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# Preoperative Survival Prediction in Patients With Glioblastoma by Routine Inflammatory Laboratory Parameters

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**Abstract.** *Background: Glioblastoma (GBM) is the most common malignant brain tumor in adults and still carries a dismal prognosis. As several studies detected a connection between inflammation and GBM prognosis, we sought to explore possible associations between routinely investigated inflammatory parameters and GBM outcome. Patients and Methods: Patients treated for GBM at our Institution between 2004 and 2014 were included. White blood cell count (WBC), C-reactive protein (CRP) and the ratio of platelets and WBC (Plt/WBC) were evaluated preoperatively. Medical records were reviewed for clinical parameters (age, sex, preoperative clinical condition, genetic alterations). Study endpoints were overall (OS) and 1- and 2-year survival. Results: In the final cohort consisting of 565 individuals with GBM, univariate analysis showed significant associations for WBC, CRP and Plt/WBC ratio with OS. Kaplan–Meier survival plot confirmed significantly poorer OS in patients with WBC>12/nl and with CRP≥2.9 mg/dl. In multivariate analysis, a WBC of >12/nl was an independent prognostic factor for all three outcome parameters and CRP≥2.9 mg/dl for OS and 1-year survival. Conclusion: Preoperative WBC and CRP values were confirmed as independent predictors of GBM outcome. This emphasizes the need for further evaluation of the role of inflammation in the prognosis of GBM.*

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*Key Words:* Glioblastoma, inflammation, routine laboratory parameter.

Glioblastoma is the most common malignant primary brain tumor in adults and carries a poor prognosis. Despite extensive research, survival remains relatively short with a median overall survival (OS) of between 16 and 21 months (1). Treatment options comprise surgical resection or biopsy followed by radiotherapy and chemotherapy. However, survival differs significantly between individuals (2, 3). Several prognostic factors have been identified, including methylation of the $O^6$-methylguanine-DNA-methyltransferase gene (*MGMT*) promotor (4), mutation of isocitrate-dehydrogenase gene 1 (*IDH1*) (5), younger age and a good clinical performance status (6, 7).

Early and reliable estimation of a patient's survival, preferably prior to surgery, is of eminent importance. Laboratory markers of disease progression and survival are already being used in clinical practice for different cancer types (8-10). In a recent systematic review analyzing blood-based markers of GBM (11), a large panel of laboratory parameters predicting outcome of patients with GBM was identified. Among promising markers, inflammatory parameters were significantly associated with survival GBM in this review.

Inflammation has long been linked to cancer. It is well known that inflammatory conditions promote cancer development in various tissues. It was shown that inflammation is present in the microenvironment of cancer and several markers for systemic inflammation, such as lymphocyte count and serum albumin have been linked to prognosis in different cancer types (12, 13). Finally, the predictive value of the white blood cell (WBC) count at admission has been shown for outcome of different cardiovascular and cerebrovascular diseases (14-16).

In this study, we sought to assess routinely investigated blood-based inflammatory markers in an institutional cohort of patients with GBM and explore possible associations with patient outcome.

## Patients and Methods

*Study population*. A retrospective longitudinal cohort study was conducted. All patients with histologically confirmed diagnosis of GBM that were treated at our Institution between 2004 and 2014 were eligible for this study. After surgery (microsurgical tumor resection or stereotactic biopsy), patients were treated with standard chemoradiation therapy. The study was approved by the Institutional Ethics Committee (BO-15-6504).

*Data management*. The primary objective of the study was to assess the association between routinely analyzed preoperative inflammatory laboratory markers and survival in GBM. As outcome endpoints, OS and 1- and 2-year survival were investigated.

Preoperative blood samples were routinely collected 1-2 days prior to surgery. Assessed inflammatory markers included WBC count, C-reactive protein (CRP) and the ratio of platelets to WBC (Plt/WBC). Cutoff values used were determined using receiver operating characteristic (ROC) curve analysis and Youden's Index. Medical records were reviewed for patient age at diagnosis, sex, preoperative clinical condition (Karnofsky Performance Scale, KPS), extent of resection, methylation status of the *MGMT* gene promotor and mutational status of the *IDH1* gene.

