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ORIGINAL ARTICLE

Prognostic factors in patients with glioblastoma multiforme: focus on the pathologic variants

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Abstract

The aim of this study was to offer predicting factors for survival in adult patients with glioblastoma multiforme. 153 consecutive patients with high-grade glioma (WHO grade IV) were studied in Imam Reza hospital, Kermanshah University of Medical Science, Kermanshah, Iran, between April 2003 and April 2017. All patients treated with surgical resection and standard postoperative radiotherapy (54 Gy). Using the patients' charts and electronic medical records system, the following data were obtained: gender, age, Karnofsky performance status (KPS) score on admission, primary vs. secondary type, extent of surgery, tumor location, tumor size, necrosis size, use of Temozolomide (TMZ), pathology subtype, and immunohistochemistry results. Patients were followed from the time of the surgery until the death occurred. Overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan–Meier method. Survival time curves for various subgroups were compared by the log-rank test. The impact of the suggested prognostic factors on survival was evaluated by univariate and multivariate analyses. Age, gender, KPS, extent of surgery, tumor location, necrosis size, and reoperation in recurrence had not any statistically significant effect on survival. Univariate analysis revealed a significant impact on outcome for pathology subtype (PFS: $P<0.001$, OS: $P<0.001$), tumor type (primary vs. secondary) (PFS: $P=P<0.001$, OS: $P<0.001$), tumor size (PFS: $P=0.044$, OS: $P=0.04$), TMZ therapy (PFS: $P<0.001$, OS: $P<0.001$), P53 (PFS: $P<0.001$, OS: $P<0.001$), and Ki67 (PFS: $P<0.001$, OS: $P<0.001$). In multivariate analysis, independent favorable prognostic factors for survival were pathology subtype (PFS: $P<0.001$, OS: $P<0.001$), type (PFS: $P<0.001$, OS: 0.012), TMZ (PFS: $P<0.001$, OS: $P<0.001$), P53 (PFS: $P<0.001$, OS: $P<0.001$), and Ki67 (PFS: $P<0.001$, OS: $P<0.001$). The results suggest that pathology subtype, primary vs. secondary type, TMZ therapy, P53, and Ki 63 may play an important role in the survival of patients with glioblastoma multiforme. There is no relationship detected between age, gender, KPS, tumor size and location, necrosis size, extent of surgery, reoperation in recurrence, and patient survival.

Keywords Glioblastoma multiforme · Prognostic factors · Overall survival · Progression-free survival · Karnofsky performance status

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Background

Glioblastoma (GBM) is the most common primary malignant central nervous system (CNS) tumor in adults [1, 2]. GBM comprises about 25% of primary CNS tumors and 50–55% of adult gliomas [3]. In spite of technical advances in surgery and adjuvant therapy modalities, median survival time is reported as less than 15 months in the most of the cases [4, 5]. Survival longer than 3 years and 5 years have been reported for approximately 3–5% and 0.5% of GBM patients, respectively. Some prognostic factors have been suggested for GBM, including age, Karnofsky performance status (KPS), tumor size and location, necrosis size, and

extent of resection [6]. Several different subtypes were reported for GBM, including: Gliosarcoma, Giant cell GBM, GBM with oligodendroglioma component (GBMO), small cell GBM, and Granular cell astrocytoma (GCA) [7, 8].

Several studies reported that patients with different histopathological patterns have different response to treatment and have different survival [9].

The aim of this study was to evaluate the effect of suggested predicting factors on survival of adult patients with glioblastoma multiforme.

Materials and methods

This retrospective study evaluated 153 consecutive patients with high-grade.

glioma (WHO grade IV) in Imam Reza Hospital, Kermanshah University of Medical Science, Kermanshah, Iran, from April 2003 to April 2017. All patients treated with surgical resection and standard postoperative radiotherapy (54 Gy). Before data collection and analysis, approval for this study was obtained from the Scientific Research Board, University of Kermanshah.

Using the patients' charts and electronic medical records system (hospital information system), the following data were obtained: gender, age, KPS score on admission, primary vs. secondary type, extent of resection, tumor location, tumor size, necrosis size, use of temozolomide (TMZ), pathology subtype, and immunohistochemistry results.

Inclusion criteria were: histologically proven glioblastoma multiforme, age $\geq$ 18 years at time of first surgery, and Karnofsky performance status $\geq$ 50. Patients with optic, cerebellar, pineal, or brain stem GBM were excluded. Patients that received no postoperative radiotherapy were excluded, too.

The surgical sample of each patient was studied by an experienced pathologist meticulously.

Preoperative and postoperative MRI and computerized tomography recordings were obtained. Follow-up MRI was performed every 3 months. In case of contraindications in performing MRI, patients followed with CT scan. Neuroimaging features of tumor including largest tumor diameter, diameter of necrosis, and tumor location were determined by an experienced neuroradiologist. Volumetric assessments were performed in all patients based on preoperative and postoperative MR images obtained within 2 days after operation. Tumor mass was measured based on the globoid scale (i.e., $A \times B \times C/2$) [10, 11].

