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Original article

Treatment outcome and prognostic factors of adult glioblastoma multiforme

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KEYWORDS

Glioblastoma multiforme;
Outcome;
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Chemotherapy

Abstract *Introduction:* This study aimed to report the characteristics, prognostic factors and treatment outcome of 223 patients with glioblastoma multiforme (GBM).
Subjects and method: This retrospective study was carried out by reviewing the medical records of 223 adult patients diagnosed at a tertiary academic hospital between 1990 and 2008. Patients' follow up ranged from 1 to 69 months (median 11 months). Surgery was attempted in all patients in whom complete resection in 15 patients (7%), subtotal resection in 77 patients (34%), partial resection in 73 patients (33%) and biopsy alone in 58 patients (26%) were done. In addition, we performed a literature review of PubMed to find out and analyze major related series. In all, we collected and analyzed the data of 33 major series including more than 11,000 patients with GBM.
Results: There were 141 men and 82 women. The median progression free- and overall survival were 6 (95% CI = 5.711–8.289) and 11 (95% CI = 9.304–12.696) months respectively. In univariate analysis for overall survival, age ($P = 0.003$), tumor size ($P < 0.013$), performance status ($P < 0.001$), the extent of surgical resection ($P = 0.009$), dose of radiation ($P < 0.001$), and adjuvant chemotherapy ($P < 0.001$) were prognostic factors. However, in multivariate analysis, only

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radiation dose, extent of surgical resection, and adjuvant chemotherapy were independent prognostic factors for overall survival.

Conclusion: The prognosis of adult patients with GBM remains poor; however, complete surgical resection and adjuvant treatments improve progression-free and overall survival.

Introduction

Glioblastoma multiforme (GBM) is the most common malignant brain tumor in adults and accounts for 17% of intracranial tumors [1]. Overall survival in GBM is usually less than 12 months and long-term survival is rare. Currently, safe optimal surgical resection followed by adjuvant radiotherapy and chemotherapy is considered as standard treatment approach for patients with GBM. However, despite advances in the last 3 decades, outcome remains poor and long-term survival is exceptional [2]. A ray of hope was temozolomide, a chemotherapeutic agent that was introduced into the clinic in the 21st century. It is simply used, well tolerated and clearly improved survival. By progressive increase in temozolomide use, a modest, but meaningful, survival improvement is observed [2,3]. A new horizon is targeted therapy, particularly bevacizumab, a recombinant humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody. It is the first antiangiogenic agent that has been clinically proven in the treatment of human cancer. Investigation in this regard is continuing; however, results are not translated into clinical application so far [2,3]. The aim of this retrospective study was to define the characteristics, prognostic factors and treatment outcomes of 223 adult patients with GBM treated and followed-up in a single institution over a 19-year period and to perform a literature review.

Material and method

This retrospective study was carried out at a tertiary academic hospital. We analyzed the characteristics, prognostic factors and survival of adult patients (aged $\geqslant$ 20 years) with histologically proven glioblastoma GBM who were treated and followed-up between January 1990 and December 2008 at the Shiraz University of Medical Sciences. In addition, to find out and analyze the major related series, a literature review of PubMed was performed. In all, we collected the data of 33 major series including more than 11,000 patients with GBM.

Patients' evaluation

All patients were pathologically-proven newly diagnosed GBM. In all, 223 patients were eligible to enter the study. Preoperative performance status was defined according to the Eastern Cooperative Oncology Group (ECOG). A preoperative and postoperative computed tomography (CT) scan and/or magnetic resonance imaging (MRI) study was performed for all patients.

Surgery

Surgery was attempted in all patients in whom complete resection (defined as resection of more than 98% of the tumor) in 15 patients (7%), subtotal resection (defined as resection of more than 50% of the tumor but less than complete resection) in 77 patients (34%), partial resection (any debulking surgical resection less than subtotal resection but more than open or stereotactic biopsy) in 73 patients (33%) and biopsy alone in 58 patients (26%) were done. Preoperative and postoperative imaging studies including computed tomography (CT) scan and/or magnetic resonance imaging (MRI) were performed for all patients. The extent of surgical resection and the size of postoperative residual disease were defined based on the imaging findings and operative note.

