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Survival rate of patient with glioblastoma: a population-based study

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Abstract

Introduction Glioblastoma, as the most common and lethal primary malignant brain tumor, has estimated mean survival of 15 months. GBM is reported more in men. Malignant glioma is the cause of 2.5% of cancer deaths. The standard therapy for patients with newly diagnosed GBM includes tumor resection surgeries, followed by radiotherapy and chemotherapy. The prognosis of glioma is a major challenge, and the outcome of GBM has remained almost unchanged for past years. The present study aimed to determine patient survival.

Methods Patients with glioblastoma tumors who visited Al-Zahra and Kashani hospitals from 2013 to 2021 were included in this study. All patients were classified with morphological codes according to the International Classification of Diseases for Oncology. The patients' information was recorded in the checklist, and then, the patients were followed up by phone. The data were measured regarding age, gender, exposure to chemicals, body mass index (BMI), and survival from the patient's surgery to death. Several questions were asked from the families of deceased patients and survivors based on the KPS Status Scale. Finally, the sample was analyzed with SPSS version 26.

Result The patient's mean age was 51.93 years, and the male–female ratio was 1:1.7. The patients' mean overall survival was 29 months and a total of 9 patients survived. There was a significant difference between the age groups in terms of 1-year survival so that more deaths were observed in the age group of more than 50 years. The mean tumor size was 5.2 ± 2.1 cm. The survival analysis indicated that the temporal lobe was more than the other in 2-year survival. The most common symptom of patients before surgery was headache (31.8%) followed by motor dysfunction. The 1-year, 2-year, 5-year, and overall survival of the patients was 4.5%, 18.38%, 37.13%, and 33.68%, respectively.

Conclusions The results of the present study indicated that the patients' survival improved over time with the advancement of adjuvant therapies. Therefore, if patients care get better for the first year after surgery, their survival will improve from the second year after the operation.

Keywords Glioblastoma, Malignant brain tumor, Survival, Karnofsky performance status

Introduction

Glioblastoma, as the most common and lethal primary malignant brain tumor, accounts for approximately 54% of gliomas and has an incidence of 3 to 4 per 100,000 individuals with an estimated mean survival of 15 months [1]. Gliomas are classified as different histological subgroups such as astrocytes and oligodendrocytes depending on the original glial cell [2].

According to studies, the 5-year overall survival is less than 20% for glial tumors and approximately 5% for glioblastoma multiforme (GBM) [3]. Survival generally decreases with increasing age at diagnosis, so that the incidence of glioblastoma increases with reaching the peak of age at 75 to 84 years and decreases after 85 years [4]. The age at diagnosis for the primary GBM (the mean age of 55 years and the average age of 64 years) is

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higher than that for the secondary GBM (the mean age of 40 years) [5]. Its incidence is 0.85 per 100,000 in the pediatric population (0–18 years), and the pediatric glioblastoma multiforme (p-GBM) accounts for 3–15% of primary brain tumors [6].

GBM is reported more in men, and the incidence rate is 1.57%; the rate is higher in males than in females [7]. The frequency of the primary GBM is more common in males, and the second type is more common in females [8].

More than 90% of patients have histological diagnoses; however, it is less than 60% in cases over 70 years of age [9]. The World Health Organization classification is the current international standard for nomenclature and diagnosis of glioma, dividing glioma into grades I to IV depending on the level of malignancy determined by histopathological criteria. Grade-I gliomas are related to lesions with low proliferative potential and can be treated with surgery, while grade II to grade IV gliomas are extremely malignant and aggressive [10, 11].

Malignant glioma is the cause of 2.5% of cancer deaths and the third leading cause of cancer deaths in people aged 15 to 34 years [12]. The difference in survival results with the mean survival of 6 to 10 months in registry databases and 14.6 to 21.1 months in individuals treated with standard treatment in clinical trials, have led to ambiguities, and the mean survival is 3 months in untreated patients [13, 14].

Only 3–5% of patients survive for 5 years, and patients surviving more than 24 years from the initial diagnosis of glioblastoma are known as "long-term survivors (LTS)" [15]. Filho (2017) described the increasing rates of CNS cancers in South American, Eastern, and Southern European countries, while reported a decreasing rate only in Japan [16]. Lam (2018) reported that 46.9% of people survived up to 2 years after glioblastoma diagnosis [17].

