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Original Article

Correlation between EGF and VEGF expression levels and the efficacy of radiosurgery in recurrent glioma

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Abstract: Objective: To investigate the expression levels of epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF) in patients with recurrent glioma and to explore their correlation with patient prognosis following radiosurgery. Methods: A retrospective analysis was conducted on 83 patients with recurrent glioma who received radiosurgery treatment (observation group). An additional 83 patients who underwent decompressive craniectomy for traumatic brain injury were included as the control group. EGF and VEGF concentrations in cerebrospinal fluid (CSF) were measured and compared between the two groups. In the observation group, EGF and VEGF levels were further analyzed according to various clinical parameters. After a 1-year follow-up, patients in the observation group were categorized into a survival group (n = 44) and a death group (n = 39) based on prognosis. Differences in clinical characteristics and EGF/VEGF expression between the two subgroups were compared, and prognostic factors were analyzed. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive value of EGF and VEGF for patient prognosis, and Kaplan-Meier survival analysis was conducted based on high and low expression levels of these biomarkers. Results: CSF levels of EGF and VEGF were significantly elevated in the observation group compared to the control group. Among patients with glioma, those with WHO grade III-IV tumors exhibited higher EGF levels than those with grade II tumors. EGF and VEGF levels were also significantly higher in patients with a Karnofsky Performance Status (KPS) score <80 and in the death group compared to those with a KPS ≥80 and the survival group (P<0.05). Multivariate logistic regression analysis identified VEGF ≥300.94 ng/L, EGF ≥102.50 ng/L, and WHO grade III-IV glioma as independent predictors of poor prognosis following radiosurgery. ROC analysis showed optimal prognostic cutoff values of 301.48 ng/L for VEGF (AUC = 0.747) and 100.98 ng/L for EGF (AUC = 0.793). Combined analysis of EGF and VEGF yielded an AUC of 0.803 for prognosis prediction. Kaplan-Meier survival curves showed that patients with low VEGF expression had significantly longer overall survival than those with high VEGF expression (P<0.05). Conclusion: Elevated CSF levels of EGF and VEGF are closely associated with tumor severity and poor prognosis in recurrent glioma. These biomarkers may serve as valuable indicators for predicting radiosurgical outcomes and guiding clinical decision-making.

Keywords: Recurrent glioma, EGF, VEGF, radiosurgery

Introduction

Glioma is the most common primary tumor of the central nervous system and is characterized by a high incidence, frequent recurrence rate, and poor prognosis [1, 2]. Despite advances in therapeutic strategies that have improved patient quality of life, the clinical outcomes of glioma - particularly in cases of recurrence - remain unsatisfactory [3-5]. Patients with recurrent glioma often face limited treatment efficacy and reduced survival, underscoring the urgent need for improved therapeutic approaches and prognostic evaluation. Radiosurgery is a precise, localized treatment modality that delivers high-dose irradiation to tumor tissue while minimizing damage to surrounding healthy brain structures, thereby achieving tumor control [6, 7]. However, treatment responses and prognoses vary significantly among patients, even when radiosurgery is employed. This variability has prompted increased research interest in understanding the underlying mechanisms of glioma recurrence and identifying reliable biomarkers for prognostic assessment in the neurosurgical field.

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Epidermal growth factor (EGF) is a biologically active polypeptide that binds to specific cell membrane receptors, activating intracellular signaling pathways that regulate cell proliferation, differentiation, migration, and apoptosis inhibition [8]. Overexpression of EGF and its receptors has been reported in multiple malignancies and is often associated with tumor progression and poor prognosis [9]. Similarly, vascular endothelial growth factor (VEGF) promotes angiogenesis by increasing vascular permeability, facilitating tumor growth and metastasis [10-12].

Although aberrant expression of EGF and VEGF has been documented in gliomas, studies specifically addressing their expression profiles in recurrent gliomas and their association with radiosurgical outcomes are relatively scarce. Therefore, this study aims to investigate the expression levels of EGF and VEGF in patients with recurrent gliomas and to evaluate their potential as prognostic biomarkers following radiosurgical treatment. The findings are expected to provide a reference for optimizing prognostic assessment and guiding clinical management in a challenging patient population.

