping and Prognosis Prediction. MedComm (2020). 2025;6(5):e70138. [DOI: 10.1002/mco2.70138] [PMID: 40264576]
4. Santosh V, Rao S. A review of adult-type diffuse gliomas in the WHO CNS5 classification with special reference to Astrocytoma, IDH-mutant and Oligodendroglioma, IDH-mutant and 1p/19q codeleted. Indian J Pathol Microbiol. 2022;65(Supplement):S14–S23. [DOI: 10.4103/ijpm.ijpm_34_22] [PMID: 35562130]
5. Levine AB, Nobre L, Das A, Milos S, Bianchi V, Johnson M, et al. Immuno-oncologic profiling of pediatric brain tumors reveals major clinical significance of the tumor immune microenvironment. Nat Commun. 2024;15(1):5790. [DOI: 10.1038/s41467-024-49595-1] [PMID: 38987542]
6. Li J, Ross JL, Hambardzumyan D, Brat DJ. Immunopathology of Glioblastoma. Annu Rev Pathol. 2026;21(1):135–62. [DOI: 10.1146/annurev-pathmechdis-042524-025950] [PMID: 41061166]

7. Chung MW, Tzeng CC, Huang YC, Wei KC, Hsu PW, Chuang CC, et al. Neutrophil-to-lymphocyte ratio dynamics: prognostic value and potential for surveilling glioblastoma recurrence. BMC Cancer. 2025;25(1):709. [DOI: 10.1186/s12885-025-14118-8] [PMID: 40241016]
8. Yang C, Wen HB, Zhao YH, Huang WH, Wang ZF, Li ZQ. Systemic Inflammatory Indicators as Prognosticators in Glioblastoma Patients: A Comprehensive Meta-Analysis. Front Neurol. 2020;11:580101. [DOI: 10.3389/fneur.2020.580101] [PMID: 33117267]
9. Han S, Liu Y, Li Q, Li Z, Hou H, Wu A. Pre-treatment neutrophil-to-lymphocyte ratio is associated with neutrophil and T-cell infiltration and predicts clinical outcome in patients with glioblastoma. BMC Cancer. 2015;15:617. [DOI: 10.1186/s12885-015-1629-7] [PMID: 26341881]
10. Zheng Y, Saffari SE, Low DCY, Lin X, Ker JRX, Ang SYL, et al. Lobectomy versus gross total resection for glioblastoma multiforme: A systematic review and individual-participant data meta-analysis. J Clin Neurosci. 2023;115:60–5. [DOI: 10.1016/j.jocn.2023.07.016] [PMID: 37487449]
11. Mier-García JF, Ospina-Santa S, Orozco-Mera J, Ma R, Plaha P. Supramaximal versus gross total resection in Glioblastoma, IDH wild-type and Astrocytoma, IDH-mutant, grade 4, effect on overall and progression free survival: systematic review and meta-analysis. J Neurooncol. 2023;164(1):31–41. [DOI: 10.1007/s11060-023-04409-0] [PMID: 37561356]
12. Chambless LB, Kistka HM, Parker SL, Hassam-Malani L, McGirt MJ, Thompson RC. The relative value of postoperative versus preoperative Karnofsky Performance Scale scores as a predictor of survival after surgical resection of glioblastoma multiforme. J Neurooncol. 2015;121(2):359–64. [DOI: 10.1007/s11060-014-1640-x] [PMID: 25344883]
13. Ohba S, Teranishi T, Matsumura K, Kumon M, Kojima D, Fujiwara E, et al. Factors involved in maintaining Karnofsky Performance Status (≥ 50%) in glioblastoma, IDH-wildtype patients treated with temozolomide and radiotherapy. Sci Rep. 2025;15(1):1750. [DOI: 10.1038/s41598-025-85339-x] [PMID: 39799218]
14. Yang PH, Tao Y, Luo J, Paturu M, Lu HC, Ramkissoon S, et al. Multivariate analysis of associations between clinical sequencing and outcome in glioblastoma. Neurooncol Adv. 2022;4(1):vdac002. [DOI: 10.1093/noajnl/vdac002] [PMID: 35156038]
15. Mohammad AH, Sakalla R, Davalan W, Ruiz-Barerra MA, Jatana S, Khalaf R, et al. Rise in post-resection neutrophil-to-lymphocyte ratio correlates with decreased survival in glioblastoma patients. Neurooncol Adv. 2025;7(1):vdaf014. [DOI: 10.1093/noajnl/vdaf014] [PMID: 40051660]
16. Qi Z, Cai J, Meng X, Cai S, Tang C, Lang L. Prognostic value of preoperative inflammatory markers among different molecular subtypes of lower-grade glioma. J Clin Neurosci. 2022;96:180–6. [DOI: 10.1016/j.jocn.2021.10.006] [PMID: 34802893]
17. Lee S, Kim M. Analysis of Patients with Glioblastoma Treated with Standard 6-Week Chemoradiation Followed by Temozolomide: Treatment Outcomes and Prognostic Factors. Medicina (Kaunas). 2025;61(3):376. [DOI: 10.3390/medicina61030376] [PMID: 40142187]
18. Nikova AS, Vlotinou P, Karelis L, Karanikas M, Birbilis TA. Gross total resection with fluorescence could lead to improved overall survival rates: a systematic review and meta-analysis. Br J Neurosurg. 2022;36(3):316–22. [DOI: 10.1080/02688697.2021.1950637] [PMID: 34313526]
19. Li B, Gao B, Zhu HJ, Luwor RB, Lu J, Zhang L, et al. The Prognostic Value of Preoperative Inflammatory Markers for Pathological Grading of Glioma Patients. Technol Cancer Res Treat. 2024;23:15330338241273160. [DOI: 10.1177/15330338241273160] [PMID: 39099463]
20. Ma L, Li G, Wei M. Neutrophil-to-Lymphocyte Ratio and Its Changes are Related to Grade II-IV Glioma Recurrence. Cancer Manag Res. 2020;12:9429–34. [DOI: 10.2147/CMAR.S267523] [PMID: 33061630]
21. Jarmuzek P, Kozlowska K, Defort P, Kot M, Zembron-Lacny A. Prognostic Values of Systemic Inflammatory Immunological Markers in Glioblastoma: A Systematic Review and Meta-Analysis. Cancers (Basel). 2023;15(13):3339. [DOI: 10.3390/cancers15133339] [PMID: 37444448]
22. Mahmud Z, Rahman A, Mishu ID, Kabir Y. Mechanistic insights into the interplays between neutrophils and other immune cells in cancer development and progression. Cancer Metastasis Rev. 2022;41(2):405–32. [DOI: 10.1007/s10555-022-10024-8] [PMID: 35314951]
23. Szlachetko JA, Hofmann-Vega F, Budeus B, Schröder LJ, Dumitru CA, Schmidt M, et al. Tumor cells that resist neutrophil anticancer cytotoxicity acquire a prometastatic and innate immune escape phenotype. Cell Mol Immunol. 2025;22(5):527–40. [DOI: 10.1038/s41423-025-01283-w] [PMID: 40155451]
24. Liu Y, Zhou F, Ali H, Lathia JD, Chen P. Immunotherapy for glioblastoma: current state, challenges, and future perspectives. Cell Mol Immunol. 2024;21(12):1354–75. [DOI: 10.1038/s41423-024-01226-x] [PMID: 39406966]
25. Serban GM, Tamas CI, Tamas F, Balasa AF. Preoperative Immune-Inflammatory Status of the Patients With Newly-Diagnosed Glioblastoma – Could It Genuinely Predict Their Survival? Cureus. 2023;15(8):e43802. [DOI: 10.7759/cureus.43802] [PMID: 37731450]
26. Jamshidi P, Brat DJ. The 2021 WHO classification of central nervous system tumors: what neurologists need to know. Curr Opin Neurol. 2022;35(6):764–71. [DOI: 10.1097/WCO.0000000000001109] [PMID: 36226717]
27. Eid M, Alset D, Timoshkina N, Gvaldin D, Rostorguev E, Kavitskiy S, et al. IDH mutation and MGMT methylation status in glioblastoma and other gliomas patients: a Russian retrospective cohort study. J Egypt Natl Canc Inst. 2025;37(1):36. [DOI: 10.1186/s43046-025-00296-w] [PMID: 40377745]