The location of glioblastoma multiforme is in frontal, temporal, and parietal lobes in most cases, and it affects other structures in some cases. In the last two decades, the increase in the number of diagnosed cases has been significant, especially in frontal and temporal lobes. The most common and the least common regions are frontal, temporal, parietal, and occipital lobes, as well as other brain structures [18].

The standard therapy for patients with newly diagnosed GBM includes surgery and tumor resection, followed by postoperative radiotherapy with concomitant and adjunctive temozolomide therapy. Recurrence is inevitable in this therapy, and almost all patients suffer from tumor recurrence despite their initial aggressive therapy [19]. Studies indicate that the mean time of recurrence is approximately 32 to 36 weeks after the initial multimodal therapy, and this is often the result of continued neoplastic growth within 2 to 3 cm of the original neoplasm [20].

The prognosis of glioma is a major challenge, and the management and treatment outcome of GBM have remained almost unchanged for the past four decades; however, it is still the most malignant primary brain tumor with a clear male predominance [21]. Nevertheless, new advances in genetic and molecular research will broaden new horizons in the future management and outcome of this devastating tumor [22]. The present study aimed to determine the demographic characteristics of patients, who were histologically diagnosed with GBM tumors, and to evaluate the determinants of patient survival.

Methods

The present study was descriptive-analytical and retrospective and investigated patients with glioblastoma tumors, who visited the neurosurgery departments of Al-Zahra and Kashani hospitals from 2013 to 2021.

This study is perfectly consistent with the Helsinki Declaration of Human Rights. Therefore, the researcher went to the hospitals and identified patients after receiving an ethical code from the Ethics Committee of Isfahan University of Medical Sciences.

All patients were classified with morphological codes according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3). Gliomas were classified under the following groups: pilocytic astrocytoma (Grade I: ICD-O-3, code 9421), diffuse astrocytoma (Grade II: code 9400, 9410, 9411, 9420), anaplastic astrocytoma (Grade III: code 9401, Grade IV: code 9440-9442), all other astrocytomas (9424, 9384), oligodendrocyte gliomas (9450, 9451), mixed gliomas (9382), ependymal tumors (9383, 9391-9394), and choroid tumors (3994).

The patients' information was recorded based on the medical record in the checklist, and then, the patients were followed up by phone. To this end, they were contacted by contact numbers in their file. The researcher explained the research objectives and told the patients or their families that they would receive questions if they had consent to participate in the study. The patients were excluded from the study if they or their families refused to answer the questions. Finally, the data were collected from 179 patients (Fig. 1).

Two inclusion criteria were considered for the study: All patients should be residents of Isfahan City and follow the treatment processes in this city. Second, the patient's age should be older than 18 years. Diagnosis of glioma in most cases was based on the patient's pathology and according to radiological findings (MRI, CT scan) in others.

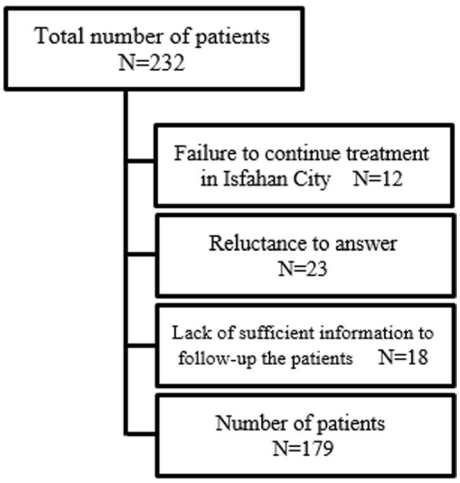

Fig. 1 Patient selection process. In this regard, 94.9% of the patients died during the data analysis

The exclusion criteria of the study were as follows: patients with other brain tumors or systemic diseases, those with spinal involvement, and deaths unrelated to this disease like deaths from COVID-19.

The data were measured regarding age, gender, exposure to chemicals, body mass index (BMI), and survival from the patient's surgery to death.

Eloquent area refers to temporo-parietal, parieto-occipital, thalamus, parietal, temporal, hypothalamus, fronto-temporal, basal ganglion, fronto-parietal lobe. Non-eloquent area refers to frontal and occipital lobes.

Furthermore, several questions were asked from the families of deceased patients and survivors based on the Karnofsky Performance Status Scale (KPS), and they examined the patient's status one week before and after surgery. The current KPS of the survivors was examined, and the KPS status of patients, who were alive up to one month after surgery, was questioned before their death.