On the basis of the surgeon's intraoperative impression and postoperative images, extent of resection was categorized into three groups: biopsy group (less than 10% resected), subtotal group (10–90% resected), or total resection (greater than 90% resected) [9, 12].

The immunostaining was examined for the presence of p53 and Ki67, and individually observed and counted by an experienced pathologist using a microscope. The labeling index for Ki-67 was determined as the percentage of positive cells per 1000 cells. The presence of p53 was determined using the percentage of immunostained cells per 200 cells in 5 fields. The p53 scoring system (based on the number of positive cells) was as follows: negative (< 50%) and positive cells (> 50) [13, 14].

Patients were followed from the time of the surgery until the death occurred. Overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan–Meier method. OS was defined from the date of first surgery until the day of death and PFS was determined from the date of first craniotomy until the diagnosis of progression based on imaging or until tumor-related death. The impact of the suggested prognostic factors on survival was evaluated by univariate and multivariate analyses.

Statistical analysis

All the statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 24.0. Continuous variables were measured as mean $\pm$ standard deviation, and categorical variables were expressed as frequency or percentages. Independent t and Chi square tests were used to analyze the difference of continuous variables and categorical data, respectively. Univariate and multivariate Cox regression models were used for analyses of the effects of suggested variables on patients' survival time. Statistical significance was defined as $P < 0.05$.

Overall survival and progression-free survival rates were calculated by Kaplan–Meier method. Survival time curves for various subgroups were compared by the log-rank test.

Results

Of total 153 patients in this study, 93 (60.8%) patients were male and 60 patients (39.2%) were female (Table 1). Mean and standard deviation of age, overall survival, and progression-free survival were 56.32 ± 9.22 years, 18.13 ± 6.84, and 11.42 ± 4.85 months, respectively. Overall survival rates for 1, 2, and 3 year(s) were 73.2, 57.5, and 15.7% respectively.

On the basis of the pathologic assessment, 138 (90.2%) patients had primary GBM and 15 (9.8%) patients had secondary GBM. 93 (60.8%) of patients had classic GBM, 22 (14.4%) had small cell GBM, 13 (8.5%) had gliosarcoma, 8 (5.2%) had granular cell GBM, 9 (5.9%) had giant cell GBM, and 8 (5.2%) had oligodendroglia GBM (Table 1). Patients with oligodendroglia and giant cell variants had

Table 1 Descriptive statistics of the variables

Variables	Frequency (%)
Age	
> 50	98 (64.1)
< 50	55 (35.9)
Gender	
Male	93 (60.8)
Female	60 (39.2)
KPS	
> 70	132 (86.3)
< 70	21 (13.7)
Type	
Primary	138 (90.2)
Secondary	15 (9.8)
Extent of surgery	
Gross total resection	107 (69.9)
Partial resection	32 (20.9)
Biopsy	14 (9.2)
Tumor location	
Frontal	26 (17)
Temporal	53 (34.6)
Parietal	26 (17.0)
Occipital	11 (7.2)
Insular	9 (5.9)
Other	13 (8.5)
Multicenter	15 (9.8)
Tumor size	
< 3 cm	33 (21.6)
3< × < 5 cm	75 (49.0)
5 cm and above	45 (29.4)
Necrosis size	
Non	12 (7.8)
< 2 cm	90 (58.8)
2 < × < 4	37 (24.2)
4 and above	14 (9.2)
Pathology	
Classic GBM	93 (60.8)
Small cell GBM	22 (14.4)
Gliosarcoma	13 (8.5)
Granular cell	8 (5.2)
Giant cell	9 (5.9)
Oligodendroglia	8 (5.2)
Reoperation in recurrence	
Yes	117 (76.5)
No	36 (23.5)
TMZ	
Yes	131 (85.6)
No	21 (13.7)
P53	
< 50%	78 (51.0)
> 50%	46 (30.0)
Unavailable	29 (19.0)
Ki67	
< 25%	76 (49.7)
> 25%	49 (32.0)
Unavailable	28 (18.3)

longer OS and PFS, while patients with granular cell variant had shorter OS and PFS ($P < 0.001$) (Table 2).

Based on preoperative KPS, 132 (86.3%) patients had preoperative KPS more than 70 and 21 (13.7%) patients had KPS less than 70.

Among these patients, 131 (85.6%) patients received concurrent TMZ during their radiation therapy and after the completion of radiation therapy. The median PFS and OS were 19.56 ± 3.05 months and 9.19 ± 2.85 for temozolomide receiving and non-receiving groups, respectively.