Materials and methods

General information

Patients with cerebral glioma who underwent radiosurgical treatment at our hospital between 2022 and 2024 were enrolled in the observation group. During the same period, patients who underwent decompressive craniectomy for traumatic brain injury were selected as the control group. This study was approved by the General Hospital of Theater Command's ethics committee.

Sample size calculation

To detect a difference in cerebrospinal fluid VEGF and EGF levels between glioma patients and patients with traumatic brain injury, a sample size calculation was performed based on preliminary data. The mean VEGF concentrations in the two groups were estimated at 100 ng/L and 85 ng/L, respectively, with a standard deviation of 20 ng/L in both groups. A two-sided test was used with a significance level (α) of 0.05 and a statistical power (1-β) of 90%. Using PASS version 15.0 software, the minimum required sample size was calculated to be 78 subjects per group. Allowing for a 6% dropout rate, the final sample size was set at 83 participants in each group.

Inclusion and exclusion criteria

Inclusion criteria: Patients in the observation group were included based on the following criteria: (1) Histopathologically confirmed diagnosis of recurrent glioma (WHO grade II-IV); (2) Availability of complete clinical data; (3) Karnofsky Performance Status (KPS) score ≥70; (4) Eligibility for and receipt of radiosurgical treatment; (5) Age ≥18.

Patients in the control group were included if they met the following conditions: (1) Underwent decompressive craniectomy for traumatic brain injury; (2) No history or evidence of malignant tumors; (3) Age ≥18 years; (4) Availability of complete clinical data.

Exclusion criteria: Patients in the observation group were excluded if they met any of the following conditions: (1) Presence of other malignancies or severe systemic diseases; (2) Prior treatment with anti-angiogenic agents or targeted therapies involving the EGF/VEGF pathway; (3) History of psychiatric disorders; (4) Estimated survival less than 3 months; (5) Poor compliance with treatment; (6) Incomplete clinical data.

Exclusion criteria for the control group were as follows: (1) Presence of intracranial infection; (2) History of neurological tumors or neurodegenerative diseases; (3) Psychiatric disorders.

Methods

Data collection: For patients in the observation group, the following clinical data were collected: age, sex, pathological type, location of tumor recurrence, diameter of recurrent lesion, WHO grade, pre-treatment Karnofsky Performance Status (KPS) score, and primary tumor type.

Biomarker detection: Cerebrospinal fluid (CSF) samples were obtained from both the observation and control groups. The concentrations of VEGF and EGF in the CSF were measured using enzyme-linked immunosorbent assay (ELISA).

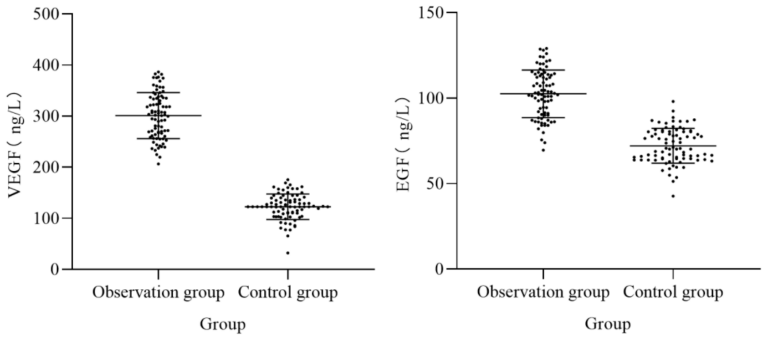

Figure 1. Comparison of VEGF and EGF levels between the observation group and the control group. Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor.

Treatment methods: All patients in the observation group received radiotherapy. Thermoplastic head masks were used for patient immobilization, and CT simulation was performed for positioning. Irradiation was delivered using 6MV X-rays via intensity-modulated radiotherapy (IMRT). The radiotherapy treatment plan was designed using the Philips Pinnacle 3.0 planning system.

