

Preoperative peripheral blood routine indicators as predictors of prognosis and diagnosis in glioma under the 2021 World Health Organization classification

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Abstract. Multiple hematological indicators have been shown to be associated with the prediction and prognosis of gliomas. The present study aimed to explore the value of 22 preoperative peripheral blood routine indicators in the diagnosis and prognosis prediction of glioma. Patients with glioma were grouped according to the 2021 World Health Organization (WHO) guidelines for glioma. The correlations among preoperative peripheral blood routine indicators in all patients with glioma were assessed using Spearman's rank correlation analysis. The relationships between these indicators and glioma molecular subtypes were evaluated using ANOVA, independent samples t-test and logistic regression analysis. Analysis of prognosis prediction was conducted using multivariate Cox regression. Based on the WHO 2021 guidelines, patients with glioma were classified into 92 cases of astrocytoma, 77 cases of oligodendroglioma and 402 cases of glioblastoma. Among 22 routine blood indicators, 10 low-correlation indicators were identified, 9 of which demonstrated significant value for the diagnosis of glioma. Among them, the neutrophil percentage (NEUT%)

showed a notable predictive power in glioma molecular subtypes classification. In the study of overall survival (OS) prediction in patients with glioma, 6 biomarkers were found to be significantly associated with OS. Through statistical analysis, 4 independent biomarkers were selected to construct a multivariable Cox regression model. However, in the regression model, NEUT% was identified as the sole statistically significant biomarker. Despite its statistical significance, the results indicated that NEUT% had limited effectiveness in predicting OS in patients with glioma. Certain preoperative blood indicators had significant predictive value for glioma diagnosis, with NEUT% emerging as a key biomarker for predicting the presence of glioma. For prognosis, although NEUT% showed a modest effect size, it was significantly associated with poor outcomes in patients with glioma. Monitoring preoperative NEUT% levels is therefore clinically important for glioma diagnosis and prognosis.

Introduction

Glioma, originating from brain glial cells, is the most common malignant primary brain tumor in adults, accounting for 4% of primary central nervous system tumors and 81% of malignant brain tumors (1-3). According to the World Health Organization (WHO) classification of central nervous system tumors (4), gliomas are named and classified based on a combination of molecular characteristics-such as mutations in the IDH1/2 genes, 1p/19q codeletion, TERT promoter mutation, and homozygous deletion of CDKN2A/2B-along with histological phenotypes, which together provide precise guidance for glioma treatment and improve prognosis.

Currently, histopathological examination of tumor specimens obtained through surgical resection or stereotactic biopsy is considered the gold standard for the classification and grading of gliomas (3). Medical imaging techniques, such as computed tomography (CT) (5) and magnetic resonance imaging (MRI) (6), are important for cancer staging and follow-up after glioma treatment (7). However, these methods are often expensive and not widely accessible, typically only

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Abbreviations: HCT, hematocrit; RDW-CV, red cell distribution width-coefficient of variation; LYMPH#, lymphocyte count; MCH, mean corpuscular hemoglobin; BASO#, basophil count; EOS#, eosinophil count; PLT, platelet count; PDW, platelet distribution width; PCT, plateletcrit; NEUT%, neutrophil percentage; NEUT#, neutrophil count

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being performed on patients who already exhibit adverse symptoms (8).

By contrast, blood indicators have been well established for cancer screening and early diagnosis, monitoring treatment response and predicting recurrence (9-11). Inflammation and immunity are important aspects of the hallmarks of cancer, playing a notable role in tumor development and progression (12). In previous years, several studies have shown that some inflammation-related biomarkers derived from preoperative peripheral blood routine tests such as the neutrophil-to-lymphocyte ratio (NLR) (13,14), lymphocyte-to-monocyte ratio (15), platelet-to-lymphocyte ratio (PLR) (16) and their combinations are able to refine patient stratification for treatment and predict survival outcomes in various cancers, including gastric cancer, colorectal cancer, hepatocellular carcinoma, ovarian cancer and non-small cell lung cancer (17-19). However, preoperative peripheral blood routine tests typically include >20 biomarkers, and the combined effects of all these indicators on the diagnosis and prognosis of gliomas have not yet been systematically studied under the new WHO 2021 guidelines (4).

Based on the role of systemic inflammation in tumor progression, the present study hypothesized that preoperative blood indicators could predict glioma diagnosis and prognosis. The present study aimed to systematically evaluate 22 routine blood indicators for their diagnostic and prognostic value in glioma under the WHO 2021 classification.

Patients and methods

Patients and healthy controls (HCs). The preoperative peripheral blood routine tests were conducted and retrospectively analyzed. All patients were confirmed to have glioma by the pathology department of the First Affiliated Hospital of Nanjing Medical University (Nanjing, China), and were classified according to the 2021 WHO classification of central nervous system tumors (4). The inclusion criteria were as follows: i) Patients had no previous antitumor treatments, including surgery, radiotherapy or chemotherapy; and ii) they underwent routine blood tests and biochemical examinations within 1 week prior to surgery. The exclusion criteria were: i) Patients with a history of other malignant tumors; ii) patients with acute or chronic inflammatory diseases; iii) individuals with diabetes, heart disease, hypertension, thyroid dysfunction or autoimmune diseases; iv) patients who received steroid treatment within the last 6 months; and v) patients with incomplete case and follow-up data.