The Karnofsky Performance Status Scale is widely used to quantify the functional status of cancer patients. The percentages of the KPS describe three states (conditions): A (100–80%), B (70–50%), and C (40–0%). These states describe different levels of performance. "Functionality" and "performance" comprise the core concerns of the KPS (Table 1).

The sample was analyzed with SPSS version 26. A comparison between nominal variables was made with the X^2 test. Kaplan–Meier survival analysis assessed survival. Continuous variable correlations have been investigated with Pearson's bivariate correlation. The threshold of statistical significance was considered $p < 0.05$.

Result

Patients and treatment characteristics

This study consisted of 179 cases diagnosed with GBM. The patient and treatment characteristics in terms of mean survival rate using Kaplan–Meier method are summarized in Tables 2 and 3.

According to the results in Table 2, the patient's mean age was 51.93 ± 15.76 years, and the male–female ratio was 1:1:7. The mean body mass index was in the overweight range. A total of 9 patients (5.02%) survived, and the death of all patients was due to glioblastoma tumors. The patients' mean overall survival was 29 months.

As the table shows, there was a significant difference between the age groups in terms of 1-year survival (one and less than 1-year survival) ($P < 0.05$), so that more deaths were observed in the age group of more than 50 years.

Table 1 Karnofsky performance status

Condition	Percentage	Comments
A: Able to carry on normal activity and to work. No special care is needed	100	Normal, no complaints, no evidence of disease
	90	Able to carry on normal activity, minor signs or symptoms of disease
	80	Normal activity with effort, some signs or symptoms of disease
B: Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed	70	Cares for self, unable to carry on normal activity or to do active work
	60	Requires occasional assistance, but is able to care for most of his needs
C: Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly	50	Requires considerable assistance and frequent medical care
	40	Disabled, requires special care and assistance
	30	Severely disabled, hospitalization is indicated although death not imminent
	20	Hospitalization necessary, very sick, active supportive treatment necessary
	10	Moribund, fatal processes progressing rapidly
	0	Dead

Table 2 Patients' characteristics in terms of mean survival rate using Kaplan–Meier method

Characteristics		12 months *N* (%) MSP** (95% CL)	24 months *N* (%) MSP (95% CL)	60 months *N* (%) MSP (95% CL)	> 60 months *N* (%) MSP (95% CL)
Age group (year), *n* (%)					
18–50	84 (46.9)	42 (23.5) 183.57 (152.73–214.4)	16 (8.9) 172 (134.53–209.64)	10 (5.6) 182.11(139.34–224.89)	16 (8.9) 117 (88.53–146.74)
> 50	95 (53.1)	63 (35.2) 82.16 (61–103.26)	15 (8.4) 115.71 (83.87–147.56)	11 (6.1) 95 (56.97–133)	6 (3.4) 111.33 (66.54–156.12)
*P**		0.0001	0.431	0.078	0.759
Median age (range); years	52 (18–87)				
Gender, *n* (%)					
Male	113 (63.1)	71 (39.66) 144.21 (116.78–171.64)	11 (6.14) 134 (108.5–159.59)	15 (8.37) 106.45 (76.61–136.29)	16 (8.93)
Female	66 (36.9)	34 (19) 89.07 (66.41–111.72)	24 (13.4) 138.17 (101.39–174.96)	4 (2.23) 160.43 (113–207.8)	4 (2.23)
*P**		0.763	0.034	0.993	0.179
BMI (Mean± SD); Kg/m^2	25.13 ± 2.75	25.05 ± 2.71	25.45 ± 2.79	25.26 ± 3.13	24.74 ± 2.37
*P**		0.609	0.484	0.828	0.484
Smoking, *n* (%)	50 (27.9)	27 (15.1) 98.95 (70.98–126.92)	11 (6.1) 114.17 (76.65–151.69)	4 (2.2) 146.58 (102.15–191)	7 (3.9) 124.6 (78.93–170.25)
*P**	0.408	0.547	0.257	0.817	
Death, n (%)	170 (94.9)	105 (58.7) –	31 (17.3) –	21 (11.7) –	13 (7.2) –

*Log-rank test-p value

***MSP* mean survival per

Gender exhibited a significant difference between the two groups in a 2-year survival period ($P < 0.05$), so that women died more than men did (Figs. 2, 3).

