Clinical and Translational Oncology
https://doi.org/10.1007/s12094-026-04251-6

RESEARCH ARTICLE

Longitudinal analysis of systemic inflammatory biomarkers in glioblastoma patients: an exploratory single-center analysis

Yener Şahin[1] · Dilek Gül[2] · Mustafa Şenses[1] · Onur Erdoğan[1] · Mustafa Sakar[1] · Beste Melek Atasoy[3]

Received: 15 November 2025 / Accepted: 21 January 2026
© The Author(s) 2026

Abstract

Purpose To explore the systemic inflammatory biomarker changes throughout the entire treatment period from the perspective of the extent of surgical resection and their possible role in predicting survival in glioblastoma.

Methods A retrospective analysis was performed on 41 glioblastoma patients who underwent either gross total resection (GTR, n = 14) or subtotal resection (STR, n = 27), followed by adjuvant radiotherapy (60 Gy) with concurrent and adjuvant temozolomide. Inflammatory biomarkers, including neutrophil–lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR), systemic inflammatory index (SII), and systemic inflammation response index (SIRI), were calculated from routine blood tests. These biomarkers were measured at specific times: preoperatively, before radiotherapy, after chemoradiotherapy, at the sixth cycle of temozolomide, and at radiological and/or clinical progression. Survival outcomes were analyzed using the Kaplan–Meier method.

Results Median follow-up was 21 months. Patients with GTR had significantly better 2-year progression-free survival (42.9% vs. 18.5%, p = 0.033) and overall survival (50% vs. 33.3%, p = 0.045) compared to those with STR. Inflammatory biomarker levels remained higher in the STR group both after RT and following the sixth cycle of temozolomide than in the GTR group. Changes in biomarker levels were not affected by the interval between surgery and radiotherapy, Ki-67 status, the number of chemotherapy cycles, age, or gender.

Conclusion Long-term patterns of systemic inflammatory biomarkers may reflect a higher inflammatory burden and a poorer prognosis in patients with glioblastoma. The predictive role of these biomarkers should be evaluated in prospectively collected, molecularly characterized cohorts.

Keywords Glioblastoma · Inflammatory biomarkers · Radiotherapy · Surgical resection · Temozolomide

Introduction

Glioblastomas (GBM, IDH-wild type, CNS WHO grade 4) are the most common primary malignant brain tumors. Standard therapy includes maximal safe resection, radiation therapy, and temozolomide [1]. Despite these treatments, the median survival is about 14 months [2]. In glioblastomas, malignant cells induce inflammation in the tumor microenvironment and invade surrounding structures. The tumor microenvironment contains high levels of inflammatory mediators, including monocyte chemotactic proteins (MCPs) and granulocyte colony-stimulating factor (G-CSF) [3]. Recent studies have shown that inflammatory biomarkers can predict progression-free survival (PFS) and overall survival (OS) in GBMs, as in most cancer types [4]. Inflammatory biomarkers are blood-based markers that reflect the level of systemic inflammation. In cancer patients, these markers are commonly used to estimate tumor-related inflammatory activity and the interaction between the tumor and the immune system. Simple ratios calculated from routine blood counts include the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Monocyte-to-Lymphocyte Ratio (MLR), Systemic Immune Inflammation

✉ Beste Melek Atasoy
bmatasoy@yahoo.com

[1] Department of Neurosurgery, Marmara University School of Medicine, Istanbul, Türkiye

[2] Clinic of Radiation Oncology, Ministry of Health-Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye

[3] Department of Radiation Oncology, Marmara University School of Medicine, Fevzi Çakmak Mah. Muhsin Yazıcıoğlu Cad. No: 8Pendik, 34899 Istanbul, Türkiye

Index (SII), and Systemic Immune Response Index (SIRI), which are the main blood cell count-derived inflammatory biomarkers associated with systemic inflammation [5, 6, 7].