Data collection. The present study included clinical data from 571 patients with glioma who visited The First Affiliated Hospital of Nanjing Medical University between December 2014 and September 2021, along with 1,899 HCs from the hospital's Health Examination Center during the same period (Table I). Retrospective analysis compared a total of 22 indicators between the HC group and glioma group, including: Hemoglobin concentration (HGB); mean corpuscular hemoglobin concentration (MCHC); hematocrit (HCT); monocyte count (MONO#); white blood cell count (WBC); monocyte percentage (MONO%); red blood cell count (RBC); red cell distribution width-coefficient of variation (RDW-CV);

lymphocyte percentage (LYMPH%); lymphocyte count (LYMPH#); mean corpuscular volume (MCV); mean corpuscular hemoglobin (MCH); mean platelet volume (MPV); basophil percentage (BASO%); basophil count (BASO#); eosinophil count (EOS#); eosinophil percentage (EOS%); platelet count (PLT); platelet distribution width (PDW); plateletcrit (PCT); neutrophil percentage (NEUT%); and neutrophil count (NEUT#). Hematological indicators were measured using 3 ml of fasting venous blood collected in the morning that was subsequently mixed in a sodium citrate anticoagulant tube and analyzed with a Sysmex AC-500 (Sysmex Corporation) fully automated immunoassay analyzer. All data were obtained from the last test conducted within the week prior to surgery. Enrolled patients were followed up via outpatient visits or phone calls. Follow-up occurred every 3 months for the first 2 years post-surgery, every 6 months from the third to the fifth year, and then twice annually thereafter until death or loss to follow-up. The survival endpoint for the present study was tumor-related death or the date of the last follow-up, with the last follow-up date being May 1, 2023. Overall survival (OS) was defined as the time from the first day after surgery until death or the date of the last follow-up.

Statistical analysis. Categorical variables were presented as case numbers, while continuous variables were expressed as the mean $\pm$ standard deviation. One-way ANOVA tests were performed to compare continuous variables across multiple groups, followed by Tukey's post-hoc test for pairwise comparisons. To address multicollinearity, the correlations among 22 preoperative peripheral blood routine indicators were analyzed using Spearman correlation analysis, and biomarkers with a correlation coefficient $|r| < 0.35$ were retained to reduce redundancy. The optimal thresholds for preoperative blood indicators were determined using receiver operating characteristic (ROC) curves and binary logistic regression was applied. Survival analysis was performed using the Kaplan-Meier (K-M) method and differences between groups were assessed with log-rank tests. Biomarkers with multicollinearity were excluded based on variance inflation factor (VIF) calculations and the remaining biomarkers were included in the Cox proportional hazards model. The proportional hazards assumption was verified by plotting Schoenfeld residuals. The model's performance was evaluated using the concordance index (C-index) and calibration curves for 3-year survival rates. All statistical analyses were conducted using R software (version 4.2.2; R Foundation for Statistical Computing). $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Clinical characteristics of patients. The HC group comprised 1,034 males (54.45%) and 865 females (45.55%), with an age range of 18 to 84 years and a median age of 48 years. The glioma group included 332 males (58.14%) and 239 females (41.86%), with an age range of 19 to 84 years and a median age of 56 years (Table I). Age was higher in the glioma group compared with the HC group (mean $\pm$ SD: 54.19 $\pm$ 13.77 vs. 47.54 $\pm$ 13.97 years, $P = 0.002$). The sex distribution did not differ between groups (male, 58.14 vs. 54.45%; $\chi^2 = 3.21$,

Table I. Clinical characteristics of glioma patients by World Health Organization grade.

Group	Total cases, n	Age, mean $\pm$ standard deviation	Gender, n (%)	Cases with prognostic information, n (%)	Survival/death, n (%)
Glioma	571	54.19 $\pm$ 13.77	Male 332 (58.14) Female 239 (41.86)	397 (69.53)	185/212 (46.60/53.40)
Astrocytoma	92	43.02 $\pm$ 12.42	Male 51 (55.43) Female 41 (44.57)	67 (72.8)	45/22 (67.16/32.84)
Oligodendroglioma	77	46.86 $\pm$ 10.12	Male 44 (57.14) Female 33 (42.86)	63 (81.8)	60/3 (95.24/4.76)
Glioblastoma	402	58.16 $\pm$ 12.87	Male 267 (66.41) Female 155 (33.59)	267 (66.4)	79/188 (29.59/70.41)
Healthy controls	1899	47.54 $\pm$ 13.97	Male 1034 (54.45) Female 865 (45.55)	-	-

$P=0.073$). The distribution of patient data was as follows: i) Patients were separated into the HC group ($n=1,899$) and the glioma group ($n=571$); and ii) within the glioma group, patients were divided into three molecular subtypes: Astrocytoma ($n=92$), oligodendroglioma ($n=77$) and glioblastoma ($n=402$). Peripheral blood routine data (comprising 22 indicators) from 1,899 HCs and 571 patients with glioma were analyzed using one-way ANOVA, with results presented as the mean $\pm$ standard deviation (Table SI).