Follow-up

Patients in the observation group were stratified into high-expression and low-expression subgroups based on the median VEGF and EGF levels. All patients were followed up after treatment, and overall survival (OS) was recorded. OS was defined as the time interval from the completion of treatment to death or the last follow-up date.

Statistical analysis

Data analyses were performed using SPSS 22.0 software. Categorical data were expressed as n (%) and compared using the chi-square test. Continuous data were presented as mean ± standard deviation (SD), and comparisons among multiple groups were conducted using one-way analysis of variance (ANOVA). Logistic regression analysis was employed to identify independent factors associated with patient prognosis. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of CSF VEGF and EGF levels for clinical outcomes. Kaplan-Meier survival analysis was used to compare OS between high-expression and low-expression groups of VEGF and EGF. A *P* value <0.05 was considered statistically significant.

Results

Comparison of VEGF and EGF levels between the observation and control groups

A total of 83 patients were included in each group. The mean CSF VEGF level was significantly higher in the observation group (300.94±44.90 ng/L) compared to the control group (122.78±24.97 ng/L). Similarly, the EGF level was significantly elevated in the observation group (102.50± 13.95 ng/L) versus the control group (72.11± 10.24 ng/L). These differences were statistically significant (t = 31.593 and 15.999, respectively; both P = 0.000). See **Figure 1**.

Comparison of VEGF and EGF levels among patients with different clinical characteristics in the observation group

Within the observation group, patients with WHO grade III-IV gliomas exhibited significantly higher EGF levels compared to those with grade II tumors (P<0.05). Additionally, patients with pre-treatment KPS scores <80 had significantly higher levels of both EGF and VEGF than those with a KPS ≥80 (P<0.05). See **Table 1**.

Comparison of VEGF and EGF levels between survival subgroups in the observation group

By the end of the follow-up period, 39 patients in the observation group had died, resulting in a survival rate of 53.01%. The mean VEGF level in the deceased subgroup was 320.44±44.48 ng/L, significantly higher than that in the surviving subgroup (283.65±38.03 ng/L). Likewise, the EGF level was significantly higher in the deceased group (109.83±11.56 ng/L) than in the surviving group (96.00±12.69 ng/L). These differences were statistically significant (t = 4.062 and 5.165, respectively; both P = 0.000). See **Figure 2**.

Comparison of clinical characteristics between survival subgroups in the observation group

Statistically significant differences were observed between the deceased and surviving patients regarding WHO grade and pre-treatment KPS scores (P<0.05). See **Table 2**.

Table 1. Comparison of VEGF and EGF levels among patients with different clinical characteristics in the observation group

Index	n	VEGF (ng/L)	EGF (ng/L)
Age			
≥60	52	304.96±47.35	101.96±15.50
<60	31	294.18±40.30	103.41±11.05
t		1.059	0.458
P		0.293	0.648
Sex			
Male	49	299.59±46.32	102.37±15.06
Female	34	302.88±43.39	102.68±12.40
T		0.326	0.098
P		0.746	0.922
Tumor location			
Cerebral lobe	39	299.61±45.31	102.69±14.81
Brainstem and cerebellum	44	302.11±45.03	102.33±13.31
T		0.252	0.117
P		0.802	0.907
WHO Classification			
Grade II	35	304.39±47.34	104.67±11.48
Grade III-IV	48	296.20±41.53	99.52±10.80
T		0.819	2.089
P		0.415	0.040
Pre-treatment KPS score			
≥80	42	318.27±46.13	105.88±14.02
<80	41	288.90±40.69	99.20±13.23
T		2.555	2.233
P		0.013	0.028
Maximum diameter of tumor			
≥3 cm	41	308.51±48.03	104.35±15.06
<3 cm	42	293.55±40.86	100.69±12.70
T		1.530	1.198
P		0.130	0.234
Primary tumor type			
Anaplastic astrocytoma	4	305.97±74.19	108.37±19.68
Glioblastoma	67	301.28±43.84	101.3±13.91
Oligodendroglioma	5	297.19±54.75	106.43±14.40
Diffuse midline cell tumor	7	297.48±40.32	106.99±11.26
F		0.042	0.744
P		0.988	0.529

Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor; KPS, Karnofsky Performance Status.