Univariate analysis revealed a significant impact on outcome for pathology subtype (PFS: $P < 0.001$, OS: $P < 0.001$), tumor type (primary vs. secondary) (PFS: $P = P < 0.001$, OS: $P < 0.001$), tumor size (PFS: $P = 0.044$, OS: $P = 0.04$), TMZ (PFS: $P < 0.001$, OS: $P < 0.001$), P53 (PFS: $P < 0.001$, OS: $P < 0.001$), and Ki67 (PFS: $P < 0.001$, OS: $P < 0.001$) (Table 2). In multivariate analysis, independent favorable prognostic factors for survival were pathology subtype (PFS: $P < 0.001$, OS: $P < 0.001$), type (PFS: $P < 0.001$, OS: 0.012), TMZ (PFS: $P < 0.001$, OS: $P < 0.001$), P53 (PFS: $P < 0.001$, OS: $P < 0.001$), and Ki67 (PFS: $P < 0.001$, OS: $P < 0.001$) (Table 3). Age, gender, KPS, extent of surgery, tumor location, necrosis size, and reoperation in recurrence had not any statistically significant effect on survival (Table 2). Survival time curves for various subgroups are showed in Figs. 1, 2, 3, 4 and 5.

Discussion

The results of our study suggest that pathology subtype, primary vs. secondary type, TMZ therapy, P53, and Ki 63 may play an important role in the survival of patients with glioblastoma multiforme.

Several different subtypes were reported for GBM, including: classic GBM, gliosarcoma, giant cell GBM, GBM with oligodendroglioma component (GBMO), small cell GBM, and granular cell astrocytoma (GCA) [15].

There was reported that patients with different histopathological patterns had different survivals [2, 3, 16]. Classic GBM including infiltrating, pleomorphic, hyperchromatic cells with glassy, astrocytic cytoplasm, frequent presence of pseudo palisading necrosis, neoepithelialization, mitotic figures, and hypercellularity. Areas of focal pseudopalisading

Table 2 Relationship between survival, progression free survival and the variables

Variables	Overall survival			Progression free survival		
	Mean (months)	Mean rank	Statistics test	Mean	Mean rank	Statistical test
Age						
> 50	18.18	77.02	$Z = -0.275$	11.55	76.21	$Z = -0.153$
< 50	18.36	75.13	$P = 0.676$	11.96	77.89	$P = 0.770$
Gender						
Male	18.17	77.82	$Z = -0.285$	11.33	76.53	$Z = -0.163$
Female	18.08	75.73	$P = 0.776$	11.56	77.73	$P = 0.870$
KPS						
> 70	18.27	77.80	$Z = -0.563$	11.42	76.84	$Z = -0.114$
< 70	17.28	71.95	$P = 0.573$	11.42	78.02	$P = 0.909$
Type						
Primary	17.26	71.46	$Z = -4.69$	10.95	72.47	Z = − 3.853
Secondary	26.13	127.93	$^*P < 0.001$	15.73	118.70	$^*P < 0.001$
Extent of surgery						
Gross total resection	18.69	80.94	K2 = 2.94	11.56	79.11	K2 = 0.916
Partial resection	17.03	69.31	$P = 0.23$	10.56	70.70	$P = 0.632$
Biopsy	16.42	64.46		12.35	75.29	
Tumor location						
Frontal	18.88	79.21	K2 = 4.172	11.42	78.67	K2 = 5.180
Temporal	17.67	74.38	$P = 0.653$	11.37	76.92	$P = 0.521$
Parietal	17.88	75.06		11.11	76.04	
Occipital	21.18	97.82		12.54	88.95	
Insular	19.11	84.94		10.88	76.11	
Other	18.30	78.08		14.23	89.92	
Multicenter	15.93	64.83		9.20	56.60	
Tumor size						
< 3 cm	17.48	71.15	K2 = 5.84	11.81	74.95	K2 = 6.430
3< × < 5 cm	19.36	85.67	$P = 0.054$	12.08	85.19	$^*P = 0.04$
5 cm and above	16.57	66.83		10.04	64.12	
Necrosis size						
Non	18.33	79.13	K2 = 6.01	12.16	81.13	K2 = 6.23
< 2 cm	18.88	81.74	$P = 0.111$	11.60	79.69	$P = 0.101$
2 < × < 4	17.81	74.64		11.83	79.73	
4 and above	14.00	50.96		8.57	48.96	
Pathology						
Classic GBM	19.29	84.76	K2 = 79.46	11.86	84.17	K2 = 73.27
Small cell GBM	10.68	29.45	$^*P < 0.001$	7.13	30.75	$P < 0.001$
Gliosarcoma	16.84	65.54		10.53	72.85	
Granular cell	7.25	8.88		4.50	8.69	
Giant cell	27.33	140.44		17.66	130.83	
Oligodendroglia	27.87	132.94		19.50	135. 38	
Reoperation in recurrence						
Yes	18.02	76.09	$Z = -0.459$	11.32	75.77	$Z = 0.622$
No	18.50	79.96	$P = 0.646$	11.75	81.00	$P = 0.534$
TMZ						
Yes	19.56	85.50	$Z = -6.30$	12.25	85.55	$Z = -6.007$
No	9.19	20.36	$^*P < 0.001$	6.19	23.26	$^*P < 0.001$