Correlation analysis of preoperative peripheral blood routine indicators. Due to the presence of multiple interrelated preoperative peripheral blood routine indicators, such as the NEUT% and NEUT#, EOS% and EOS#, retaining all indicators would affect the accuracy of subsequent analyses. Therefore, the present study first performed a Spearman correlation analysis of the 22 biomarkers and visualized the results in a heatmap (Fig. 1A). A total of 10 indicators with low correlation coefficients ($|r|<0.35$) (Fig. 1B) were retained for further study. The present study assessed the distribution differences of the same biomarkers between HCs and different glioma molecular subtypes (astrocytoma, oligodendroglioma and glioblastoma) (Fig. 1C-L, Table SI). HCs displayed significantly higher levels in HCT, RDW-CV, MCH, BASO#, EOS# and PDW compared with all glioma subtypes ($P<0.0001$). Conversely, NEUT% demonstrated a significant increase in value with the progression of glioma grades when compared with the HC group, and patients diagnosed with glioblastoma showed the highest levels compared with lower-grade gliomas and HCs ($P<0.0001$) (Fig. 1K). Despite significant differences between HCs and oligodendroglioma ($P=0.0364$) and between oligodendroglioma and glioblastoma ($P=0.0181$), no statistically significant difference was observed in MONO% with the progression of glioma grades (Fig. 1E).

Binary logistic regression model for differentiating glioma molecular subtypes using preoperative peripheral blood routine indicators. To construct the binary logistic regression model, all of the biomarkers were first transformed into binary classification data based on their optimal cut-off values. Data greater than or equal to the optimal threshold were recorded

as high-level, while the remaining data were classified as low-level (Table SII). Subsequently, a binary logistic regression model was used to test the classification performance of the remaining 10 biomarkers between the HC group and glioma group. The results indicated that, except for EOS#, all other biomarkers showed significant associations with the classification outcomes (Fig. 2A). Among them, the odds ratios (OR) for WBC, MONO% and NEUT% were 2.20 (95% CI: 1.73-2.80; $P<0.001$), 1.71 (95% CI: 1.37-2.14; $P<0.001$) and 3.26 (95% CI: 2.60-4.09; $P<0.001$), respectively, which means that as the levels of these biomarkers increased, the risk of developing glioma also increased significantly. By contrast, a decrease in the levels of the remaining six biomarkers indicated that the likelihood of developing glioma in healthy individuals significantly increased. This suggested that lower levels of these biomarkers were negatively associated with health. The ROC curve analysis for the classification model showed an area under the curve (AUC) of 0.9293 ($P<0.0001$), indicating excellent classification performance in differentiating the HC group from the glioma group (Fig. 2B).

A similar model was also constructed for the classification of the low-grade glioma (LGG) and high-grade glioma (HGG) groups using the nine biomarkers that showed significant effects in the aforementioned binary logistic regression model. Astrocytoma and oligodendroglioma were classified as LGGs, while glioblastoma was classified as a HGG. The results showed that the PLT (OR, 0.63; $P=0.025$) and NEUT% (OR, 3.17; $P<0.001$) were identified as key biomarkers for distinguishing between LGG and HGG. A decrease in PLT was associated with a significantly higher risk of developing HGG in patients with glioma, while an increase in NEUT% indicated a significantly elevated risk of HGG progression. However, the remaining biomarkers did not show any significant differences ($P>0.05$) (Fig. 2C). The ROC analysis yielded an AUC of 0.6900 ($P<0.0001$), suggesting some discriminative potential; however, the sub-0.70 AUC indicates limited performance and should not be taken as evidence of a strong diagnostic marker (Fig. 2D).

Association of preoperative blood routine indicators with survival outcomes in patients with glioma. To evaluate whether preoperative blood routine indicators can predict survival (OS)