Logistic regression analysis of prognostic factors

A logistic regression analysis was conducted to identify independent factors associated with patient prognosis. Survival status was set as the dependent variable (survival = 0, death = 1), while the following were included as independent variables: WHO grade (grade II = 0, grade III-IV = 1), pre-treatment KPS score (≥80 = 0, <80 = 1), VEGF level (categorized by the mean: <300.94 ng/L = 0, ≥300.94 ng/L = 1), and EGF level (<102.50 ng/L = 0, ≥102.50 ng/L = 1). The analysis revealed that VEGF ≥300.94 ng/L, EGF ≥102.50 ng/L, and WHO grade III-IV glioma were independently associated with poor prognosis in patients with recurrent glioma treated with radiosurgery. See **Table 3**.

ROC curve analysis results

ROC curve analysis showed that the cutoff values were 301.48 ng/L for VEGF and 100.98 ng/L for EGF, corresponding to areas under the curve (AUC) of 0.747 and 0.793, respectively. When both biomarkers were combined, the AUC increased to 0.803. See **Table 4** and **Figure 3**.

Comparison of survival between high and low VEGF expression groups

Patients with VEGF levels ≥300.94±44.90 ng/L ng/L were classified into the high-expression group (n = 44), while those with levels <300.94 44.90 ng/L were classified into the low-expression group (n = 39). In the high-expression group, 30 patients died, and the median OS was 8.28 months (7.44, 9.12). In contrast, the low-expression group had 9 deaths, with a median OS of 11.07 months (10.42, 11.72). The difference in OS between the two groups was statistically significant (Log-rank test = 22.091, P<0.05). See **Figure 4**.

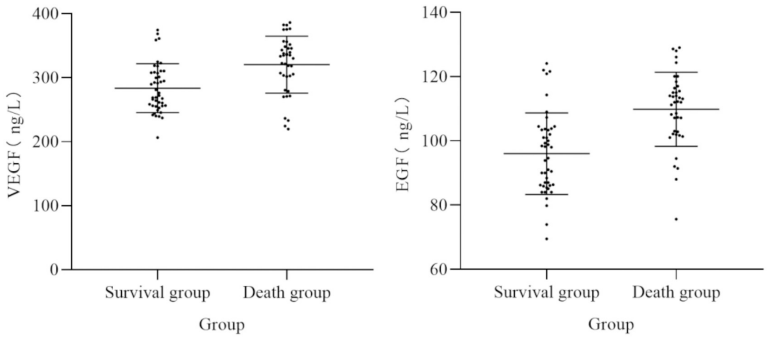

Figure 2. Comparison of VEGF and EGF levels between the survival group and the death group. Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor.

Table 2. Comparison of clinical characteristics between survival and death groups in the observation cohort

Index	Survival group (n = 44)	Death group (n = 39)	X^2	P
Age				
≥60	27 (61.36)	25 (64.10)	0.066	0.797
<60	17 (35.90)	14 (35.90)		
Sex				
Male	25 (56.82)	24 (61.54)	0.191	0.663
Female	19 (43.18)	15 (38.46)		
Tumor location				
Cerebral lobe	21 (47.73)	18 (46.15)	0.021	0.886
Brainstem and cerebellum	23 (52.27)	21 (53.85)		
WHO Classification				
Grade II	25 (56.82)	10 (25.64)	8.241	0.004
Grade III-IV	19 (43.18)	29 (74.36)		
Pre-treatment KPS score				
≥80	29 (65.91)	13 (33.33)	8.777	0.003
<80	15 (34.09)	26 (66.67)		
Maximum diameter of tumor				
≥3 cm	20 (45.45)	21 (53.85)	0.582	0.445
<3 cm	24 (54.55)	18 (46.15)		
Primary tumor type				
Anaplastic astrocytoma	2 (4.55)	2 (5.13)	0.416	0.937
Glioblastoma	36 (81.82)	31 (79.49)		
Oligodendroglioma	2 (4.55)	3 (7.69)		
Diffuse midline cell tumor	4 (9.09)	3 (7.69)		

Note: KPS, Karnofsky Performance Status.