Recent research has shown that, in some tumor types, inflammatory biomarkers are associated with the Ki-67 proliferation index, and higher levels of these biomarkers are linked to higher tumor grade and shorter progression-free and overall survival [8]. However, this relationship has not been clearly established in glioblastoma. In this cohort, Ki-67 was analyzed together with inflammatory biomarkers [1, 2]. Moreover, the systemic inflammatory dynamics during multimodal treatment remain has not been defined in glioblastoma. Most previous studies have assessed inflammatory biomarkers at a single preoperative or postoperative time point, without considering their longitudinal behavior [3].

The extent of surgical resection in glioblastoma is among the most important prognostic indicators. The literature reports that gross total resection (GTR) is superior to subtotal resection (STR) or biopsy. This study aims to examine systemic inflammatory biomarker changes throughout the entire treatment period, from the perspective of the extent of surgical resection, and their possible role in predicting survival in glioblastoma. and to assess their clinical significance.

Materials and methods

This retrospective study was approved by our faculty's ethics committee (date: September 2024, number: 09.2024.1002) to analyze and publish the data from patients who completed treatment and follow-up. The medical records of patients who underwent surgical intervention for GBM at our center between 2016 and 2021 were reviewed retrospectively. Forty-one patients who underwent surgery and completed all follow-up and adjuvant treatments at our institution were included in the analysis. To avoid interference, patients who were hospitalized or in intensive care for any reason during any treatment were excluded. All patients received adjuvant radiotherapy (range, 34–60 Gy) with concurrent temozolomide (75 mg/m^2/day) and at least 6 cycles of adjuvant temozolomide (200 mg/m^2 on days 1–5 of each month). Karnofsky Performance Status was 70 or higher at the time of surgical resection, during adjuvant radiotherapy, and at follow-up since the blood test results were obtained. All patients received a standardized corticosteroid regimen in accordance with institutional practice. Hence, dexamethasone was administered at a dose of 16 mg/day in the preoperative period. Postoperatively, corticosteroids were tapered with dose reduction every five days and discontinued by approximately 20 days after surgery. During radiotherapy, dexamethasone was administered at a dose of 2 to 4 mg/day.

A single tumor was defined as one contrast-enhancing lesion on preoperative MRI. Multiple tumors were defined as two or more separate, nonconnected contrast-enhancing lesions at diagnosis. Diffuse infiltrative tumors without clearly distinct lesions were not considered multiple tumors. The extent of resection was assessed using early postoperative MRI (within 24–48 h). Gross total resection was defined as no visible residual contrast-enhancing tumor, whereas subtotal resection was defined as residual contrast enhancement.

Molecular data were retrieved retrospectively from routine pathology reports. Epidermal growth factor receptor (EGFR) amplification was available for approximately half of the cohort and was recorded only when present in patient files. Methylated-DNA–protein-cysteine methyltransferase (MGMT) promoter methylation analysis was available in only one patient, and telomerase reverse transcriptase (TERT) promoter mutation and cyclin-dependent kinase inhibitors (CDKN)2A/B statuses were not assessed because they were not part of routine testing during the study period.

Neutrophil, platelet, monocyte, and lymphocyte counts were obtained from complete blood counts (CBC) performed at five time points: the day before surgery (Preop), before radiotherapy (Pre-RT), after radiotherapy (Post-RT), after chemotherapy at the end of treatment (Post-CT), and at disease progression. Disease progression was defined based on radiological and/or clinical progression during routine follow-up, in accordance with the Response Assessment in Neuro-Oncology (RANO) criteria. Subsequently, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) values were calculated.

The inflammatory biomarkers were calculated from absolute peripheral blood cell counts obtained from complete blood counts as follows:

- Neutrophil-to-lymphocyte ratio (NLR) = neutrophil count/lymphocyte count
- Platelet-to-lymphocyte ratio (PLR) = platelet count/lymphocyte count
- Monocyte-to-lymphocyte ratio (MLR) = monocyte count/lymphocyte count
- Systemic immune-inflammation index (SII) = (platelet count × neutrophil count)/lymphocyte count
- Systemic inflammation response index (SIRI) = (neutrophil count × monocyte count)/lymphocyte count

Statistical analyses

All statistical analyses were conducted using BM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro–Wilk test. Non-parametric data were analyzed using the Mann–Whitney rank correlation coefficient. Survival was defined as the time from surgery to the last follow-up or death. Progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan–Meier curves and compared among groups using the log-rank test. Within-group temporal changes were analyzed via the Wilcoxon signed-rank test, while between-group comparisons (GTR vs. STR) for each time interval were performed using the Mann–Whitney U test. NLR, PLR, MLR, SII, and SIRI were compared between the GTR and STR groups across different treatment phases using non-parametric tests. Due to the small sample size and incomplete longitudinal measurements, more complex longitudinal models were not used. All p-values were two-tailed, and $p < 0.05$ was considered statistically significant.