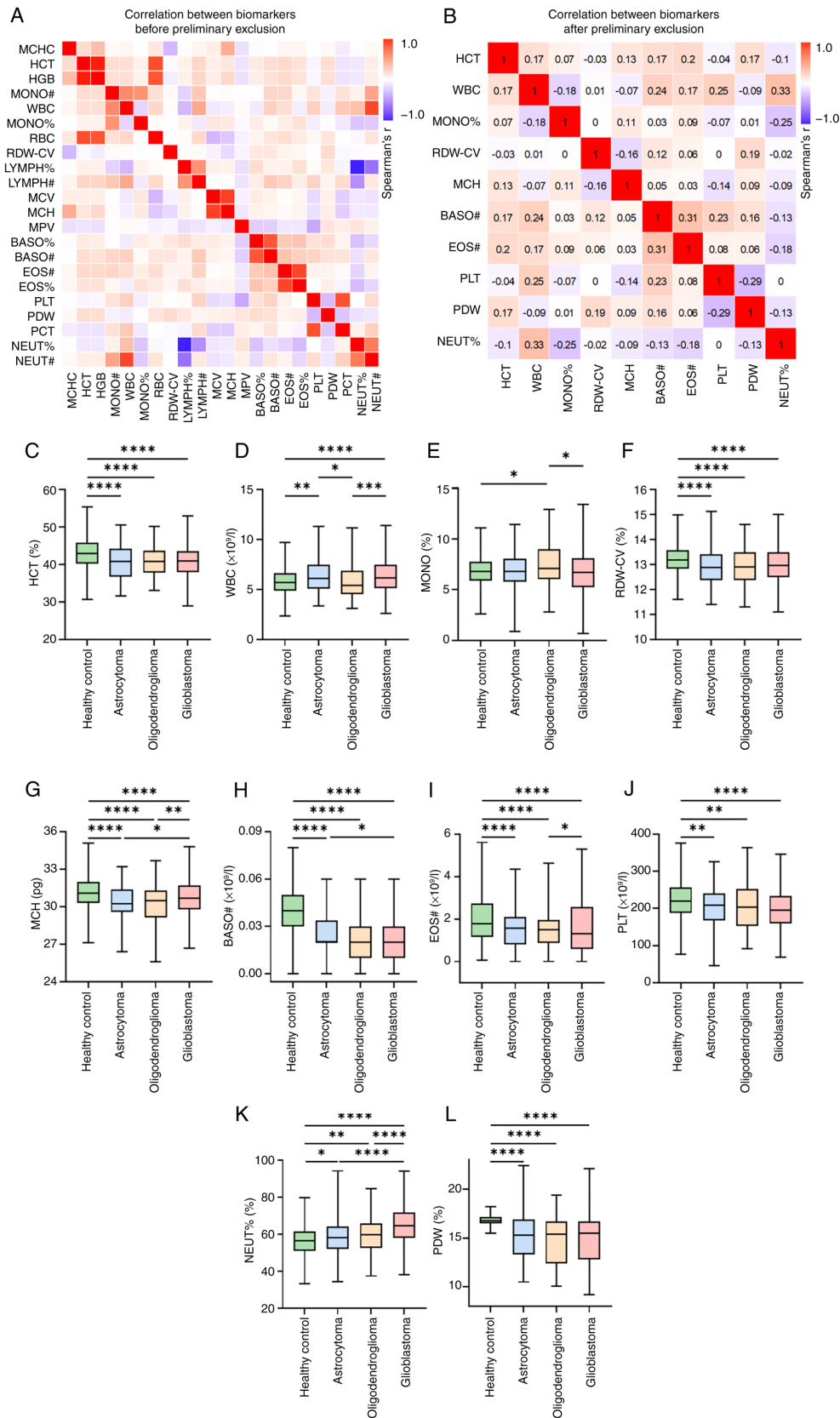


Figure 1. Correlations between preoperative peripheral blood routine indicators. (A) Spearman correlation coefficients for all 22 biomarkers from preoperative peripheral blood routine tests. (B) Spearman correlation coefficients among 10 biomarkers after preliminary exclusion. A correlation coefficient of $|r| < 0.35$ was used as the screening criterion. (C) Distribution of HCT across healthy controls, astrocytoma, oligodendroglioma and glioblastoma. Distribution of (D) WBC, (E) MONO, (F) RDW-CV, (G) MCH, (H) BASO#, (I) EOS#, (J) PLT, (K) NEUT% and (L) PDW across the four groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ and **** $P < 0.0001$. MCHC, mean corpuscular hemoglobin concentration; HCT, hematocrit; HGB, hemoglobin; MONO#, monocyte count; WBC, white blood cell count; MONO%, monocyte percentage; RBC, red blood cell count; RDW-CV, red cell distribution width-coefficient of variation; LYMPH%, lymphocyte percentage; LYMPH#, lymphocyte count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MPV, mean platelet volume; BASO%, basophil percentage; BASO#, basophil count; EOS#, eosinophil count; EOS%, eosinophil percentage; PLT, platelet count; PDW, platelet distribution width; PCT, plateletcrit; NEUT%, neutrophil percentage; NEUT#, neutrophil count.