Imaging of one of the patients is shown in Fig. 4.

According to the results in Table 3, the mean tumor size was 5.2 ± 2.1 cm. The extent of tumors was more than one lobe in 105 patients (58.7%). The tumor was observed alone in the frontal lobe in 31 patients (17.3). The survival analysis indicated that the temporal lobe was more than the other lobe of the deceased patient, being statistically significant ($P < 0.05$) in the 2-year survival period of the patients (Fig. 5).

Also, 121 (67.6%) patients had undergone lobectomy with no significant difference in 12-month, 24-month, or 60-month survival rate compared to the control group ($P > 0.05$).

Table 4 presents the patients' KPS status one week before and after surgery, as well as before death or their current status, symptoms and follow-up time.

According to the results in Table 4, the patients' mean follow-up period (from surgery until now) was 7.38 ± 3.46 years. The mean scores of KPS did not demonstrate any significant difference from admission to immediately after surgery ($P = 0.635 > 0.05$); however, the mean score of KPS during the patient evaluation was significantly different from immediately after surgery ($P = 0.012 < 0.05$). After headache, motor dysfunction was the most common symptom of patients before surgery and it remained in 4 (44.5%) survivors. A total of 57 patients (31.8%) visited the physician with the initial symptom of headache.

Discussions

The present study examined 179 patients with glioblastoma, among whom 9 (5.02%) survived after 7 years of follow-up. The 1-year, 2-year, 5-year, and overall survival of patients was 4.5%, 18.38%, 37.13%, and 33.68%, respectively. In other words, the patient's survival greatly decreased in the first year after the surgery, but the survivors lived for more years from the second to the fifth year after the surgery.

Several studies have been conducted on the survival of glioblastoma patients; for example, Armocida (2019) (15) examined 177 patients in a study in Italy. In this study, the male–female ratio was 1:1:2 and the patients' mean age was 61 years. The presence of tumors in the left lobe was more common than in the right, and the frontal region had the highest involvement. Furthermore, seizure was the most common symptom of the patients. The 2-year survival of patients was 16.9%. In

Table 3 Treatment characteristics in terms of mean survival rate using Kaplan–Meier method

Characteristics		12 months *N* (%) MSP** (95% CL)	24 months *N* (%) MSP (95% CL)	60 months *N* (%) MSP (95% CL)	> 60 months *N* (%) MSP (95% CL)
Tumor size (cm.)					
Median (range)	5.3 (2.2–13.7)				
Mean ± SD	5.2 ± 2.1	5.8 ± 1.1	5.1 ± 0.98	4.8 ± 0.99	4.6 ± 0.85
*P**		0.069	0.112	0.325	0.023
Tumor location, *n* (%)					
Confined to single lobe	74 (41.3)	45 (25.14) 16 (8.1–23.8)	11 (6.15) 18 (3.2–21.3)	7 (3.91) 33 (21.3–36.9)	11 (6.15) 11 (9.9–12.6)
Involved more than one lobe	105 (58.7)	60 (33.52) 41.8 (24.6–59)	20 (11.17) 21 (19.1–25.8)	14 (7.82) 15 (10.2–26.7)	11 (6.15) 10.3 (9.7–11.6)
*P**		0.678	0.369	0.139	1.000
Eloquent area	120 (67)	72 (40.22) 100.37 (68.49–132.26)	20 (11.17) 128.87 (86.6–171.1)	13 (7.26) 146.8 (102.4–191.1)	15 (8.38) 109 (67.3–151.5)
Non-eloquent area	59 (33)	33 (18.44) 136.32 (107.6–165)	11 (6.15) 165.2 (127.3–203)	8 (4.47) 141.3 (94.2–188.4)	7 (3.91) 124.4 (86.9–161.9)
*P**		0.826	0.807	0.241	0.747
Hemisphere					
Right	86 (48)	57 (31.84) 94.1 (68.5–119.8)	14 (7.82) 131.6 (97.3–165.9)	10 (5.59) 88.3 (50.4–126.2)	5 (2.79) 111 (97.3–124.9)
Left	93 (52)	48 (26.82) 143.5 (109.8–177.2)	17 (9.5) 169.3 (125.1–213.5)	11 (6.15) 197.7 (149.9–245.5)	17 (9.5) 136.2 (120.3–148.9)
*P**		0.450	0.999	0.147	0.269
Lobe					
Frontal	31 (41.9)	17 (9.5) 96.2 (82.3–99.2)	4 (2.2) 111.7 (79.1–144.2)	1 (0.55) 172.1 (117–227.2)	9 (5) 104.1 (67.9–140.4)
Temporal	28 (37.8)	16 (8.9) 98.8 (75.5–179.4)	7 (3.9) 189 (143.1–234.8)	3 (1.7) 113.7 (75.7–151.6)	2 (1.1) 128.8 (88.4–169.1)
Parietal	15 (20.3)	12 (6.7) 141.9 (104.5–179.4)	0	3 (1.7) 110.9 (83.6–136.8)	0
*P**		0.538	0.025	0.488	0.523
Type of surgery, *n* (%)					
Craniotomy	112 (62.5)	82 (45.81) 24 (21.4–26.8)	14 (7.82) 18 (10.2–24.5)	3 (1.67) 9 (4–0.6)	13 (7.26) 8.1 (5.2–10.8)
Craniectomy	67 (37.5)	23 (12.84) 15.2 (9.8–18.8)	17 (9.5) 12.2 (10.4–21.7)	18 (10.05) 10.6 (7.3–14.6)	9 (5.02) 3.9 (1.6–6.9)
*P**		0.362	0.147	0.313	0.087