Results

There were 25 males (61%) and 16 females (39%), with a median age of 56 years (range, 37–80 years). No significant age difference was observed between the GTR and STR groups (median (IQR): 59.5 (11.3) vs. 54.0 (14.0), $p = 0.178$). Most cases presented with a single lesion (n = 37, 90.2%), while 4 patients (9.8%) had multiple lesions. GTR was achieved in 14 patients (34.1%), and STR was performed in 27 patients (65.9%). With a median follow-up of 21 months, patients in the GTR group had significantly longer survival than those in the STR group. The median progression-free survival (PFS) was 14.5 months for the GTR group and 7 months for the STR group (Fig. 1). The median overall survival (OS) was 33 months (14–62) for patients who underwent GTR and 15 months (9–25) for those with STR (Fig. 2). At 24 months, the estimated 2-year PFS rates were 42.9% versus 18.5%, and the 2-year OS rates were 50% versus 33.3% for the GTR and STR groups, respectively ($p = 0.033$ and $p = 0.045$). No significant correlation was found between the Ki-67 proliferation index and survival outcomes.

The median values of inflammatory biomarkers at baseline and during different treatment stages are summarized in Tables 1 and 2 and shown in Fig. 3. In the GTR group, NLR increased significantly before chemoradiotherapy (preoperative: 3.24 (2.25–7.96); pre-RT: 8.14 (6.07–11.53); $p < 0.001$) and then decreased markedly after treatment (post-RT: 2.67 (1.99–4.29); post-CT: 2.67 (1.96–4.24)). Similarly, in the STR group, NLR also decreased significantly after therapy

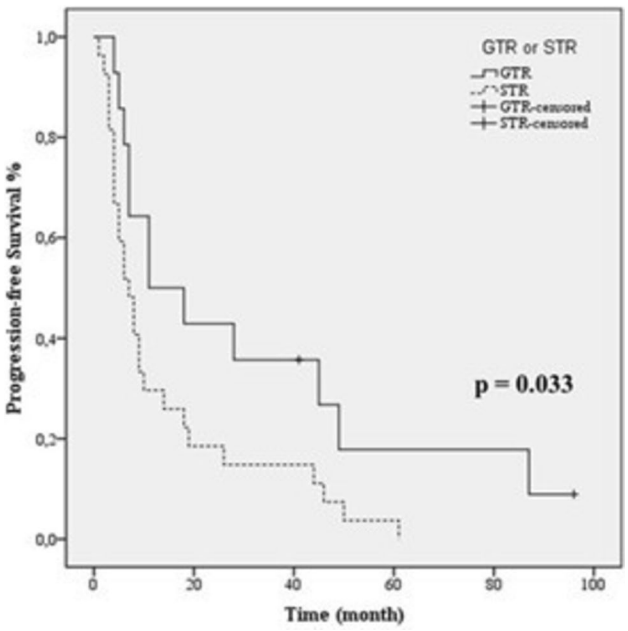


Fig. 1 Kaplan–Meier curve for progression-free survival (PFS) by extent of resection. Progression-free survival was significantly longer in patients who underwent GTR than in those who underwent STR ($p = 0.033$, log-rank test). Censored cases are indicated by a cross mark (+) on the survival curves