*Statistical analysis*. Statistical analysis was performed using SPSS (version 21; IBM, Armonk, NY, USA) and PRISM (version 5.0; GraphPad Software Inc., San Diego, CA, USA). All assessed variables were investigated in univariate and multivariate analyses. Differences with a $p$-value ≤0.05 were considered statistically significant. Firstly, all variables were evaluated using the Mann–Whitney $U$-test (two group variables) and the Kruskal–Wallis test (more than two variables) for continuous variables. The chi-square test was applied for categorical variables. All variables that reached significance for OS in the univariate analysis were then included in multivariate binary logistic (for 1- and 2-year survival) or linear regression analysis (for OS). Missing values were replaced using multiple imputation. Kaplan–Meier test and log-rank test were also used for survival analysis.

## Results

*Patient characteristics*. From 2004 to 2014, 565 patients with histologically confirmed GBM were treated at our Institution. Their mean age was 62.15 years (±12.2 years). Median survival time was 12.47 months. Of all patients, 57.3% were male. About 69% of all patients underwent tumor resection, whereas 30.8% only underwent biopsy. Patient characteristics are shown in Table I.

*Inflammatory laboratory markers*. The WBC ranged between 3.1/nl and 36.86/nl, with a mean value of 11.11/nl.

The mean CRP value was 0.46 mg/dl, ranging between 0 and 11.6 mg/dl. As an additional marker of inflammation, the ratio of Plt to WBC was also calculated. The values ranged between 6.05 and 86.79, and the mean value was 26.9.

According to the appropriate ROC curves for the association between the laboratory parameters as continuous variables and the study endpoints, the following cutoffs were defined for the analyzed laboratory parameters: WBC>12/nl and CRP≥2.9 mg/dl. For the Plt/WBC ratio, there were two cut-offs with similar diagnostic accuracy: 16 and 32. Therefore, the Plt/WBC ratio was further assessed as a categorical variable with cutoffs of <16, 16-32 and >32.

Table I. *Patient characteristics*.

| Parameter | Value |
|---|---|
| Number of patients | 565 |
| Mean age, years | 62.15 |
| Gender (female), n (%) | 241 (42.7%) |
| Tumor resection, n (%) | 391 (69.2%) |
| *IDH1* mutation (R132H), n (%) | 10 (4.2%) |
| *MGMT* methylation, n (%) | 166 (38.5%) |
| Preoperative KPS <80% | 160 (28.3%) |

IDH1: Isocitrate-dehydrogenase gene 1 *MGMT*: $O^6$-methylguanine-DNA-methyltransferase promotor methylation; KPS: Karnofsky performance scale.

*Association of inflammatory markers with GBM outcome*. Univariate analysis revealed significant shorter OS of patients with WBC >12/nl ($p$=0.036) and CRP ≥2.9 mg/dl ($p$=0.041) and patients with a higher Plt/WBC ratio had a significant shorter OS ($p$=0.042).

There was a significant negative association between 1-year survival and WBC >12/nl ($p$=0.048) and CRP ≥2.9 mg/dl ($p$=0.036), whereas the Plt/WBC ratio did not reach significance ($p$=0.252). For 2-year survival, a significant negative association was detected when comparing patients with WBC>12/nl and WBC≤12/nl ($p$=0.007) and for Plt/WBC ratio ($p$=0.027). Statistical analysis is summarized in Table II.

*Multivariate analysis of inflammatory markers*. All three inflammatory markers (WBC >12/nl, CRP≥2.9 mg/dl and Plt/WBC <16, 16-32 and >32) were also tested in multivariate analysis adjusted for patient age, sex, preoperative KPS, extent of resection and molecular genetic markers (*MGMT* promotor methylation and *IDH1* mutational status).

Accordingly, higher values of WBC [unstandardized coefficient (UC)=−2.5, 95% CI=−4.96- −0.07; $p$=0.044] and CRP (UC=−6.65, 95% CI=−12.26- −1.04; $p$=0.02) were associated with shorter OS, whereas increasing Plt/WBC ratio was associated with longer OS (UC=2.06, 95% CI=0.24-3.87; $p$=0.026). Therefore, all three inflammatory markers were confirmed as independent predictors of OS.