Comparison of survival between high and low EGF expression groups

Using a threshold of 102.50±13.95 ng/L, patients were divided into high (n = 42) and low (n = 41) EGF expression groups. The high-expression group experienced 29 deaths and had a median OS of 8.24 months (7.44, 9.04), whereas the low-expression group had 10 deaths and a significantly longer median OS of 10.98 months (10.25, 11.70). The difference was statistically significant (Log-rank test = 19.891, P<0.05). See **Figure 5**.

Discussion

EGF is a multifunctional growth factor whose overexpression has been shown to promote tumor cell growth [13, 14]. VEGF, a principal mediator of angiogenesis, facilitates tumor growth by enhancing vascular permeability [15, 16]. Accordingly, elevated levels of EGF and VEGF are closely associated with glioma progression. Measuring the CSF levels of EGF and VEGF in glioma patients provides valuable insights into the tumor's biological behavior and offers a theoretical basis for improving diagnostic and therapeutic strategies. This study found that patients with recurrent glioma exhibited significantly higher CSF levels of EGF and VEGF compared to patients who underwent decompressive craniectomy for traumatic brain injury. These findings suggest that EGF and VEGF may play a role in the initiation and progression of glioma [17, 18].

In the analysis of recurrent glioma patients stratified by clinical characteristics, EGF levels were higher in patients with WHO grade III-IV tumors compared to those with grade II, indicating a strong association between EGF expression and glioma malignancy. As tumor grade increases, the proliferative capacity, invasiveness, and metastatic potential of tumor cells are progressively enhanced. Given that EGF is a critical regulator of

Table 3. Logistic regression analysis of factors affecting patient prognosis

Index	B	SE	Wald	P	OR	OR 95% CI	
						Lower limit	Upper limit
VEGF (≥300.94 ng/L)	1.534	0.702	4.774	0.029	4.636	1.171	18.355
EGF (≥102.50 ng/L)	1.551	0.694	4.986	0.026	4.715	1.209	18.39
WHO Classification (III-IV)	1.514	0.671	5.095	0.024	4.544	1.221	16.92
Pre-treatment KPS score (<80)	1.192	0.629	3.593	0.058	3.292	0.96	11.288
Constant	-3.252	0.786	17.139				

Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor; KPS, Karnofsky Performance Status.

Table 4. ROC curve analysis for predicting patient prognosis

Index	Cutoff value	AUC (95% CI)	P	Sensitivity	Specificity
VEGF (ng/L)	301.48	0.747 (0.64, 0.86)	<0.001	0.77	0.71
EGF (ng/L)	100.98	0.798 (0.70, 0.90)	<0.001	0.87	0.66
Combined factor	-	0.803 (0.70, 0.90)	<0.001	0.87	0.71

Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor; AUC, Area under the receiver operating characteristic (ROC) curve.

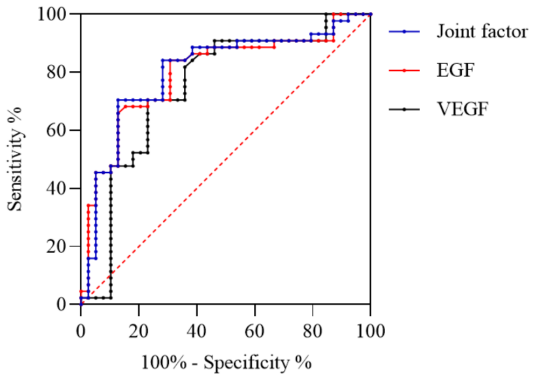

Figure 3. Receiver operating characteristic (ROC) curve analysis. Note: VEGF, vascular endothelial growth factor; EGF, epidermal growth factor.