*Log-rank test-p value, ***MSP* mean survival per

this study, old age and female gender were determinants of patient survival. The mean follow-up of the patients was 3 years, and 53 patients (30%) were still alive after three years, and 4 of them experienced recurrence. The results of this study were consistent with the results of the present study in some findings. Furthermore, the 2-year survival of patients was 18.38%, the left lobe was more than the right, and the frontal region was the most involved in the present study. Furthermore, there was inconsistency in other findings. In the present study, the patient age was ten years younger and males were more than females.

In 2008, Stummer [23] reported that the mean survival was 11.8 months for patients with residual tumors after surgery and 16.9 months for patients with no residual tumors.

Witthayanuwat (2018) [24] studied 77 patients with a male–female ratio of 1:1:9, a mean age of 53 years, and a mean survival of 12 months in Thailand. Furthermore, the mean 2-year survival of patients was estimated to be 17.2%. The patients' mean 2-year survival and the mean age were almost similar in both studies, but the patients' mean overall survival was 17 months in the present study. The patients' mean follow-up was 54 months which was

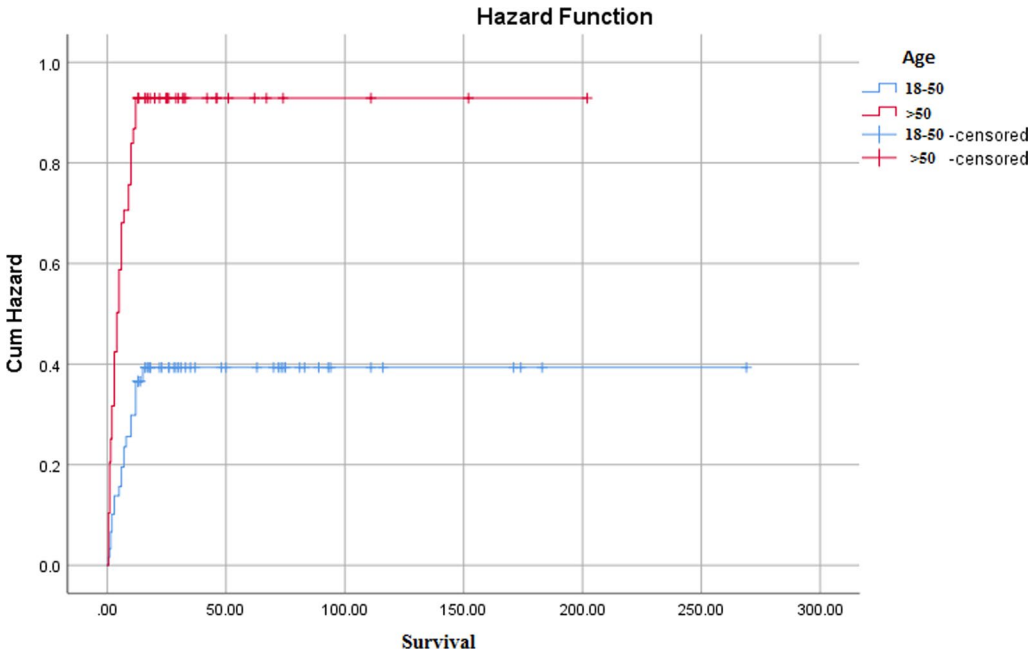

Fig. 2 The results of Kaplan–Meier analysis for age (mean survival per 12 months).