WBC>12/nl [adjusted odds ratio (aOR)=0.61, 95% CI=0.40-0.93; $p$=0.022] and CRP≥2.9 mg/dl (aOR=0.20, 95% CI=0.06-0.7; $p$=0.012) were also significant in the multivariate analysis of 1-year survival. Finally, only

Table II. *Univariate analysis*.

| Parameter | Survival | | | | | |
|---|---|---|---|---|---|---|
| | Overall, months | | 1-Year | | 2-Year | |
| WBC >12/nl *vs*. ≤12/nl | 11.20 *vs*. 13.35 | $p$=0.036 | 31.9% *vs*. 40.4% | $p$=0.048 | 8.7% *vs*. 16.9% | $p$=0.007 |
| CRP ≥2.9 mg/dl *vs*. <2.9 mg/dl | 6.1 *vs*. 12.76 | $p$=0.041 | 15% *vs*. 38.1% | $p$=0.036 | 0% *vs*. 14.2% | $p$=0.069 |
| Plt/WBC ratio >32 *vs*. 16-32 *vs*. <16 | 15.68 *vs*. 12.1 *vs*. 9.94 | $p$=0.042 | 41.3% *vs*. 37.2 *vs*. 31.1% | $p$=0.252 | 19.3% *vs*. 13.0% *vs*. 8.4% | $p$=0.027 |

WBC: White blood cell count; CRP: C-reactive protein; Plt: platelet count.

WBC>12/nl was significantly associated with 2-year survival (aOR=0.41, 95% CI=0.22-0.75; $p$=0.004). Results of multivariate analysis are accessible as supplementary material (S1-3) (https://figshare.com/s/04c24f993d67252bffb8).

*Analysis of survival according to inflammatory markers*. Survival analysis was performed using Kaplan–Meier curves and survival was compared using log-rank test. Log-rank test revealed significantly shorter survival to be associated with all three variables ($p$=0.041, $p$=0.003, and $p$=0.019, respectively). Figure 1 shows Kaplan–Meier curves for survival according to WBC, CRP and Plt/WBC ratio.

## Discussion

Inflammation has been repeatedly linked to carcinogenesis, tumor progression and metastasis. Whereas the exact mechanisms have not been fully explored so far, there are multiple tumor systems with a pathogenic role of inflammation (17, 18). Examples for the link between inflammation and cancer are the inflammation-driven development of gastric cancer (19) and the carcinogenic potential of hepatitis B or C infection for hepatocellular carcinoma (20, 21).

In glioma, there are several lines of evidence for a role of inflammation in glioma diagnosis, progression and prognosis. One recent multicenter cohort study detected high sensitivity and specificity of preoperative inflammatory markers for glioma diagnosis and differential diagnosis of low-grade glioma from GBM (22). Concerning prognosis, several studies established a relation between inflammatory laboratory markers and survival (23-25). A high preoperative systemic immune-inflammation index and a low albumin/globulin ratio were associated with a poorer prognosis in 169 newly-diagnosed GBM cases (26). Bao and colleagues showed that high neutrophil-to-lymphocyte, platelet-to-lymphocyte and monocyte-to-lymphocyte ratios were independent prognostic factors for OS in patients with GBM (27). This was supported by a recent meta-analysis that found an association between high neutrophil-to-lymphocyte ratio with unfavorable prognosis in 2,275 patients with glioma (28).

The aim of the present study was to assess inflammatory laboratory markers that are routinely investigated preoperatively in GBM and to examine possible associations with outcome parameters. In our large institutional GBM cohort, all three tested inflammatory markers (WBC, CRP and Plt/WBC ratio) were confirmed as independent predictors of OS in the multivariate analysis. Regarding long-term outcome after diagnosis of GBM, only WBC>12/nl had a robust significant association with 1-year and 2-year survival.

Our findings are in line with some studies of WBC and CRP in other entities. In a prospective population-based cohort study, WBC and CRP values were assessed and found to be inflammation-related biomarkers for prostate cancer risk and prognosis (29). Furthermore, a positive association was found between pre-diagnostic high-sensitivity CRP and overall mortality in breast cancer (30). In gliomas, a recent meta-analysis found the CRP value to be associated with glioma risk as well as with a poor prognosis (31). Significant associations between increased CRP with OS of patients with glioma was also shown by Strojnik and colleagues (32). For WBC values, patients with GBM with preoperative dexamethasone-induced leukocytosis showed poorer OS in the study of Dubinski et al. (33).

## Limitations

Several limitations of this study should be considered when interpreting the presented data. The major limitation is the retrospective design of the database. Therefore, the quality of our analysis depended strongly on the accuracy of the assessed items in the database. It was not possible to incorporate several factors that are associated with an increase or decrease of WBC, such as preoperative dexamethasone therapy, smoking or autoimmune disease, into our analysis. Our results will have to be confirmed in a prospective study addressing a larger number of inflammatory markers.