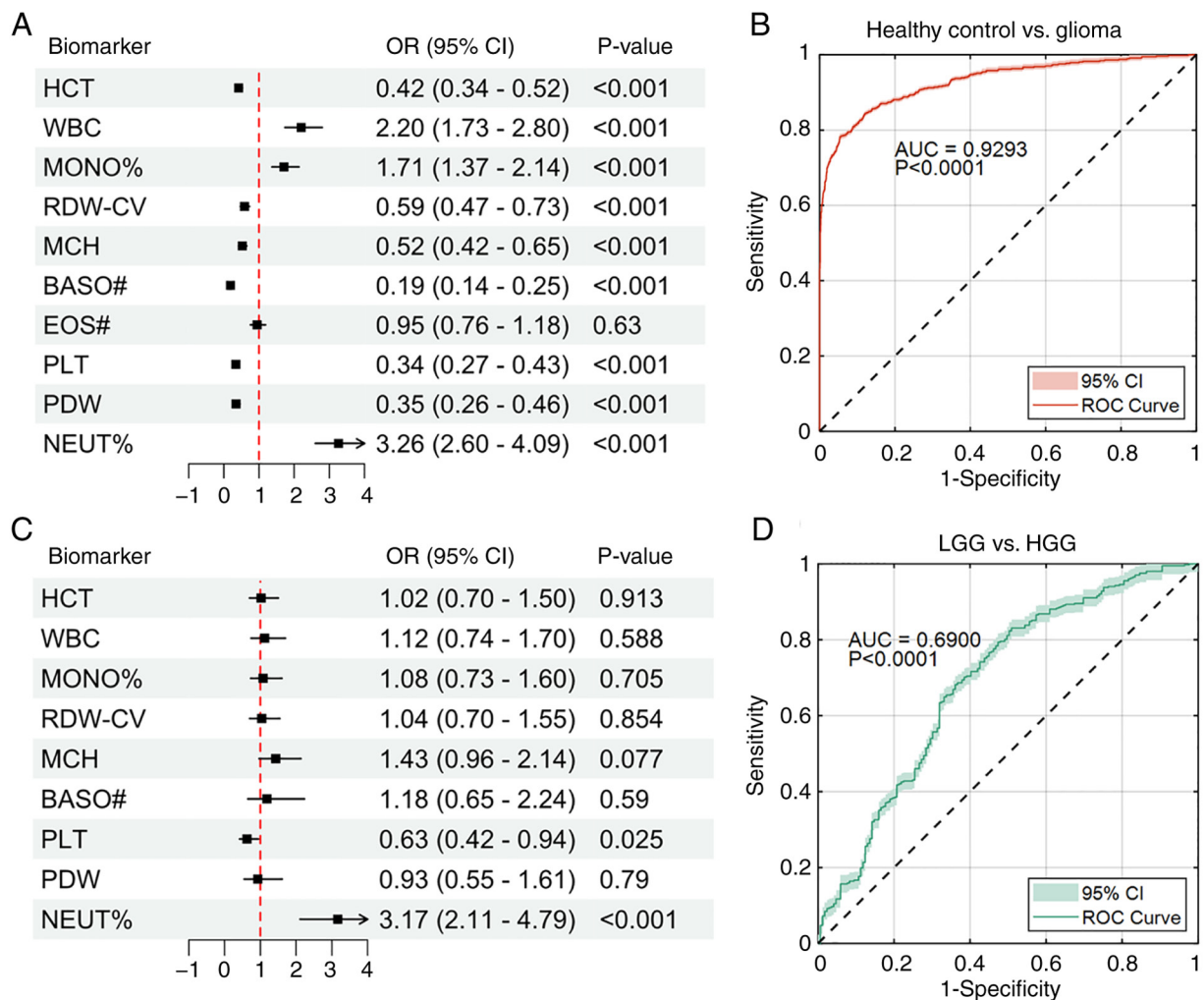


Figure 2. Results of binary logistic regression between different groups with preoperative blood routine indicators. (A) Forest plot of binary logistic regression comparing the effects of biomarkers in classification of healthy control group vs. glioma group. (B) ROC curve analysis for the classification model in A. (C) Forest plot of binary logistic regression comparing the effects of biomarkers in the classification of LGG vs. HGG. (D) ROC curve analysis for the classification model in C. ROC, receiver operating characteristic; LGG, low-grade glioma; HGG, high-grade glioma; OR, odds ratio; CI, confidence interval; AUC, area under curve; HCT, hematocrit; WBC, white blood cell count; MONO%, monocyte percentage; RDW-CV, red cell distribution width-coefficient of variation; MCH, mean corpuscular hemoglobin; BASO#, basophil count; PLT, platelet count; PDW, platelet distribution width; NEUT%, neutrophil percentage.

in patients with glioma, patients with complete prognostic information were selected in the present study based on the WHO 2021 glioma grading guidelines (4). The group included 67 patients with astrocytoma, 63 patients with oligodendroglioma and 267 patients with glioblastoma. Survival analysis was first performed using the K-M method, with log-rank tests assessing intergroup differences. K-M survival curves were plotted for all 22 preoperative blood routine indicators and 6 biomarkers were statistically significant, as shown in Fig. 3 (all $P<0.05$). The results showed that these 6 biomarkers significantly affected the OS of the patients with glioma. Since LYMPH% and LYMPH#, NEUT% and NEUT# were highly clinically correlated (Fig. 1A), it was decided to include LYMPH#, MONO%, PCT and NEUT% in the multivariate Cox regression analysis. Previously, the VIF was calculated for these indicators and plotted in Table II, which showed that all Variance Inflation Factor (VIF) values were low (MONO%=1.34, LYMPH#=1.88, PCT=1.09, NEUT%=1.16), indicating that multicollinearity was not a concern in the present model.