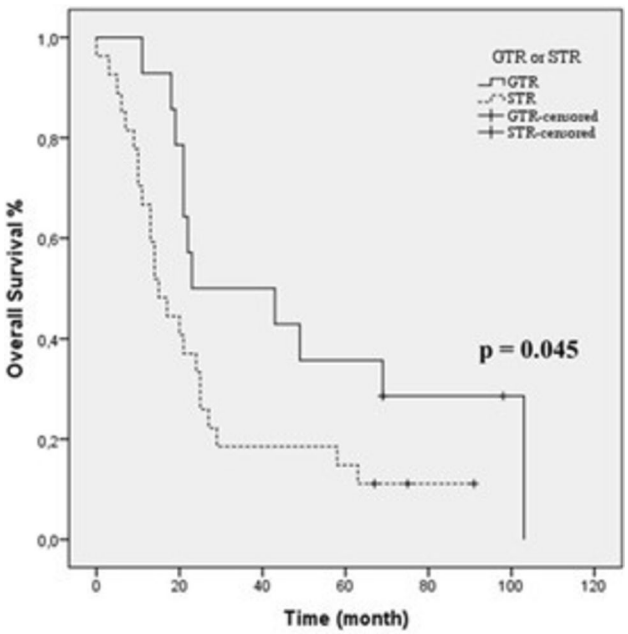


Fig. 2 Kaplan–Meier curve for overall survival (OS) by extent of resection. Overall survival was significantly longer in patients who underwent GTR than in those with STR ($p = 0.045$, log-rank test). Censored cases are indicated by a cross mark (+) on the survival curves

Table 1 Patient and study characteristics

Gender (Male: Female)	25:16
Median age (range) years	56 (37–80)
GTR median age [IQR]	59.5 [11.3]
STR median age [IQR]	54.0 [14.0]
Tumor characteristic	
Single	37
Multiple	4
Resection type	
STR (Male/Female)	27 (14/13)
GTR (Male/Female)	14 (11/3)
Median weeks from surgery to RT [IQR]	5.07 [3.68–6.57]
Median RT dose (range) Gy	60 (34–60)
Median values of inflammatory indices [IQR]	
NLR	3.2 [2.3–7.6]
PLR	132 [104–213]
MLR	0.29 [0.24–0.53]
SII	853 [597–1594]
SIRI	1.9 [1.2–5.7]

RT Radiotherapy, *NLR* Neutrophil–lymphocyte ratio, *PLR* Platelet-lymphocyte ratio, *MLR* Monocyte-lymphocyte ratio, *SII* Systemic inflammatory index, *SIRI* Systemic inflammatory response index

(pre-RT: 9.7 (7.5–11.9); post-RT: 4.1 (3.1–6.0); post-CT: 4.5 (3.4–6.5); all $p < 0.001$). Although the reduction in NLR was greater in the GTR group, the difference between the groups was not statistically significant ($p = 0.341$ for pre-RT–post-RT, $p = 0.455$ for pre-RT–post-CT).

In the overall cohort, PLR decreased slightly after treatment (preoperative: 176.6 (105.2–215.6); post-CT: 164.6 (102.3–202.1); $p = 0.417$). When analyzed by surgical extent, the GTR group showed a minor, nonsignificant reduction in PLR throughout the treatment course. In contrast, the STR group exhibited a significant increase between pre-radiotherapy and post-chemotherapy measurements ($p = 0.012$).

MLR values remained stable throughout treatment. In the GTR group, MLR medians were 0.29 (0.23–0.52) before surgery and 0.38 (0.26–0.47) after chemotherapy ($p = 0.407$). Similarly, in the STR group, pre- and post-treatment MLR values did not change significantly.

In the GTR group, SII showed notable reductions during therapy. Median values decreased from 857 [668–2048] before surgery to 626 (462–902) after radiotherapy ($p = 0.025$) and to 617 (376–928) after chemotherapy ($p = 0.007$). Conversely, the STR group did not show statistically significant changes over the same periods ($p = 0.365$ and $p = 0.427$, respectively).

In the GTR group, SIRI values decreased significantly after treatment. The median SIRI dropped from 1.9 (1.3–5.7) before surgery to 1.5 (1.1–2.1) after radiotherapy ($p = 0.020$) and to 1.6 (1.1–2.5) after chemotherapy ($p = 0.027$). In contrast, the STR group showed no statistically significant change (preoperative: 3.3 (1.1–3.7), after chemotherapy: 2.3 (1.1–2.6), $p = 0.552$).