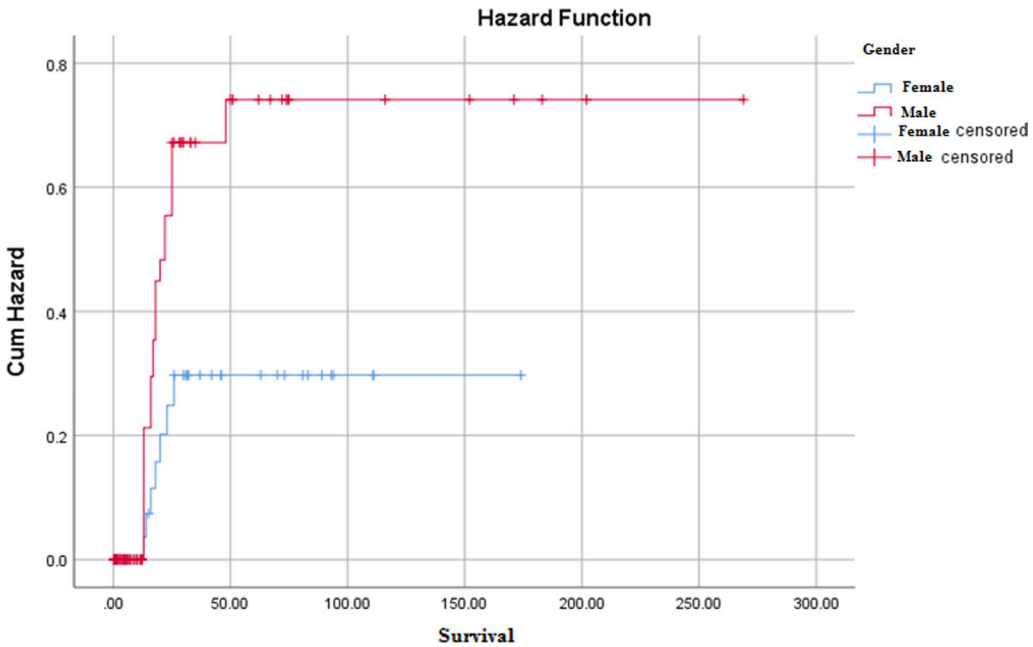

Fig. 3 The results of Kaplan–Meier analysis for gender (mean survival per 24 months).

30 months less than the present study. The tumor size was more than 5 cm in 48 patients (62.3%), and the mean tumor size was about 5 cm in the present study. A total of 36 patients (46.7%) had a KPS score of 90 to 100, but the KPS score was lower than and equal to 74 in the present study.

In a descriptive study in Massachusetts, Bi (2014) [25] studied determinants of differential survival in GBMs and reported that old age, preoperative neurological disorder, and poor functional status were associated with worse outcomes after surgery in patients.