Subsequently, a multivariable Cox regression analysis was performed, and residual plots were generated using the Schoenfeld residuals method (Fig. 4A). These plots indicated that the residual distributions of the remaining 4 indicators were uniform, suggesting independence from time and their suitability for inclusion in the multivariable Cox regression analysis (Table II). PCT showed a protective trend but did not reach statistical significance ($P=0.116$). NEUT% was the only independent prognostic factor with statistical significance ($P<0.001$). Although the associated hazard ratio of 1.035 indicated a relatively small effect size, NEUT% elevation was consistently and significantly associated with poor prognosis.

The model showed good overall fit (likelihood ratio $\chi^2=22.45$, $df=4$, $P<0.0001$), acceptable discrimination (C -index=0.62, $SD=0.02$) (data not shown) and good 3-year calibration (Fig. 4B). The predicted probabilities, indicated by the red curve in Fig. 4B, align well with the actual observed outcomes, depicted by the gray dashed line, indicating that the model has relatively high predictive accuracy.

Table II. Results of VIF between different biomarkers and multivariable Cox regression analysis.

Biomarker	VIF	β	$S_{\bar{x}}$	Wald χ^2	HR	95% CI	P-value
MONO%	1.341141	0.017	0.039	0.186	1.017	0.943-1.097	0.666
LYMPH#	1.878677	0.119	0.175	0.462	1.126	0.798-1.588	0.496
PCT	1.091518	-2.198	1.398	2.469	0.111	0.007-1.253	0.116
NEUT%	1.163272	0.035	0.009	12.776	1.035	1.016-1.055	<0.001

VIF, variance inflation factor; β , regression coefficient; $S_{\bar{x}}$, sample mean; HR, hazard ratio; CI, confidence interval; MONO%, monocyte percentage; LYMPH#, lymphocyte count; PCT, plateletcrit; NEUT%, neutrophil percentage.