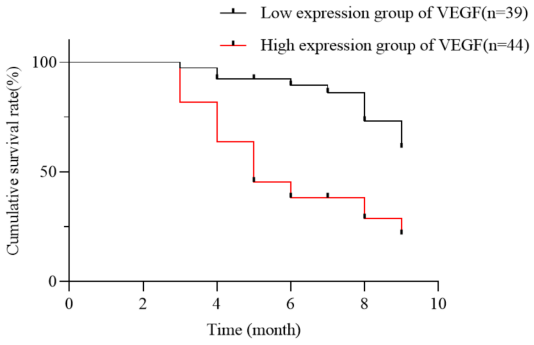

Figure 4. Kaplan-Meier survival curves comparing the high-expression and low-expression VEGF groups. Note: VEGF, vascular endothelial growth factor.

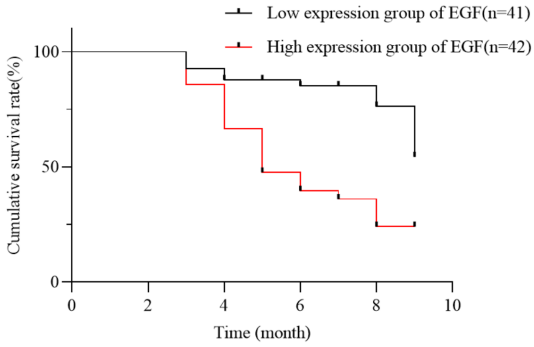

Figure 5. Kaplan-Meier survival curves comparing the high-expression and low-expression EGF groups. Note: EGF, epidermal growth factor.

cell proliferation and migration, its elevated expression may serve as a key biological marker indicating increased tumor aggressiveness [19]. Moreover, patients with a KPS score <80 exhibited higher levels of both EGF and VEGF compared to those with scores ≥80. The KPS score is widely used to assess patients' functional status and quality of life, with lower scores reflecting poorer physical condition and quality of life [20]. The results of this study demonstrate a negative correlation between EGF and VEGF levels and KPS scores, which may be explained by the tumor-promoting effects of these factors leading to accelerated tumor growth and invasion. This, in turn, likely contributes to the deterioration of patients'

physical condition and quality of life, resulting in decreased KPS scores.

In recent years, stereotactic radiosurgery has become a key treatment modality for recurrent gliomas, garnering increasing attention regarding its therapeutic efficacy and prognostic factors. This technique achieves localized tumor control by precisely delivering high-dose radiation, making it especially suitable for recurrent lesions located deep within the brain or adjacent to critical functional areas. Nevertheless, treatment outcomes are influenced by a variety of factors, including tumor molecular characteristics, alterations in the tumor microenvironment, and treatment-related toxicities [21, 22]. Therefore, elucidating the factors that influence the efficacy of stereotactic radiosurgery is essential for optimizing treatment strategies and improving patient prognosis.

In this study, a one-year follow-up of patients with recurrent glioma revealed that 39 patients died, with the deceased group showing higher levels of EGF and VEGF. ROC curve analysis indicated that both individual and combined detection of EGF and VEGF yielded AUC exceeding 0.7 for prognostic prediction. These findings suggest a strong association between EGF and VEGF expression and clinical outcomes in glioma patients, suggesting that integrating these biomarkers with clinical characteristics can enhance prognostic accuracy in clinical practice. Multivariate logistic regression further identified VEGF ≥300.94 ng/L, EGF ≥102.50 ng/L, and WHO glioma grade III-IV as independent predictors of poor prognosis following stereotactic radiosurgery. This underscores the critical role of elevated EGF and VEGF expression, alongside advanced higher tumor grade, as key prognostic factors in patients with recurrent glioma.

Additionally, Kaplan-Meier survival curve analysis was performed to compare overall survival between high and low expression groups of VEGF and EGF. Patients in the high-expression groups exhibited significantly shorter cumulative survival times compared to those in the low-expression groups, further confirming the strong association between elevated EGF and VEGF levels and glioma progression [23-25]. Consequently, clinical strategies aimed at inhibiting the expression of EGF and VEGF or blocking their signaling pathways may hold potential to prolong survival and improve outcomes in glioma patients.