Discussion

Changes in systemic inflammatory biomarkers during multidisciplinary treatment have received less attention, and their potential predictive role has not been described in glioblastoma. The present study shows that tracking systemic inflammatory biomarkers may help predict progression status and survival in glioma patients. All measured parameters—NLR, PLR, MLR, SII, and SIRI—generally decreased after treatment, indicating a reduction in tumor-related inflammatory activity following multimodal therapy. However, this decrease was more substantial and sustained in patients who underwent GTR, whereas those with STR showed consistently elevated biomarker levels during and after adjuvant therapy. These findings also suggest that incomplete resection may be linked to ongoing systemic inflammation, reflecting the presence of residual tumor tissue and potentially worse disease behavior.

Inflammation plays a crucial role in gliomagenesis and tumor progression by regulating cytokine signaling, immune cell recruitment, and angiogenesis. Previous studies have shown that elevated inflammatory biomarkers, including NLR, PLR, and SII, are associated with poorer prognosis and shorter survival in GBM and other solid tumors [2, 4]. The current study's findings align with earlier reports, showing that patients with persistently high inflammatory indices, particularly after STR, had shorter PFS and OS.

Table 2 Median [IQR] biomarker values at treatment stages

	Median [IQR]				
	PRE-OP	PRE-RT	POST-RT	POST-CT	PROGRESSION
NLR	3.2 [2.3–7.6]	8.1 [6.1–11.5]	2.7 [2.0–4.3]	2.7 [2.0–4.2]	4.4 [2.0–6.0]
PLR	132 [104–213]	138 [102–178]	169 [115–209]	145 [102–202]	172 [108–221]
MLR	0.29 [0.24–0.53]	0.35 [0.24–0.45]	0.31 [0.26–0.50]	0.38 [0.26–0.47]	0.33 [0.20–0.62]
SII	853 [597–1594]	597 [473–1584]	626 [462–902]	617 [376–928]	756 [488–1552]
SIRI	1.9 [1.2–5.7]	1.6 [1.1–3.6]	1.5 [1.1–2.1]	1.6 [1.1–2.5]	1.6 [0.9–3.8]

PRE-OP Preoperative, *PRE-RT* Before radiotherapy, *POST-RT* After radiotherapy, *POST-CT* after completion of the treatment