Table 2 (continued)

Variables	Overall survival			Progression free survival		
	Mean (months)	Mean rank	Statistics test	Mean	Mean rank	Statistical test
P53						
< 50%	21.11	95.67	K2 = 52.78 *$P < 0.001$	13.53	99.02	K2 = 58.59 *$P < 0.001$
> 50%	12.00	37.54		7.50	36.47	
Unavailable	19.86	89.36		11.96	82.07	
Ki67						
< 25%	20.92	94.46	K2 = 40.46 *$P < 0.001$	13.34	96.77	K2 = 41.69 *$P < 0.001$
> 25%	13.06	44.09		8.28	44.65	
Unavailable	19.46	87.20		11.71	79.95	

*Statistically significant ($P < 0.05$)

Table 3 Multivariate analyses of the factors associated with survival rate and PFS

Factor (indicator)	OS		PFS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Type	0.35 (0.201–0.609)	*< 0.001	0.50 (0.292–0.857)	0.012
Pathology (classic GBM)				
Small cell GBM	11.36 (5.97–21.61)	*< 0.001	7.54 (4.30–13.22)	*< 0.001
Gliosarcoma	2.27 (1.23–4.16)	*0.008	1.58 (0.877–2.86)	0.127
Granular cell	52.47 (19.66–140.05)	*< 0.001	36.48 (14.59–91.17)	*< 0.001
Giant cell	0.276 (0.135–565)	*< 0.001	0.318 (0.154–0.657)	*0.002
Oligodendroglia	0.221 (0.099–0.494)	*< 0.001	0.284 (0.133–0.605)	*0.001
TMZ	6.74 (4.08–11.14)	*< 0.001	5.240 (3.196–8.590)	*< 0.001
P53 (< 50%)				
> 50%	4.51 (3.02–6.75)	*< 0.001	5.52 (3.58–8.52)	*< 0.001
Unavailable	0.996(0.647–1.53)	0.984	1.24 (0.809–1.91)	0.318
Ki67 (< 25%)				
> 25%	3.39 (2.30–4.99)	*< 0.001	3.11 (2.12–4.561)	*< 0.001
Unavailable	1.098 (0.708–1.70)	0.677	1.27 (0.821–1.971)	0.281
Tumor size (<3 cm)				
3 < × < 5 cm	0.835 (0.553–1.26)	0.390	0.988 (0.650–1.50)	0.954
5 cm and above	1.07 (0.680–1.68)	0.771	1.46 (0.925–2.322)	0.102

*Is significant

necrosis and microvascular proliferation are characteristic for classic GBM. Median PFS and OS of classic GBM, were reported as 5.3–10.3 months and 12.7–21.7 months, respectively [7, 17].

In our study, 60.8% of cases (93 patients) had classic GBM, and median OS and PFS were 19.29 months ($P < 0.001$) and 11.86 months ($P < 0.001$), respectively.

Gliosarcoma is one of the GBM subtypes with prevalence of 1–5% of all patients with GBM diagnosis. This subtype occurs mostly in ages between 50 and 70. Gliosarcoma commonly occurs in temporal lobes; it is a circumscribed lesion with histological features of meningioma. Mutation in P53 has been seen in both glioma and sarcoma areas of the tumor. Presentation of meningioma component increases survival greater than gliosarcoma alone [5, 18]. Gliosarcoma has potential of metastasis to extracranial organs such as lungs and liver. Gliosarcoma can occur after radiotherapy of GBM; this subtype of GBM has been also reported in spinal cord [19]. the survival of this type was reported as 4–11 months.The pathological findings include the features of GBM along with heterogeneous sarcomatous and mesenchymal components and differentiation staining for reticulin, laminin, collagen type IV, procollagen type III, fibronectin, vimentin, alfa-1 antitrypsin, and chymotrypsin A. Primary gliosarcoma could show pattern of malignant fibrous histiocytoma, osteosarcoma, or fibrosarcoma [20].

Median OS of 4–11 months was reported for gliosarcoma; in our analysis, the prevalence of patients with gliosarcoma was 8.5% (13 patients), with median OS of 16.84 months ($P < 0.001$) and PFS of 10.53 months ($P < 0.001$).