Инфламаторни композитни индикатори и клиничке карактеристике за анализу прогностичких фактора и изградњу модела за предвиђање малигнитета код болесника са глиомом

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САЖЕТАК

Увод/Циљ Циљ рада био је процена инфламаторних композитних индикатора и клиничких карактеристика као прогностичких фактора и развој модела за предвиђање степена малигнитета глиома.

Методе Спроведена је ретроспективна анализа 107 болесника са глиомом који су подвргнути хируршкој ресекцији. Прикупљени су клинички подаци, укључујући старост, пол, индекс телесне масе, Карнофски индекс, карактеристике тумора и параметре комплетне крвне слике, преоперативно и постоперативно. Коксова регресија пропорционалних ризика примењена је за идентификацију независних прогностичких фактора преживљавања без прогресије. Анализа *ROC* криве коришћена је за процену дијагностичких перформанси инфламаторних маркера у предвиђању глиома високог степена малигнитета.

Резултати Кохорта је обухватила 107 болесника (средња старост 54,3 ± 13,5 година, 53,3% мушкараца). Глиоми високог степена малигнитета (IV степен према класификацији Светске здравствене организације) чинили су 55,1% случајева. Број неутрофила у периоперативном периоду значајно је порастао, док је број лимфоцита остао стабилан. У мултиваријантној Коксовој анализи, млађа старост (*HR* = 0,93, 95% *CI* 0,89–0,98, *p* = 0,009) била је независно повезана са бољим преживљавањем без прогресије болести; *ROC* анализа показала је да старост (*AUC* = 0,632, *p* = 0,019) и преоперативни однос неутрофила и лимфоцита (*AUC* = 0,606, *p* = 0,058) показују потенцијал у предвиђању глиома високог степена малигнитета. Спирманова корелациона анализа открила је значајну негативну корелацију између Карнофског индекса и односа неутрофила и лимфоцита.

Закључак Старост представља независни прогностички фактор преживљавања без прогресије болести код болесника са глиомом. Преоперативни инфламаторни маркери, посебно однос неутрофила и лимфоцита, у комбинацији са клиничким параметрима, као што је старост, показују потенцијал у предвиђању степена малигнитета глиома.

Кључне речи: глиом; неутрофили; прогноза; упала