Radiotherapy

Different external beam radiotherapy machines (megavoltage telecobalt units or linear accelerator), radiation dose and techniques had been used. Before 2000, the patients were initially treated with 40 Gy whole brain conventional (daily fraction of 1.8–2 Gy, and five fractions per week) radiotherapy which was continued to the primary tumor, using reduced size fields, up to 54 Gy. Since 2000, involved field radiotherapy with a median dose of 54 (range 40–60) Gy was considered for all patients who were treated with a curative intent. Patients with poor general condition were treated with palliative intent and only received 30 Gy in 10 fractions. Patients with significant tumor-related or postsurgical complications such as severe anorexia, nausea, vomiting (due to persistent increased intracranial cranial pressure) weight loss, dysphagia and respiratory distress (due to midbrain and brain stem involvement) and decreased level of consciousness could not complete their radiotherapy plan. In addition, all patients received corticosteroids concurrently with radiotherapy and 9 patients received concurrent chemoradiation with temozolomide. Five patients expired before starting radiotherapy and 19 cases expired during the course of radiotherapy and could not complete their radiotherapy.

Chemotherapy

Since 1998, adjuvant nitrosourea-based chemotherapy was considered for eligible patients with acceptable performance status and without significant comorbidity. One hundred and two patients received a median of 4 (range 1–6) cycles of nitrosourea-based chemotherapy consisting of procarbazine, lomustine, and vincristine (PCV regimen). Only 21 patients received adjuvant temozolomide. Temozolomide was administered concurrently with radiotherapy with a dose of 75 mg/m^2 daily throughout the radiation course followed by 4–6 cycles of adjuvant temozolomide with a dose of 150–200 mg/m^2 daily for 5 days, every 4 weeks.

Definition of survival

Date of surgery was considered as the time of diagnosis. Progression free survival was calculated from the date of surgery

to the date of disease progression at the primary location or other sites of the brain. Overall survival was calculated from the date of surgery to date of death due to any cause.

Statistics

Clinical and pathological variables were analyzed using the SPSS for Windows version 17 statistical software (SPSS, Chicago, IL). Categorical variables of patient demographics (such as sex and performance status, categorized age), tumor characteristics (such as location, laterality, and categorized tumor size) and treatment modalities (such as type of surgery, radiotherapy techniques, and type of chemotherapy) were compared by using chi-square tests and for continuous variables such as patients' age, radiation dose and tumor size Student's *t* tests were used. Proportions were compared with Fisher's exact test for unordered or ordered categorical variables. Patients who lost to follow-up were taken into account in the survival analysis, which takes the last follow-up tumor status for the calculation. Univariate analysis for progression free survival and overall survival rates were performed using the Kaplan–Meier method and prognostic factors were compared using the log-rank test. Multiple-covariate analysis was performed using the stepwise regression hazards regression model. The hazard ratio for death (HR), with the 95% confidence interval (CI), was calculated for the variable groups. The stratified log-rank test was used to compare treatment results in each variable group. A *P* value of 0.05 or less was considered to be statistically significant.

Results

Patients' age and sex

There were 82 women and 141 men ranging in age from 20 to 75 years, with a median age at diagnosis of 53 years. The peak

Table 1 Univariate analysis of prognostic factors for progression free survival in 223 patients with glioblastoma multiforme.

Prognostic factors (patients No.)	One-year PFS (%)	Median PFS (month)	*P* value	Hazard ratio (HR)	95% CI
Age					
⩽50 years (91)	25.7	9			
>50 years (132)	20.1	5	0.003	1.504	1.121–2.018
Sex					
Male (141)	23.4	5			
Female (82)	20.9	6	0.468	1.109	0.824–1.477
Primary site					
Frontal (72)	17.7	6			
Temporoparietal (109)	24.3	6		1.488	0.783–2.825
Occipital (27)	20.9	5		1.229	0.657–2.299
Others location (15)	29.2	9	0.444	1.317	0.931–1.321
Lateralization					
Right (118)	20.1	5			
Left (105)	23.9	6	0.342	1.128	0.849–1.497
Tumor size					
<5 cm (89)	29.3	7			
⩾5 cm (134)	18.1	6	0.013	1.402	1.045–1.880
Type of surgery					
Partial or biopsy (131)	15.3	5			
Subtotal resection (77)	27.2	7		2.009	1.126–3.585
Total resection (15)	57.1	12	0.009	1.501	0.824–2.732
Chemotherapy					
Nitrosourea-based (102)	34.9	10			
Temozolomide (21)	54.5	13		1.651	1.417–1.924
No chemotherapy (110)	5.8	4	<0.001	1.280	1.146–1.430
Radiation dose					
Incomplete or palliative dose (31)	6.2	3			
>40 Gy and < 54 Gy (124)	26.9	9		4.537	2.814–7.316
⩾ 54 Gy and ⩽ 60 Gy (68)	21.7	7	<0.001	0.899	0.654–1.235
Radiation technique					
Whole brain → involved field (99)	15.7	5			
Involved field (114)	31.9	6	0.064	1.308	0.956–1.790
Performance status (ECOG)					
0 or 1 (108)	25.9	9			
2 (84)	24.0	7		1.805	0.799–1.472
3 or 4 (31)	6.2	4	<0.001	5.040	3.193–7.955

PFS, progression free survival; ECOG, eastern cooperative oncology group; HR, hazard ratio.