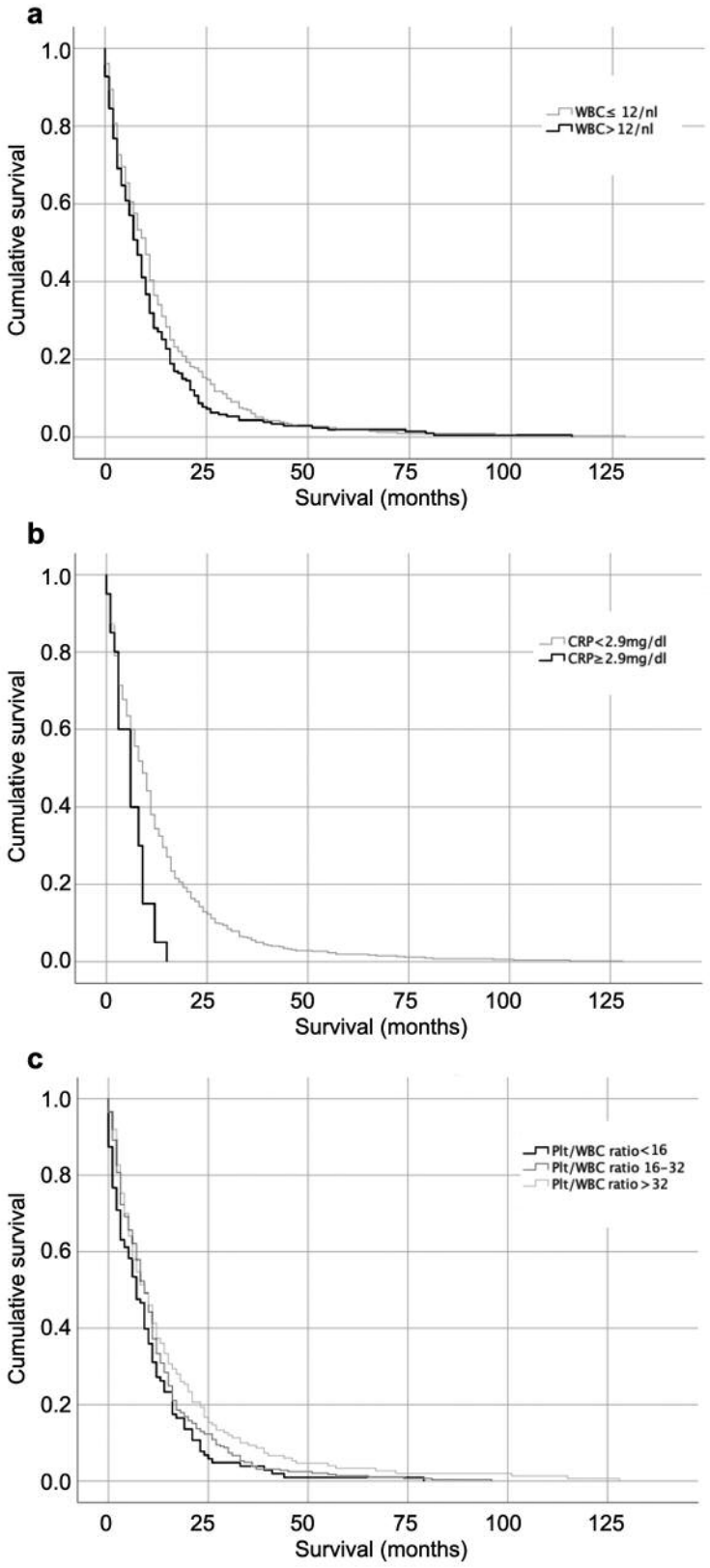


Figure 1. *Kaplan–Meier curves for overall survival according to white blood cell count (WBC) (A), C-reactive protein (CRP) (B) and platelet count (Plt)/WBC ratio (C) Log-rank test revealed a significant difference for all three variables (p=0.041, p=0.003 and p=0.019, respectively).*

## Conclusion

In our retrospective study, high preoperative WBC and CRP values were confirmed as independent outcome predictors of GBM. Our results emphasize the need for further evaluation of the role of inflammation in the prognosis of GBM.