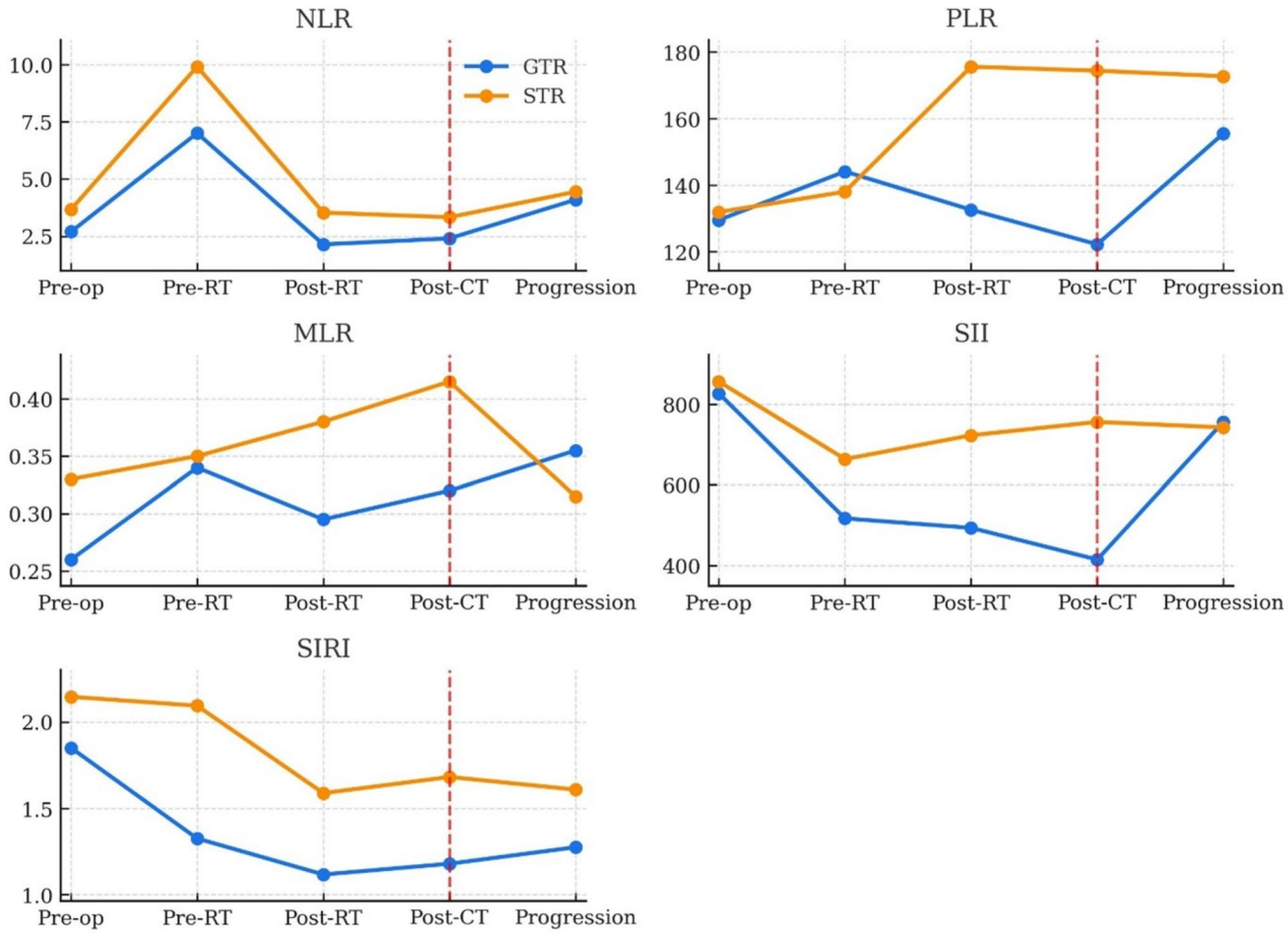


Fig. 3 Changes over time in systemic inflammatory biomarkers by extent of resection. Line graphs display the longitudinal trends of neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), monocyte–lymphocyte ratio (MLR), systemic immune–inflammation index (SII), and systemic inflammation response index (SIRI) in patients who underwent gross total resection (GTR) and subtotal resection (STR). Vertical dashed red lines mark the completion of treatment (POST-CT)

The observed postoperative decrease in NLR and SII after GTR aligns with Gonçalves et al. [6], who reported a significant reduction in blood-based inflammatory biomarkers after standard chemoradiotherapy in patients with complete resection; however, their study did not directly compare changes in inflammatory biomarkers between GTR and STR groups. Similarly, Alan et al. [1] highlighted the prognostic importance of early post-treatment normalization of systemic inflammatory biomarkers in recurrent and newly diagnosed GBMs. Persistently high NLR, PLR, and SIRI levels in our STR cohort may reflect ongoing tumor-induced immune activation, potentially exacerbated by hypoxia, necrosis, or altered cytokine signaling within residual tumor tissue. Recent research by Mohammad et al. [9] found that an increase in NLR after surgery was significantly associated with poorer survival in glioblastoma, underscoring the clinical significance of biomarker changes. Lee et al. [10] showed that a low postoperative lymphocyte-to-monocyte ratio (LMR < 3.2) was an independent predictor of worse progression-free and overall survival in glioblastoma patients treated with the Stupp regimen [11].

Limitations

For several reasons, patients may continue their adjuvant treatment outside our center. Therefore, only patients who underwent both surgery and chemoradiotherapy and had complete follow-up until progression at our institution were included in this study. This criterion limits the number of eligible patients and precludes a robust conclusion about the independent prognostic value of inflammatory markers. The modest sample size and number of events likely limit power to detect small to moderate effects and increase the risk of type I and type II errors. We think that future, larger prospective studies with systematic data collection will be required to apply mixed-effects modeling and to control for multiple testing more rigorously.