Giant cell GBM is a rare variant of GBM (with including 2–5% of GBM) that distinguished with prominent

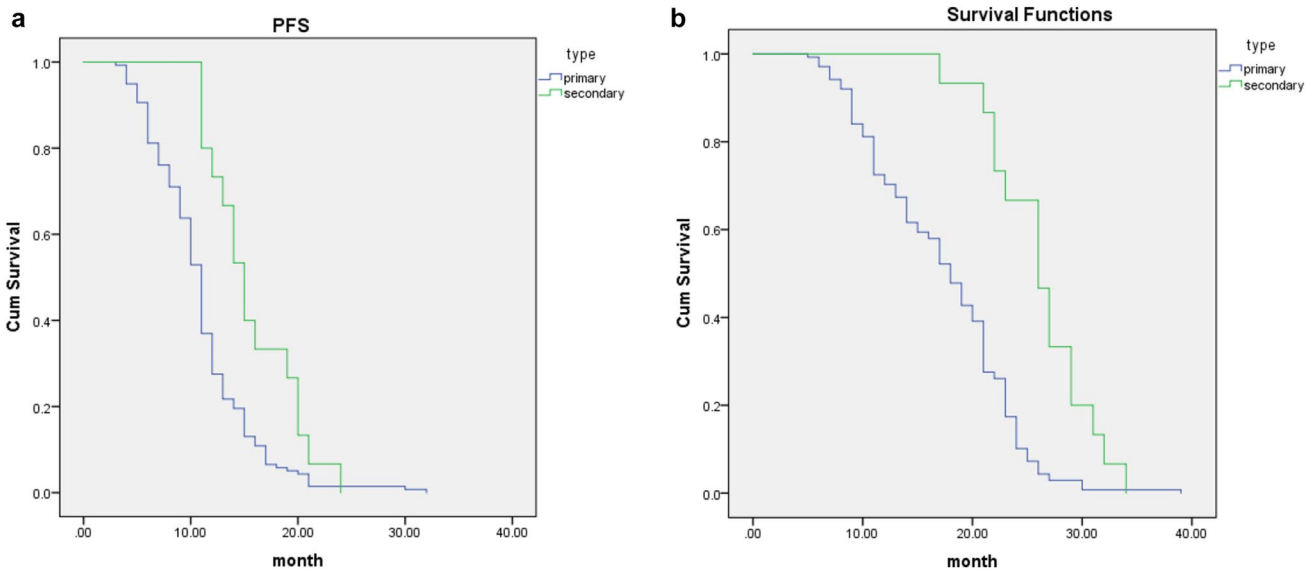

Fig. 1 Comparison of Kaplan–Meier estimates of clinical outcomes between the patients with primary tumors and the patients with secondary tumors: overall survival (**a**) and progression-free survival (**b**)

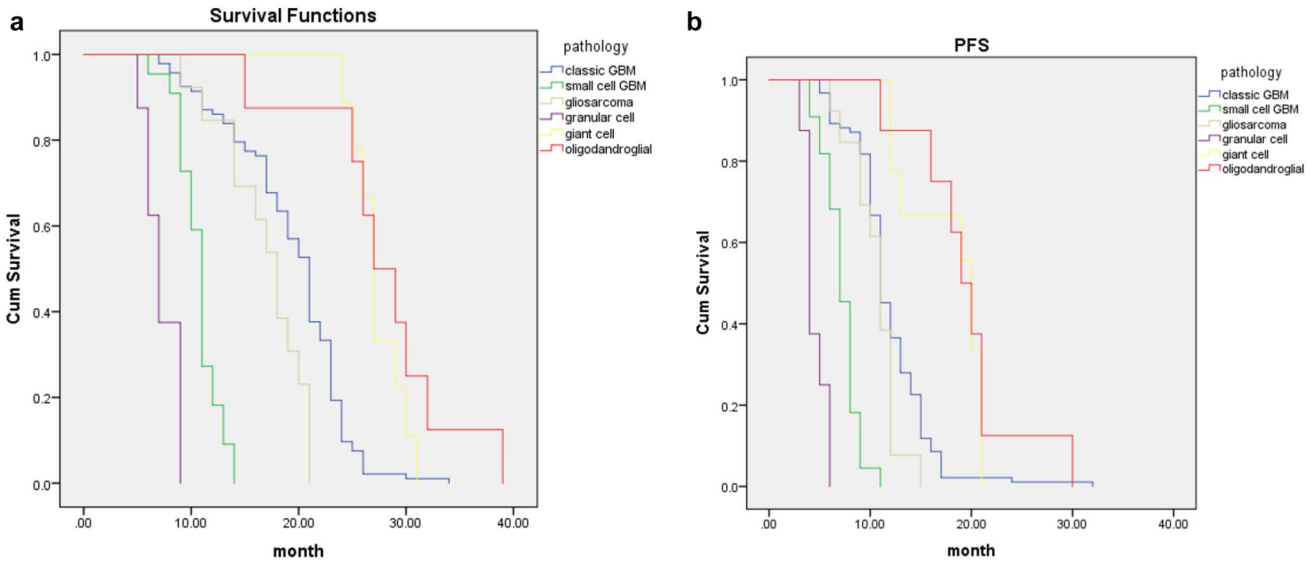

Fig. 2 Comparison of Kaplan–Meier estimates of clinical outcomes of the patients with different pathologic variants of glioblastoma: overall survival (**a**) and progression-free survival (**b**)