## Conflicts of Interest

All Authors state that there are no conflicts of interest.

## Authors' Contributions

DP and RJ: Study design, data collection, statistical analysis, preparation of the article. YA, MDO, AM, MC: Data collection, contributed to the interpretation of the results. MG, MS, US, RJ: Critical revision of the article, supervision of the project.

## References


1 Stupp R, Taillibert S, Kanner A, Read W, Steinberg D, Lhermitte B, Toms S, Idbaih A, Ahluwalia MS, Fink K, Di Meco F, Lieberman F, Zhu JJ, Stragliotto G, Tran D, Brem S, Hottinger A, Kirson ED, Lavy-Shahaf G, Weinberg U, Kim CY, Paek SH, Nicholas G, Bruna J, Hirte H, Weller M, Palti Y, Hegi ME and Ram Z: Effect of tumor-treating fields plus maintenance temozolomide vs. maintenance temozolomide alone on survival in patients with glioblastoma: A randomized clinical trial. JAMA *318(23)*: 2306-2316, 2017. PMID: 29260225. DOI: 10.1001/jama.2017.18718

2 Krex D, Klink B, Hartmann C, von Deimling A, Pietsch T, Simon M, Sabel M, Steinbach JP, Heese O, Reifenberger G, Weller M, Schackert G and German Glioma N: Long-term survival with glioblastoma multiforme. Brain *130(Pt 10)*: 2596-2606, 2007. PMID: 17785346. DOI: 10.1093/brain/awm204

3 Michaelsen SR, Urup T, Olsen LR, Broholm H, Lassen U and Poulsen HS: Molecular profiling of short-term and long-term surviving patients identifies CD34 mRNA level as prognostic for glioblastoma survival. J Neurooncol *137(3)*: 533-542, 2018. PMID: 29305787. DOI: 10.1007/s11060-017-2739-7

4 Hegi ME, Diserens AC, Gorlia T, Hamou MF, de Tribolet N, Weller M, Kros JM, Hainfellner JA, Mason W, Mariani L, Bromberg JE, Hau P, Mirimanoff RO, Cairncross JG, Janzer RC and Stupp R: *MGMT* gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med *352(10)*: 997-1003, 2005. PMID: 15758010. DOI: 10.1056/NEJMoa043331

5 Hartmann C, Hentschel B, Simon M, Westphal M, Schackert G, Tonn JC, Loeffler M, Reifenberger G, Pietsch T, von Deimling A, Weller M and German Glioma N: Long-term survival in primary glioblastoma with versus without isocitrate dehydrogenase mutations. Clin Cancer Res *19(18)*: 5146-5157, 2013. PMID: 23918605. DOI: 10.1158/1078-0432.CCR-13-0017

6 Gittleman H, Lim D, Kattan MW, Chakravarti A, Gilbert MR, Lassman AB, Lo SS, Machtay M, Sloan AE, Sulman EP, Tian D, Vogelbaum MA, Wang TJC, Penas-Prado M, Youssef E, Blumenthal DT, Zhang P, Mehta MP and Barnholtz-Sloan JS: An independently validated nomogram for individualized estimation of survival among patients with newly diagnosed glioblastoma: NRG Oncology RTOG 0525 and 0825. Neuro Oncol *19(5)*: 669-677, 2017. PMID: 28453749. DOI: 10.1093/neuonc/now208

7 Gramatzki D, Dehler S, Rushing EJ, Zaugg K, Hofer S, Yonekawa Y, Bertalanffy H, Valavanis A, Korol D, Rohrmann S, Pless M, Oberle J, Roth P, Ohgaki H and Weller M: Glioblastoma in the canton of Zurich, Switzerland revisited: 2005 to 2009. Cancer *122(14)*: 2206-2215, 2016. PMID: 27088883. DOI: 10.1002/cncr.30023

8 Dummer R, Hauschild A, Lindenblatt N, Pentheroudakis G, Keilholz U and Committee EG: Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol *26(Suppl 5):* v126-132, 2015. PMID: 26314774. DOI: 10.1093/annonc/mdv297

9 Hayes JH and Barry MJ: Screening for prostate cancer with the prostate-specific antigen test: A review of current evidence. JAMA *311(11)*: 1143-1149, 2014. PMID: 24643604. DOI: 10.1001/jama.2014.2085

10 Rasool M, Rashid S, Arooj M, Ansari SA, Khan KM, Malik A, Naseer MI, Zahid S, Manan A, Asif M, Razzaq Z, Ashraf S, Qazi MH, Iqbal Z, Gan SH, Kamal MA and Sheikh IA: New possibilities in hepatocellular carcinoma treatment. Anticancer Res *34(4)*: 1563-1571, 2014. PMID: 24692683.