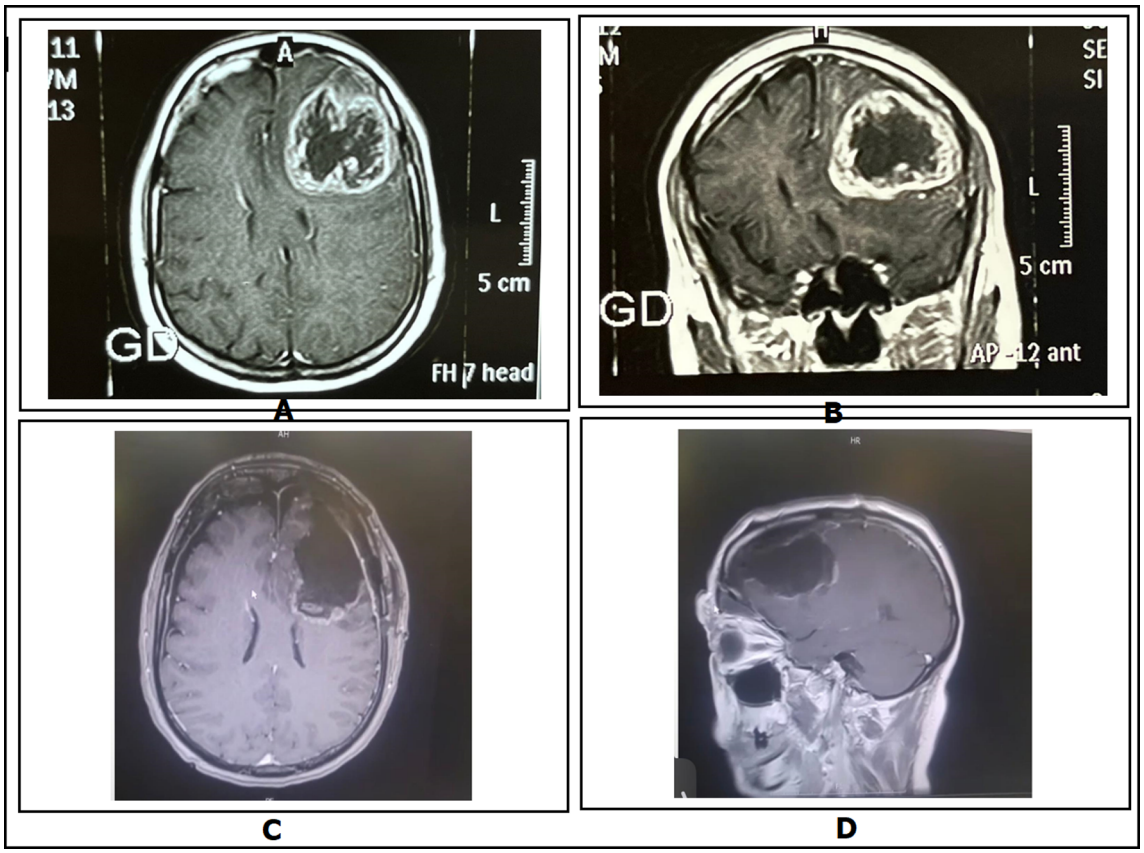

Fig. 4 Imaging of one of the patients. A 57-year-old male with 1-month history of progressive right side hemiparesis and headache. (**A**, **B** axial and coronal pre-operation post Gad T1 images) (**C**, **D** Axial and coronal post Gad T1 images 24h after operation) Pathologic and molecular examination confirmed preoperative diagnosis (GBM, grade 4 WHO).

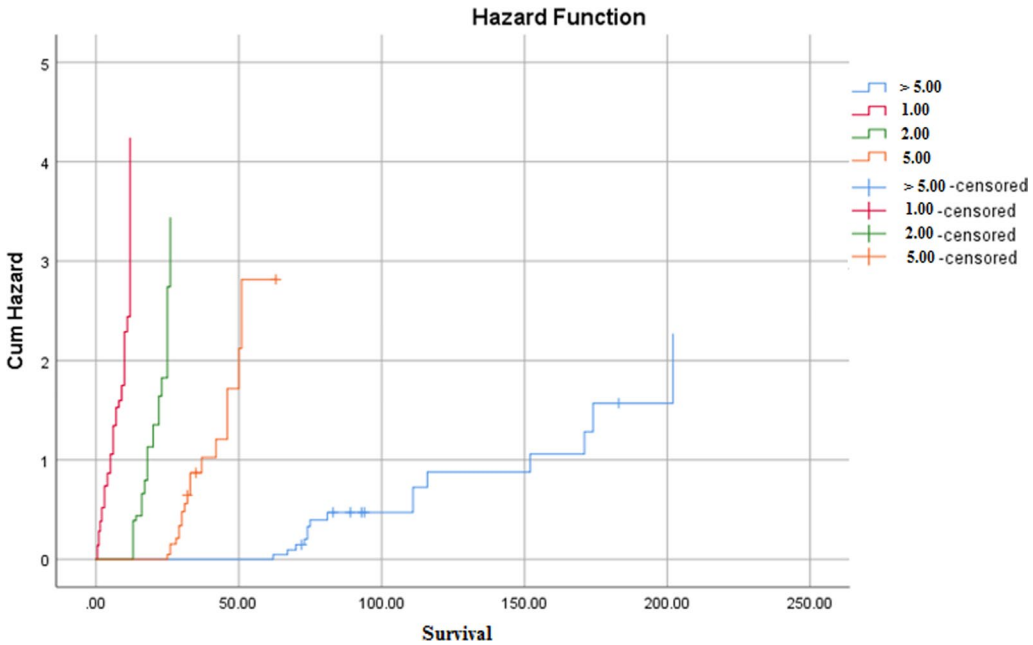

Fig. 5 The patients' overall survival. The 1-year, 2-year, 5-year, and overall survival of the patients was 4.5%, 18.38%, 37.13%, and 33.68%, respectively. Moreover, the survival of patients, who survived for more than 5 years, was 33.96%.