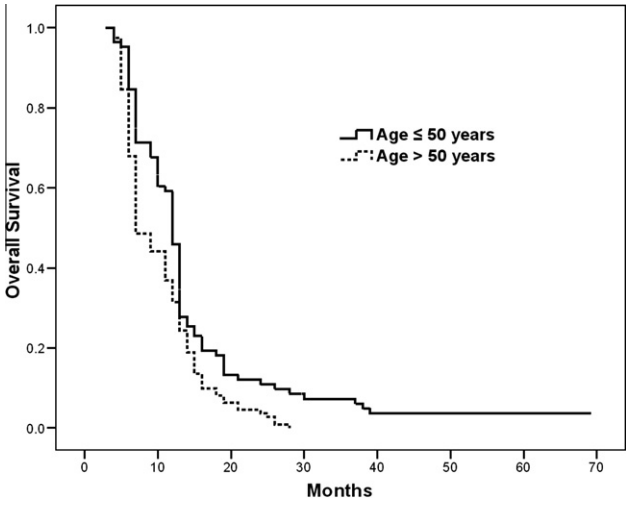

Figure 1 Kaplan–Meier survival curves of overall survival categorized according to the patients' age ($P = 0.026$).

age was during the sixth and seventh decades of life in both sexes. One hundred and thirty-two patients were more than 50 years old at presentation and 91 patients were less than or equal to 50 years old. The mean female patients' age (48.4 ± 13.22 vs. 52.6 ± 13.44, $P = 0.025$, CI = 0.534–7.849), radiation dose (53.2 ± 8.59 vs. 53.2 ± 8.31, $P = 0.555$, CI = −0.466–0.866), and tumor size (6.2 ± 2.30 vs. 6.2 ± 2.50, $P = 0.965$, CI: −2.355–2.252) were not significantly different compared with those of male patients. In addition, there was no significant difference between female and male patients according to the performance status ($P = 0.394$, CI = 0.384–0.403), type of surgery ($P = 0.874$, 0868–0.881) and chemotherapy regimen ($P = 0.115$, CI = 0.113–0.126).

Treatment outcome and survival

After a median follow-up of 11 (range 1–69) months for surviving patients, 4 patients were alive and without disease, eight were alive with disease, 184 had died due to disease and 27 lost

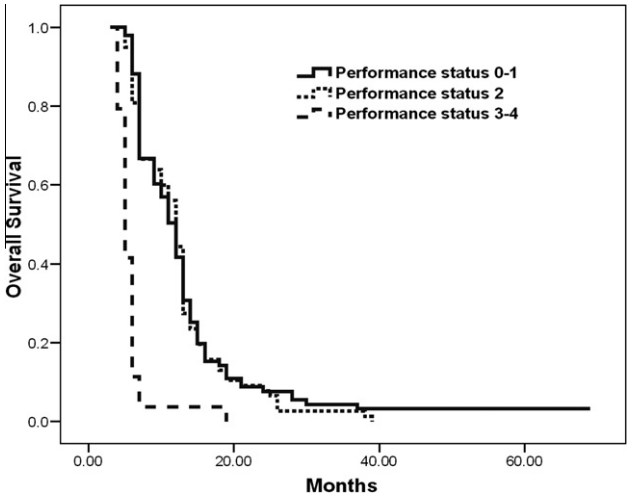

Figure 2 Kaplan–Meier survival curves of overall survival categorized according to the patients' performance status ($P < 0.001$).

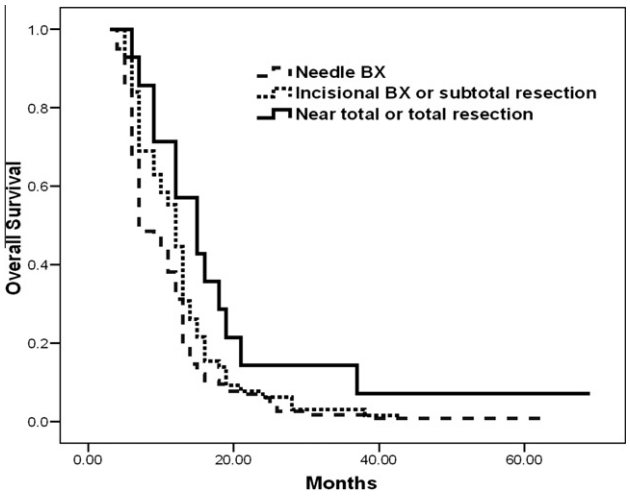

Figure 3 Kaplan–Meier survival curves of overall survival categorized according to the type of surgery ($P = 0.037$).