11 Pierscianek D, Ahmadipour Y, Oppong MD, Rauschenbach L, Kebir S, Glas M, Sure U and Jabbarli R: Blood-based biomarkers in high grade gliomas: A systematic review. Mol Neurobiol *56(9)*: 6071-6079, 2019. PMID: 30719642. DOI: 10.1007/s12035-019-1509-2

12 Asher V, Lee J and Bali A: Preoperative serum albumin is an independent prognostic predictor of survival in ovarian cancer. Med Oncol *29(3)*: 2005-2009, 2012. PMID: 21735143. DOI: 10.1007/s12032-011-0019-5

13 Hong J, Chen X, Gao W, Zhu S, Wu J, Huang O, He J, Zhu L, Chen W, Li Y, Fei X, Lin L and Shen K: A high absolute lymphocyte count predicts a poor prognosis in HER-2-positive breast cancer patients treated with trastuzumab. Cancer Manag Res *11:* 3371-3379, 2019. PMID: 31114373. DOI: 10.2147/CMAR.S187233

14 Al-Mufti F, Misiolek KA, Roh D, Alawi A, Bauerschmidt A, Park S, Agarwal S, Meyers PM, Connolly ES, Claassen J and Schmidt JM: White blood cell count improves prediction of delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. Neurosurgery *84(2)*: 397-403, 2019. PMID: 29528448. DOI: 10.1093/neuros/nyy045

15 Schuss P, Hadjiathanasiou A, Brandecker S, Guresir A, Vatter H and Guresir E: Elevated C-reactive protein and white blood cell count at admission predict functional outcome after non-aneurysmal subarachnoid hemorrhage. J Neurol *265(12)*: 2944-2948, 2018. PMID: 30317466. DOI: 10.1007/s00415-018-9091-5

16 Turner CL, Budohoski K, Smith C, Hutchinson PJ, Kirkpatrick PJ, Murray GD and collaborators S: Elevated baseline c-reactive protein as a predictor of outcome after aneurysmal subarachnoid hemorrhage: Data from the simvastatin in aneurysmal subarachnoid hemorrhage (STASH) trial. Neurosurgery *77(5)*: 786-792; discussion 792-783, 2015. PMID: 26280117. DOI: 10.1227/NEU.0000000000000963

17 Gonda TA, Tu S and Wang TC: Chronic inflammation, the tumor microenvironment and carcinogenesis. Cell Cycle *8(13)*: 2005-2013, 2009. PMID: 19550141. DOI: 10.4161/cc.8.13.8985

18 Landskron G, De la Fuente M, Thuwajit P, Thuwajit C and Hermoso MA: Chronic inflammation and cytokines in the tumor microenvironment. J Immunol Res *2014:* 149185, 2014. PMID: 24901008. DOI: 10.1155/2014/149185

19 Figueiredo C, Machado JC, Pharoah P, Seruca R, Sousa S, Carvalho R, Capelinha AF, Quint W, Caldas C, van Doorn LJ, Carneiro F and Sobrinho-Simoes M: *Helicobacter pylori* and interleukin 1 genotyping: An opportunity to identify high-risk individuals for gastric carcinoma. J Natl Cancer Inst *94(22)*: 1680-1687, 2002. PMID: 12441323. DOI: 10.1093/jnci/94.22.1680

20 Ghouri YA, Mian I and Rowe JH: Review of hepatocellular carcinoma: Epidemiology, etiology, and carcinogenesis. J Carcinog *16:* 1, 2017. PMID: 28694740. DOI: 10.4103/jcar.JCar_9_16

21 Ivanov AV, Valuev-Elliston VT, Tyurina DA, Ivanova ON, Kochetkov SN, Bartosch B and Isaguliants MG: Oxidative stress, a trigger of hepatitis C and B virus-induced liver carcinogenesis. Oncotarget *8(3)*: 3895-3932, 2017. PMID: 27965466. DOI: 10.18632/oncotarget.13904