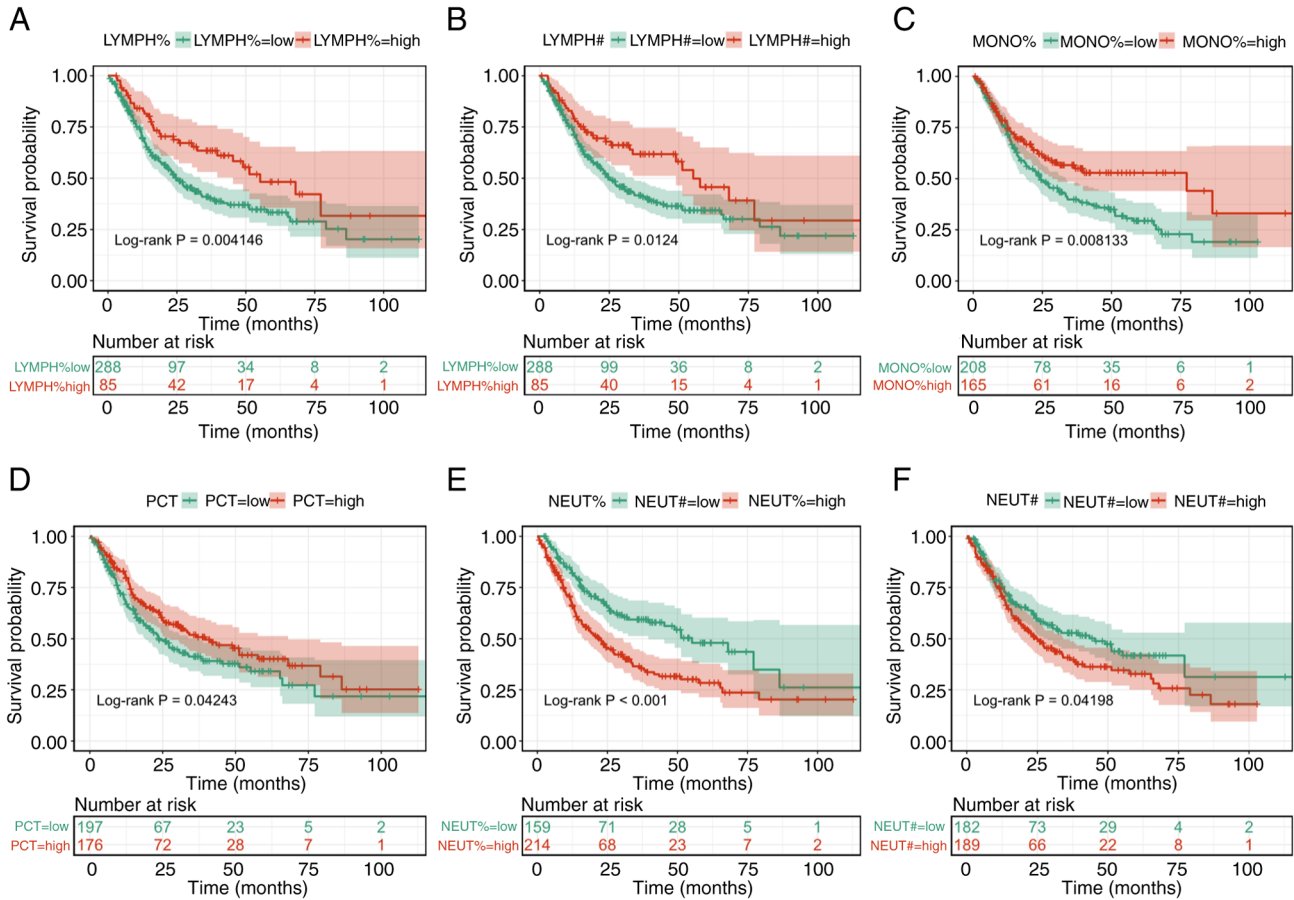


Figure 3. Kaplan-Meier survival curves for different biomarkers in the glioma group. Survival curves were stratified by baseline (A) LYMPH%, (B) LYMPH#, (C) MONO%, (D) PCT, (E) NEUT% and (F) NEUT# levels. The curves compared overall survival probabilities between low- and high-level groups defined by biomarker thresholds. LYMPH%, lymphocyte percentage; LYMPH#, lymphocyte count; MONO%, monocyte percentage; PCT, plateletcrit; NEUT%, neutrophil percentage; NEUT#, neutrophil count.

Discussion

The early diagnosis of glioma is important for patient treatment and recovery. It can be achieved via imaging modalities such as CT, MRI and positron emission tomography-CT (5,6), but routine peripheral blood examination has the advantage of simplicity and can cover a wider population. Existing studies have shown that multiple hematological indicators are associated with the prediction and prognosis of gliomas. Blood inflammatory markers, such as NLR (13,14) and PLR (16), have been identified as useful for the early detection and staging of gliomas. This study assessed preoperative peripheral blood

routine indicators and explored their correlations with the integrated diagnosis (incorporating both histology and molecular subtypes), tumor grade, and prognosis in gliomas.

In the present study, significant differences were found between the healthy group and the glioma group in the following 7 indicators: HCT, RDW-CV, MCH, BASO#, EOS#, PDW and NEUT%. Many of these indicators are known to be influenced by the systemic inflammatory and nutritional status of patients. In this context, a study by Han *et al* (20) reported that low preoperative levels of serum albumin, a well-established marker of malnutrition and inflammation (21), are associated with shorter survival

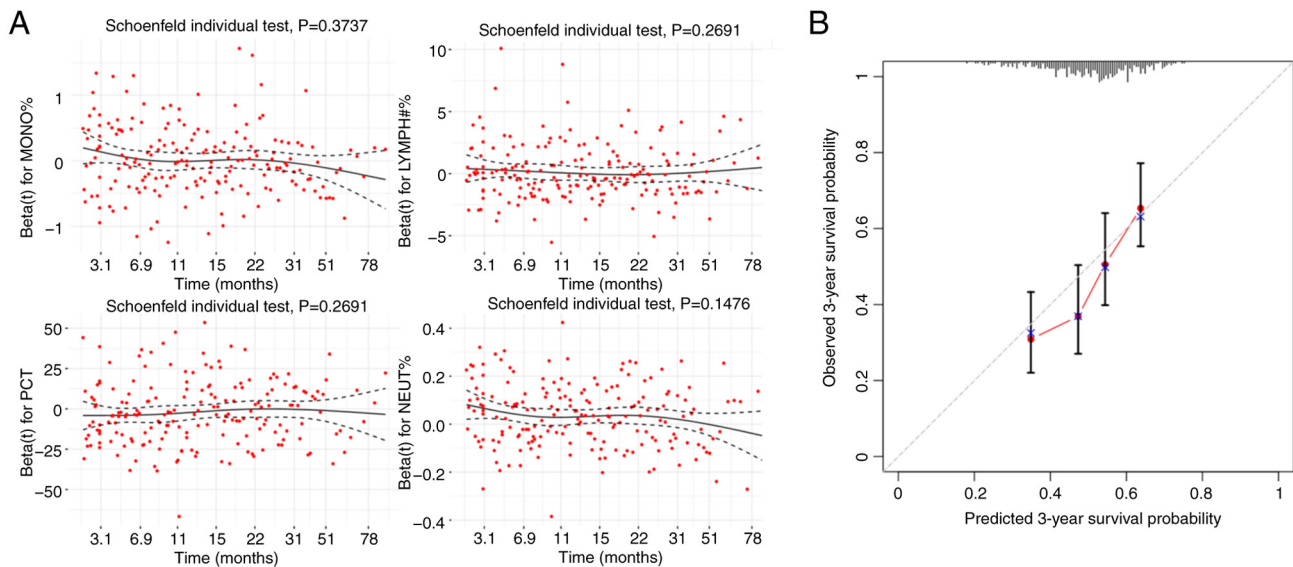


Figure 4. Evaluation of the multivariable Cox regression model. (A) The Schoenfeld residual tests for the Cox hazards model. The solid lines represented smoothing spline fits to the plot with the dashed lines representing the 95% CI around the fit. (B) 3-yearpp calibration curve for the multivariable Cox regression model. CI, confidence interval; MONO%, monocyte percentage; LYMPH#, lymphocyte count; PCT, plateletcrit; NEUT%, neutrophil percentage.