In summary, this study demonstrates that EGF and VEGF are markedly elevated in the CSF of glioma patients, and their quantification provides valuable insights into tumor malignancy and prognosis. These findings offer important implications for the diagnosis and treatment of gliomas. However, the relatively short one-year follow-up limits the ability to fully assess the long-term prognostic impact of EGF and VEGF levels. Therefore, further multicenter studies with large cohorts and extended follow-up durations are needed to validate these findings.

Disclosure of conflict of interest

None.

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References

[1] Miller KD, Ostrom QT, Kruchko C, Patil N, Tihan T, Cioffi G, Fuchs HE, Waite KA, Jemal A, Siegel RL and Barnholtz-Sloan JS. Brain and other central nervous system tumor statistics, 2021. CA Cancer J Clin 2021; 71: 381-406.

[2] Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A and Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol 2021; 23: 1231-1251.

[3] Jiang T, Nam DH, Ram Z, Poon WS, Wang J, Boldbaatar D, Mao Y, Ma W, Mao Q, You Y, Jiang C, Yang X, Kang C, Qiu X, Li W, Li S, Chen L, Li X, Liu Z, Wang W, Bai H, Yao Y, Li S, Wu A, Sai K, Li G, Yao K, Wei X, Liu X, Zhang Z, Dai Y, Lv S, Wang L, Lin Z, Dong J, Xu G, Ma X, Zhang W, Zhang C, Chen B, You G, Wang Y, Wang Y, Bao Z, Yang P, Fan X, Liu X, Zhao Z, Wang Z, Li Y, Wang Z, Li G, Fang S, Li L, Liu Y, Liu S, Shan X, Liu Y, Chai R, Hu H, Chen J, Yan W, Cai J, Wang H, Chen L, Yang Y, Wang Y, Han L and Wang Q; Chinese Glioma Cooperative Group (CGCG); Society for Neuro-Oncology of China (SNO-China); Chinese Brain Cancer Association (CBCA); Chinese Glioma Genome Atlas (CGGA) and Asian Glioma Genome Atlas (AGGA) network. Clinical practice guidelines for the management of adult diffuse gliomas. Cancer Lett 2021; 499: 60-72.