multinucleated giant cells, lymphatic infiltration, necrosis, and atypia [21, 22].This subtype often presents in younger population and shows distinct surgical borders, these findings impetus to do more aggressive surgical resections for improve survival of patients with this subtype of GBM. Giant cell GBM reported in some patients with Turcot syndrome [23]. In our study, this type was seen in only 5.9% (9 patients) of cases, and OS and PFS of them were 27.33 and 17.66 months, respectively.

Small cell astrocytoma (SCA) characterized by monomorphic proliferation of cells with small nuclei, limited cytoplasm, round nuclei, limited reticular stroma, and low mitotic index [24, 25].

Small cell astrocytoma is an aggressive lesion and compromises about 10% of GBM [4, 5].

Median survival of SCA in some studies reported about 6–12 months, in our study, and we found that SCA

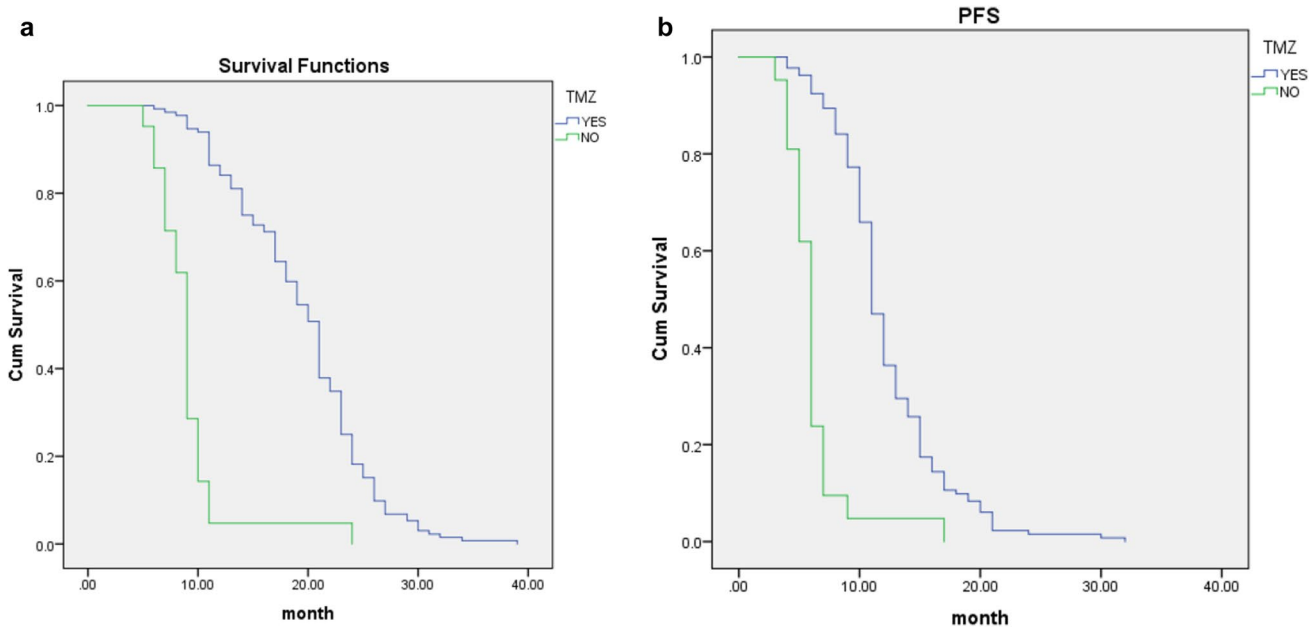

Fig. 3 Comparison of Kaplan–Meier estimates of clinical outcomes between the temozolomide receiving and non-receiving patients: overall survival (**a**) and progression-free survival (**b**)