in patients with glioblastoma. Low albumin levels typically reflect malnutrition and inflammatory status in patients (21); patients with glioma often experience significant changes in their nutritional status, especially as the tumor progresses and treatment advances, leading to a higher prevalence of malnutrition and weight loss. The present study found a significant difference in MCH between the healthy and glioma groups, consistent with prior research on anemia-related hematologic alterations in cancer, including glioma (21-24). Here, MCH is cited as a marker of anemia, linking this finding to the preceding discussion of malnutrition and inflammation (low albumin) (21). HCT, RDW-CV and MCH are highly correlated hematologic markers of anemia, which are associated with the development of a variety of tumors, such as prostate cancer (22-24). In addition to anemia- and nutrition-related markers, tumor-associated inflammation and immune responses can affect peripheral blood counts; therefore, inflammation/immune activity may manifest as changes in indicators such as BASO# and NEUT%. A study by Zheng *et al* (25) first reported elevated preoperative NLR and derived NLR in patients with glioma. Subsequent studies by Li *et al* (26) and Stepanenko *et al* (27) further supported that systemic inflammatory responses, particularly neutrophil-dominated immunity, play an important role in glioma progression. A study presented by Liang *et al* (28) reported that increased neutrophil infiltration in tumors is significantly associated with glioma grade. In the present study, it was found that the distribution levels of the neutrophil percentage gradually increased across the groups of healthy individuals, astrocytoma, oligodendroglioma and glioblastoma. This suggested that for healthy individuals, NEUT% was a risk factor for developing glioma, while for those with glioma, it was a risk factor for developing glioblastoma.

Inflammatory responses may play an important role in the progression of gliomas (29,30), particularly the elevated levels of neutrophils in preoperative peripheral blood, which may reflect chronic inflammation in the tumor microenvironment

that is closely associated with tumor growth and invasion. The NEUT% not only served as an independent prognostic factor for patients with glioma but may also be an effective indicator for early identification of high-risk patients with glioma. The present study may provide an important clinical reference and future studies could integrate other indicators for a more comprehensive prognostic assessment. In summary, NEUT% holds significant potential in the diagnosis, molecular subtyping and prognostic evaluation of gliomas, warranting further investigation into its mechanisms in glioma and clinical applications.

Despite the promising findings of the present study, several limitations should be acknowledged: i) Age differed between the glioma and HC groups, but age was not incorporated into the analyses. Because age is associated with both disease risk and outcomes, the lack of age adjustment may introduce residual confounding and could partly account for some observed associations. Future work should include age (and other baseline covariates) as adjustment variables, perform stratified analyses or apply matching/weighting approaches to mitigate this bias. ii) Sample size disparity-while the overall number of patients was substantial (n=571), subgroup analyses for rare molecular subtypes, such as oligodendroglioma (n=88) and glioblastoma (n=402), may have lacked statistical power; iii) model performance-the prognostic model exhibited moderate discriminative ability (C-index, 0.62), indicating a need for integrating complementary biomarkers, such as genetic or imaging markers, to enhance clinical utility.

In conclusion, the present study demonstrated that the combination of certain preoperative peripheral blood routine indicators has significant predictive value for glioma diagnosis. NEUT% exhibited significant predictive power for glioma diagnosis and warrants close attention. Although NEUT% showed a limited impact in the prediction of the OS of patients with glioma, it was significantly associated with poor outcomes in patients with glioma. The NEUT% level in preoperative peripheral blood tests holds clinical significance

for both the diagnosis and prognosis of glioma and should be carefully monitored in clinical practice.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YYo and YW conceived and designed the study. QY, JN and JZ acquired the clinical data. YYu and ZS assisted with patient enrollment and clinical data interpretation. QY, JN, JZ, XF and XC analyzed and interpreted the data. XF and XC performed statistical analyses, developed analysis pipelines, and ensured data reproducibility. YYu developed the data visualization pipeline. YYu and QY drafted the manuscript. YYu, ZS, YW, XF and XC critically revised the manuscript for important intellectual content. ZS provided critical expertise on the 2021 WHO classification of gliomas. YYo and YW supervised the study. YYo, YYu and YW confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was completed with ethics committee approval from The First Affiliated Hospital of Nanjing Medical University (approval no. 2024-SR-1144).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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