[4] Liu D, Liu Y, Hu X, Hu G, Yang K, Xiao C, Hu J, Li Z, Zou Y, Chen J and Liu H. Alterations of white matter integrity associated with cognitive deficits in patients with glioma. Brain Behav 2020; 10: e01639.
[5] Ostrom QT, Cioffi G, Waite K, Kruchko C and Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2014-2018. Neuro Oncol 2021; 23 Suppl 2: iii1-iii105.
[6] Kang Y, Li H, Liu Y and Li Z. Regulation of VEGF-A expression and VEGF-A-targeted therapy in malignant tumors. J Cancer Res Clin Oncol 2024; 150: 221.
[7] Minniti G, Niyazi M, Alongi F, Navarria P and Belka C. Current status and recent advances in reirradiation of glioblastoma. Radiat Oncol 2021; 16: 36.
[8] Wang P, Zhao L, Gong S, Xiong S, Wang J, Zou D, Pan J, Deng Y, Yan Q, Wu N and Liao B. HIF1α/HIF2α-Sox2/Klf4 promotes the malignant progression of glioblastoma via the EGFR-PI3K/AKT signalling pathway with positive feedback under hypoxia. Cell Death Dis 2021; 12: 312.
[9] Lou Z, Lou Z, Jiang Y and Chen Z. FGF2 and EGF for the regeneration of tympanic membrane: a systematic review. Stem Cells Int 2021; 2021: 2366291.
[10] Paskal W, Gotowiec M, Stachura A, Kopka M and Włodarski P. VEGF and other gene therapies improve flap survival-a systematic review and meta-analysis of preclinical studies. Int J Mol Sci 2024; 25: 2622.
[11] Beheshtizadeh N, Gharibshahian M, Bayati M, Maleki R, Strachan H, Doughty S and Tayebi L. Vascular endothelial growth factor (VEGF) delivery approaches in regenerative medicine. Biomed Pharmacother 2023; 166: 115301.
[12] Sun Y, Liu P, Wang Z, Zhang H, Xu Y, Hu S and Yan Y. Efficacy and indications of gamma knife radiosurgery for recurrent low-and high-grade glioma. BMC Cancer 2024; 24: 37.
[13] Cicek E, Circir A, Oyken M, Akbulut Caliskan O, Dioken DN, Guntekin Ergun S, Cetin-Atalay R, Sapmaz A, Ovaa H, Sahin O and Erson-Bensan AE. EGF-SNX3-EGFR axis drives tumor progression and metastasis in triple-negative breast cancers. Oncogene 2022; 41: 220-232.
[14] Huang JC, Duan CC, Jin S, Sheng CB, Wang YS, Yue ZP and Guo B. HB-EGF induces mitochondrial dysfunction via estrogen hypersecretion in granulosa cells dependent on cAMP-PKA-JNK/ERK-Ca2+-FOXO1 pathway. Int J Biol Sci 2022; 18: 2047-2059.
[15] Patel SA, Nilsson MB, Le X, Cascone T, Jain RK and Heymach JV. Molecular mechanisms and future implications of VEGF/VEGFR in cancer therapy. Clin Cancer Res 2023; 29: 30-39.
[16] Zhang Y and Brekken RA. Direct and indirect regulation of the tumor immune microenvironment by VEGF. J Leukoc Biol 2022; 111: 1269-1286.
[17] Bag AK, Mandloi S, Jarmalavicius S, Mondal S, Kumar K, Mandal C, Walden P, Chakrabarti S and Mandal C. Connecting signaling and metabolic pathways in EGF receptor-mediated oncogenesis of glioblastoma. PLoS Comput Biol 2019; 15: e1007090.
[18] Flavahan WA, Drier Y, Liau BB, Gillespie SM, Venteicher AS, Stemmer-Rachamimov AO, Suvà ML and Bernstein BE. Insulator dysfunction and oncogene activation in IDH mutant gliomas. Nature 2016; 529: 110-114.
[19] Hu C, Leche CA 2nd, Kiyatkin A, Yu Z, Stayrook SE, Ferguson KM and Lemmon MA. Glioblastoma mutations alter EGFR dimer structure to prevent ligand bias. Nature 2022; 602: 518-522.
[20] Luo C, Luo Q, Xu Y, Song J, Liu Y, Wang L, Dong Z, Huang W, Yu H and Li J. Analysis of clinical characteristics and risk factors of postoperative recurrence and malignant transformation of low-grade glioma. J Oncol 2022; 2022: 4948943.
[21] Bunevicius A and Sheehan JP. Radiosurgery for glioblastoma. Neurosurg Clin N Am 2021; 32: 117-128.
[22] De Pietro R, Zaccaro L, Marampon F, Tini P, De Felice F and Minniti G. The evolving role of reirradiation in the management of recurrent brain tumors. J Neurooncol 2023; 164: 271-286.
[23] Seyedmirzaei H, Shobeiri P, Turgut M, Hanaei S and Rezaei N. VEGF levels in patients with glioma: a systematic review and meta-analysis. Rev Neurosci 2020; 32: 191-202.
[24] Kashino G, Kobashigawa S, Uchikoshi A and Tamari Y. VEGF affects mitochondrial ROS generation in glioma cells and acts as a radioresistance factor. Radiat Environ Biophys 2023; 62: 213-220.
[25] Wu J, Yang H, Cheng J, Zhang L, Ke Y, Zhu Y, Wang C, Zhang X, Zhen X and Zheng LT. Knockdown of milk-fat globule EGF factor-8 suppresses glioma progression in GL261 glioma cells by repressing microglial M2 polarization. J Cell Physiol 2020; 235: 8679-8690.