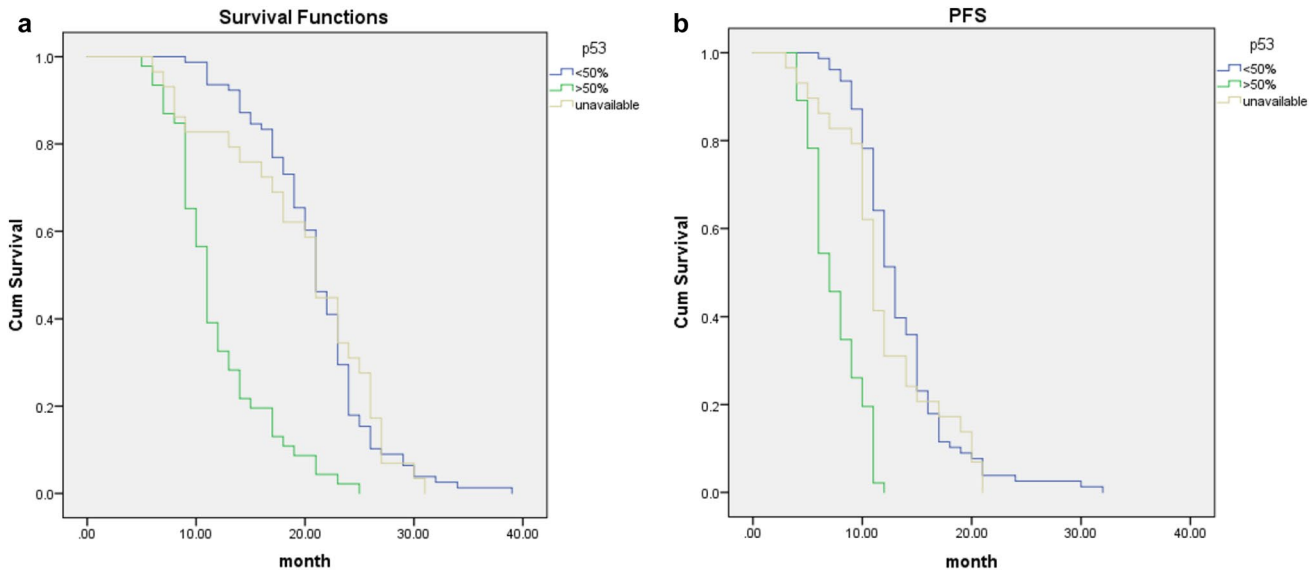

Fig. 4 Kaplan–Meier estimates of clinical outcomes on the basis of p53: overall survival (**a**) and progression-free survival (**b**)

consisted 14.4% (22 patients) of all patients, with OS of 10.6 months and PFS of 7.13 months.

GBM with oligodendroglioma component (GBMO) is one of the other variants of GBM. This histopathological pattern is resembling GBM, but it contains areas of oligodendroglioma with typical fried egg appearance [6, 14]. This category of GBM is more sensitive to chemotherapy than GBM. Finding oligodendrocytic component in pathology improve prognosis of GBM. Honey comb like pattern in GBMO predict better survival than round cell appearance. Patients with GBMO usually response to chemoradiotherapy [26]. Younger patients with GBMO have better overall survival and response better to radiotherapy than GBM [9]. Mean OS of 19–26 months and median PFS of 10.3 months reported for GBMO; in our retrospective study, only 5.2% of patients (8 cases) had this histopathology pattern and OS of 27.87 months and PFS of 19.5 months were detected.

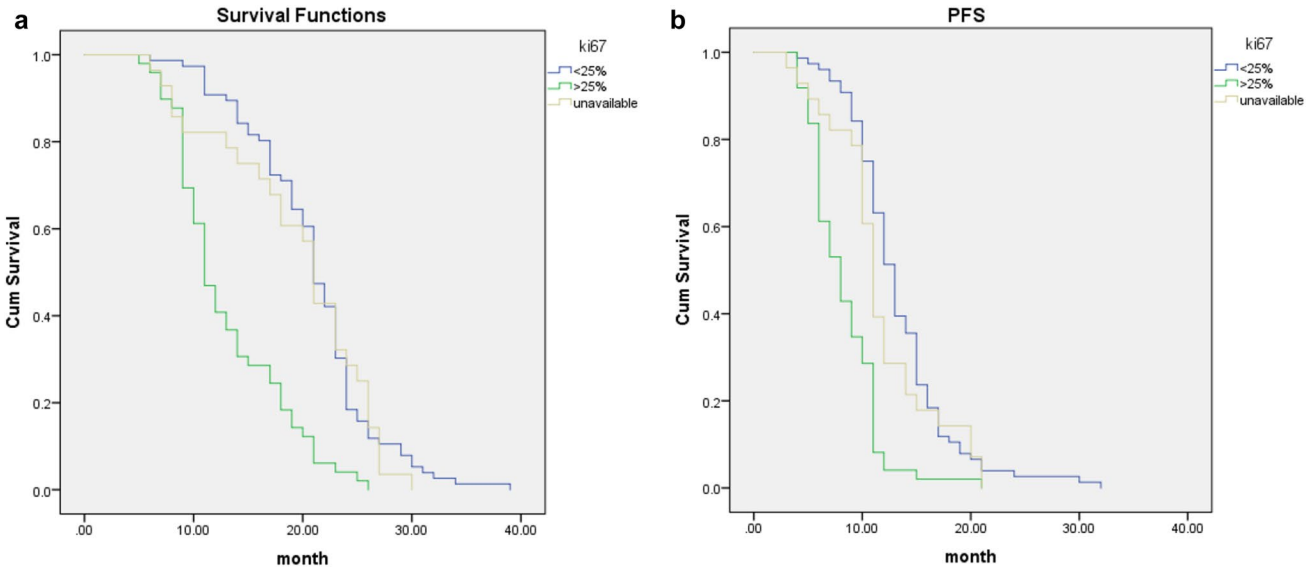

Fig. 5 Kaplan–Meier estimates of clinical outcomes on the basis of Ki67: overall survival (**a**) and progression-free survival (**b**)