22 Zheng SH, Huang JL, Chen M, Wang BL, Ou QS and Huang SY: Diagnostic value of preoperative inflammatory markers in patients with glioma: A multicenter cohort study. J Neurosurg *129(3)*: 583-592, 2018. PMID: 29099300. DOI: 10.3171/2017.3.JNS161648

23 Auezova R, Ryskeldiev N, Doskaliyev A, Kuanyshev Y, Zhetpisbaev B, Aldiyarova N, Ivanova N, Akshulakov S and Auezova L: Association of preoperative levels of selected blood inflammatory markers with prognosis in gliomas. Onco Targets Ther *9:* 6111-6117, 2016. PMID: 27785058. DOI: 10.2147/OTT.S113606

24 Mason M, Maurice C, McNamara MG, Tieu MT, Lwin Z, Millar BA, Menard C, Laperriere N, Milosevic M, Atenafu EG, Mason W and Chung C: Neutrophil-lymphocyte ratio dynamics during concurrent chemo-radiotherapy for glioblastoma is an independent predictor for overall survival. J Neurooncol *132(3)*: 463-471, 2017. PMID: 28332000. DOI: 10.1007/s11060-017-2395-y

25 Weng SY, Wang X, Vijayan S, Tang Y, Kim YO, Padberg K, Regen T, Molokanova O, Chen T, Bopp T, Schild H, Brombacher F, Crosby JR, McCaleb ML, Waisman A, Bockamp E and Schuppan D: IL-4 receptor alpha signaling through macrophages differentially regulates liver fibrosis progression and reversal. EBioMedicine *29:* 92-103, 2018. PMID: 29463471. DOI: 10.1016/j.ebiom.2018.01.028

26 Liang R, Li J, Tang X and Liu Y: The prognostic role of preoperative systemic immune-inflammation index and albumin/globulin ratio in patients with newly diagnosed high-grade glioma. Clin Neurol Neurosurg *184:* 105397, 2019. PMID: 31306893. DOI: 10.1016/j.clineuro.2019.105397

27 Bao Y, Yang M, Jin C, Hou S, Shi B, Shi J and Lin N: Preoperative hematologic inflammatory markers as prognostic factors in patients with glioma. World Neurosurg *119:* e710-e716, 2018. PMID: 30092479. DOI: 10.1016/j.wneu.2018.07.252

28 Lei YY, Li YT, Hu QL, Wang J and Sui AX: Prognostic impact of neutrophil-to-lymphocyte ratio in gliomas: A systematic review and meta-analysis. World J Surg Oncol *17(1)*: 152, 2019. PMID: 31472673. DOI: 10.1186/s12957-019-1686-5

29 Stikbakke E, Richardsen E, Knutsen T, Wilsgaard T, Giovannucci EL, McTiernan A, Eggen AE, Haugnes HS and Thune I: Inflammatory serum markers and risk and severity of prostate cancer. The PROCA-life study. Int J Cancer, 2019. PMID: 31583707. DOI: 10.1002/ijc.32718

30 Frydenberg H, Thune I, Lofterod T, Mortensen ES, Eggen AE, Risberg T, Wist EA, Flote VG, Furberg AS, Wilsgaard T, Akslen LA and McTiernan A: Pre-diagnostic high-sensitive c-reactive protein and breast cancer risk, recurrence, and survival. Breast Cancer Res Treat *155(2)*: 345-354, 2016. PMID: 26740213. DOI: 10.1007/s10549-015-3671-1

31 Feng Y, Wang J, Tan D, Cheng P and Wu A: Relationship between circulating inflammatory factors and glioma risk and prognosis: A meta-analysis. Cancer Med *8(17)*: 7454-7468, 2019. PMID: 31599129. DOI: 10.1002/cam4.2585

32 Strojnik T, Smigoc T and Lah TT: Prognostic value of erythrocyte sedimentation rate and C-reactive protein in the blood of patients with glioma. Anticancer Res *34(1)*: 339-347, 2014. PMID: 24403485.

33 Dubinski D, Won SY, Gessler F, Quick-Weller J, Behmanesh B, Bernatz S, Forster MT, Franz K, Plate KH, Seifert V, Harter PN and Senft C: Dexamethasone-induced leukocytosis is associated with poor survival in newly diagnosed glioblastoma. J Neurooncol *137(3)*: 503-510, 2018. PMID: 29349612. DOI: 10.1007/s11060-018-2761-4

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