Table 4 The patients' KPS status, symptoms, and follow-up time

Characteristics	
Follow-up time (years)	
Median (range)	7 (2–26)
KPS at admission, (mean ± SD)	74.26 ± 15.69
KPS after surgery, (mean ± SD)	66.58 ± 17.32
KPS at last evaluation, (mean ± SD)	32.36 ± 11.48
Symptoms, *n* (%)	
Headache	96 (53.6)
Seizures	17 (9.5)
Speech disturbance	23 (15.8)
Motor dysfunction	75 (41.9)
Sensory disturbance	12 (6.7)
Visual deficit	27 (15.1)

Delgado–López (2016) [26] conducted a study in Spain and reported that prognostic factors involved in survival included age, functional status, tumor resection rate, and specific genetic markers. The one-year survival of older patients decreased in the present study.

In a systematic review, Tykocki (2018) [27] estimated the ten-year survival of patients to be 0.71%. Korja (2019) [14] reported that the patient's mean age was 63.3 years and 42% were women in Finland. The mean survival time increased from 3.6 months to 4.5 months in patients over 70 years of age. The patient's mean age was lower in the present study. The results indicated that access to neurological treatments and having a better social and economic status had effects on the patient's survival.

Zreik (2020) [28] followed up patients for 3 years in a study in Rochester. The patients' 3-year survival improved significantly from 8 to 10.5% from 2004 to 2013. Patients with lower survival did not have social insurance, were older, and had underlying diseases in addition to tumors.

Abu Jaoude (2019) [29] examined 56 patients in Dallas. The patients' mean 1-year, 2-year, 3-year, and 5-year survival rates were 54%, 28.3%, 17.8%, and 4%, respectively, which were inconsistent with the results of the present study. In the present study, the one-year survival rate was shorter and the mean survival rate improved over time, but the one-year survival was longer and the mean survival decreased over time in Abou Jaoude's study.

The research limitations included the non-possibility of genetic examination of the patients as well as the lack of access to the patient's economic and social status.

Conclusion

The results of the present study indicated that the patients' survival improved over time with the advancement of adjuvant therapies such as chemotherapy and radiotherapy. Therefore, if patients can be followed up and fully cared for the first year after surgery, their survival will improve and the number of months they live will increase from the second year after the operation.

Abbreviations

GBM	Glioblastoma multiforme
CNS	Central nervous system
LTS	Long-term survivors
ICD	Implantable cardioverter defibrillator
MRI	Magnetic resonance imaging
CT scan	Computerized tomography scan
KPS	Karnofsky Performance Status Scale
BMI	Body mass index
MSP	Mean survival per
N	Number
CL	Confidence interval
SD	Standard deviation

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Author contributions

All authors read and approved the final manuscript. Mehdi Shafiei contributed as the main author with the concept of planning the study. Mehdi Shafiei and Aref Famili Dogonchi contributed in study design, patient selection and follow ups. Aref Famili Dogonchi and Donya Sheibani Tehrani performed the statistical analysis and interpreted the data Masih sabouri and Donya Sheibani Tehrani helped write the manuscript and Mehdi Shafiei mentored the edition of the final version.

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Availability of data and materials

The data that support the findings of this study are available but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of [Donya Sheibani Tehrani].

Declarations

Ethics approval and consent to participate

The current study was approved by the Isfahan University of Medical Sciences Ethics Committee with the code of IR.MUI.MED.REC.1400.361. Written consent was obtained from the families of patients to enter this study.

Consent for publication

All coauthors have seen and agree with the contents of the manuscript and each author believes that the manuscript represents honest work. All coauthors certify that the submission is not under review at any other publication. There are no previous reports that might be regarded as redundant publication of the same or very similar work. Furthermore, the authors report no conflict of interest. Written informed consent was obtained from the patient for publication of this case report and accompanying images. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Competing interests

The authors declare that they have no competing interests.

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