Granular cell astrocytoma is a rare infiltrative malignant gliomas characterized by many granular cells with large distinct cell borders, round-to-oval shape, and many eosinophilic granular cytoplasm with periodic acid-schiff (PAS: pos) [11]. GCA often displays aggressive features. [10, 18]. One-year survival for GCA was reported in 40% of patients with low-grade and 12% for high-grade lesions which extended to multiple cerebral lobes. Similar to gemistocytic astrocytoma, GCAs mimic a benign pathological pattern despite distinct molecular mechanism. In GCA, mean survival is only 7.6 months and 1-year survival in low-grade pattern is 40% and in high-grade lesions is 12% [11, 16]. In our study, 5.2% of patients (8 patients) had GCA histopathology with OS of 7.25 months and PFS of 4.5 months.

On the basis of tumor precursor cell, GBM could dichotomize into primary and secondary types [8, 13]. Primary type consists of 80–90% of all GBM and develop rapidly de novo in elderly patients, without histologic and clinical evidence of a less malignant precursor lesion. Secondary GBM progress from low-grade lesions. They present in younger patients and have a significantly better prognosis. Primary and secondary glioblastomas differ in their genetic and epigenetic profiles, but they are histologically indistinguishable [3, 14]. The median overall survival of primary and secondary glioblastoma reported 4.7 and 7.8 months, respectively ($P=0.003$) [17]. Yan and colleagues reported that secondary glioblastomas had an overall survival time of 31 months, again twice as long as primary tumors [23].

Temozolomide is a bioactive oral chemotherapeutic agent for treating high-grade glioma. TMZ could be used for treatment of newly diagnosed or recurrent lesions. There are several reports indicated improvement of survival in GBM patients that receive temozolomide in comparison to non-receiving group [12]. Although TMZ demonstrates promising activity against high-grade glioma, after a few months, drug resistance develops in most cases; thereafter, antitumor activity of TMZ lasts only a few months [8]. It was suggested that resistance to TMZ, mediated by a DNA repair enzyme, O^6-methylguanine DNA methyltransferase (MGMT), which is induced in tumor cells. Some studies reported that methylation of the MGMT promoter detected in 60% of GBM [26]. Enzyme activity is significantly correlated with the expression levels of MGMT mRNA and protein [16]. The survival time for patients who are positive for MGMT is shorter than that of patients who are negative for MGMT [3, 4].

p53 is an important molecular marker used in gliomas [2, 16]. p53 is a tumor suppressor gene that plays an important role in promoting tumor cell apoptosis. There is a controversy in the correlation between p53 immunoreactivity and the survival outcome of glioma patients. It is suggested that this difference may be a result of the various methods used to detect p53 expression in GBM samples from differing patient populations [1, 5]. Ki-67 is a cell proliferation nuclear antigen. The level of ki 67 can reflect the proliferation and malignancy of tumor cells [21]. Some studies showed that increased Ki-67 expression is positively correlated with the increased grade of malignancy and a poor prognosis in GBM patients [24]. Our study showed that a substantial increase in Ki-67 expression was correlated with a shorter OS and PFS.

There are several limitations in this study. First, this was a retrospective study and was not randomized and controlled. Second, the number of patients is relatively small,

and some data were missed. However, the results of present study could provide valuable data for helping surgeons and patients with glioblastoma multiforme.

Conclusions

The results suggest that pathology subtype, primary vs. secondary type, TMZ therapy, P53, and Ki 63 may play an important role in the survival of patients with glioblastoma multiforme. There is no relationship detected between age, gender, KPS, tumor size and location, necrosis size, extent of surgery, reoperation in recurrence, and patient survival.

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Authors' contributions EA and SRB had the idea for this study. EA and PR participated in outlining the concept and design. ZR and ASS did the data acquisition. EA and AA did the statistical analysis and wrote the first draft of the manuscript. EA, SRB, ASS, and AA revised the final manuscript. All authors have read and approved the manuscript.

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Data availability All data are available from the corresponding author upon reasonable request.

Compliance with ethical standards

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

Consent for publication Not applicable.

Ethics approval and consent to participate The study received ethics approval by the Kermanshah University of Medical Science Ethics Committee.

Informed consent All participants provided informed consent prior to their participation.

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