Although a standardized corticosteroid protocol was routinely applied, detailed information regarding steroid use outside the predefined treatment periods was not available, representing another limitation of this study. As with the steroid use status, a detailed infection history throughout the follow-up period was not available, and other clinical variables could not be incorporated into the analysis.

The absence of volumetric analysis limits more refined modeling of residual tumor burden and may reduce the biological granularity of the current findings.

Conclusion

Despite some limitations, this study may offer a novel approach to tracking systemic inflammatory biomarkers throughout the entire treatment period from the perspective of the extent of surgical resection, a well-known and strong prognostic factor in glioblastoma. Persistent elevation of these biomarkers may accomplish for a poorer prognosis. Regular monitoring of these biomarkers during various treatments may help characterize disease courses and support postoperative clinical follow-up.

Author contributions YŞ contributed to the design of the study, data acquisition, analysis, and interpretation, drafting the manuscript, editing the final version, and approving the manuscript before submission. DG, MŞ, OE, and MS were involved in the analysis and interpretation of the data, editing the final version, and approving the manuscript before submission. BMA was involved in conceptualizing and designing the study, analyzing and interpreting data, drafting the manuscript, and making the final revision prior to submission, serving as the corresponding author. All authors agree to be personally accountable for their contributions and to ensure that any questions regarding the accuracy or integrity of any part of the work, even those in which they were not directly involved, are properly investigated, resolved, and documented in the literature.

Funding None.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This retrospective study (reference number 09.2024.1002) was approved by the Marmara University School of Medicine Noninterventional Ethics Committee on September 20, 2024, to analyze and publish data from patients who completed treatment and follow-up.

Human ethics and consent to participate declarations Not applicable.

Data availability Data will be made available on request from corresponding author

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Alan O, Telli TA, Basoğlu T, Arikan R, Demircan NC, Ercelep O, et al. Impact of prognostic nutritional index on survival in recurrent glioblastoma. Neurocirugia. 2022;33(1):15–21.
2. Gurrieri L, Mercatali L, Ibrahim T, Fausti V, Dall'Agata M, Riva N, et al. Immuno markers in newly diagnosed glioblastoma patients underwent Stupp protocol after neurosurgery: a retrospective series. J NeuroOncol. 2023;164(1):55–64.
3. Basheer AS, Abas F, Othman I, Naidu R. Role of inflammatory mediators, macrophages, and neutrophils in glioma maintenance and progression: mechanistic understanding and potential therapeutic applications. Cancers. 2021;13(16):4226.
4. 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. 2023;15(13):3339.
5. Wu Z, Cao Y, Liu Z, Geng N, Pan W, Zhu Y, et al. Study on the predictive value of laboratory inflammatory markers and blood count-derived inflammatory markers for disease severity and prognosis in COVID-19 patients: a study conducted at a university-affiliated infectious disease hospital. Ann Med. 2024;56(1):2415401.
6. Gonçalves JM, Carvalho B, Tuna R, Polónia P, Linhares P. Sequential evaluation of hematology markers as a prognostic factor in glioblastoma patients. Biomedicines. 2024;12(5):1067.
7. Bayatli E, Ozgural O, Dogan I, Ozpiskin OM, Hasimoglu S, Kuzukiran YC, et al. Prediction of meningioma grade using hematological parameters. World Neurosurg. 2024;185:e893–9.
8. Wu R, Hu M, Zhang P. Predictive value of systematic immune-inflammation index combined with Ki-67 index on prognosis of prostate cancer patients after laparoscopic radical prostatectomy. BMC Urol. 2023;23(1):210.
9. 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. Neuro-Oncol Adv. 2025;7(1):vdaf014.
10. 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. https://doi.org/10.3390/medicina61030376.
11. Stupp R, Hegi ME, Mason WP, Van Den Bent MJ, Taphoorn MJ, Janzer RC, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Lancet Oncol. 2009;10(5):459–66. https://doi.org/10.1016/S1470-2045(09)70025-7.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.