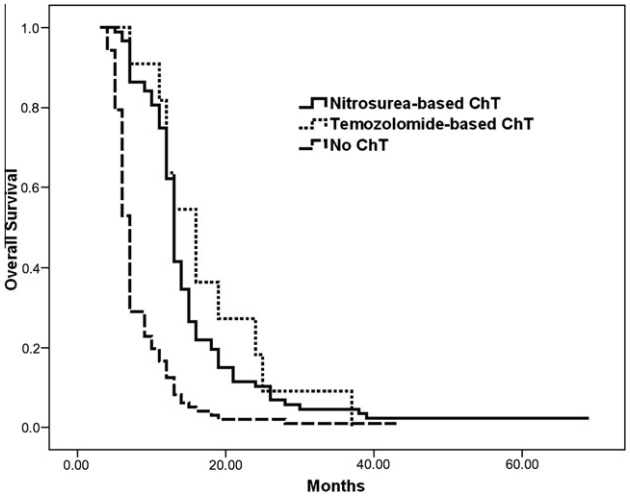

Figure 4 Kaplan–Meier survival curves of overall survival categorized according to the type of chemotherapy ($P < 0.001$).

their follow-up. The last follow-up tumor status was considered for patients who lost to follow-up and their data were incorporated to the study population for calculation. These patients were lost to follow-up during the course of RT (6 cases) or few weeks after that (21 cases). The median follow-up for these cases was 2 (range 1–4) months. Almost all recurrences occurred within radiation fields. The majority of recurrences were within 2 cm of the margin of the initial tumor bed. The median progression free- and overall survival were 6 (95% CI = 5.711–8.289) and 11 (95% CI = 9.304–12.696) months respectively for all patients. The one-, 2- and 3-year overall survival rates were 45.9%, 7.7% and 3.1% respectively. The 4-month progression free survival for patients who lost to follow-up was 52.5%.

Prognostic factors

All potential prognostic variables were analyzed to establish their effect on progression free- and overall survival rates.

Table 2 Univariate analysis of prognostic factors for overall survival in 223 patients with glioblastoma multiforme.

Prognostic factors (Patients No.)	One-year OS (%)	Median OS (month)	*P* value	Hazard ratio (HR)	95% CI
Age					
⩽50 years (91)	59.2	12			
>50 years (132)	36.9	9	0.001	1.542	1.149–2.070
Sex					
Male (141)	44.1	9			
Female (82)	49.9	11	0.400	1.121	0.838–1.500
Primary site					
Frontal (72)	42.0	10			
Temporoparietal (109)	47.8	12		1.367	0.720–2.596
Occipital (27)	40.1	7		1.113	0595–2.083
Other locations (15)	55.4	12	0.504	1.202	0.590–2.448
Lateralization					
Right (118)	40.0	7			
Left (105)	53.1	12	0.308	1.144	0.862–1.519
Tumor size					
<5 cm (89)	56.6	12			
⩾5 cm (134)	39.9	9	0.015	1.394	1.040–1.869
Type of surgery					
Partial or biopsy (131)	38.1	7			
Subtotal resection (77)	55.3	12		2.011	1.129–3.858
Total resection (15)	71.4	15	0.010	1.515	0.833–2.756
Chemotherapy					
Nitrosourea-based (102)	74.9	13			
Temozolomide (21)	81.8	16		0.845	0.450–1.587
No chemotherapy (110)	16.6	6	<0.001	2.860	2.108–3.880
Radiation dose					
Incomplete or palliative dose (31)	3.8	5			
>40 Gy and <54 Gy (124)	55.9	12		4.885	3.032–7.869
⩾54 Gy and ⩽60 Gy (68)	47.7	11	<0.001	0.916	0.667–1.259
Radiation technique					
Whole brain → involved field (99)	40.2	9			
Involved field (114)	51.1	10	0.103	1.268	0.927–1.734
Performance status (ECOG)					
0 or 1 (108)	50.4	12			
2 (84)	56.1	12		1.072	0.789–1.456
3 or 4 (31)	3.8	5	<0.001	5.332	3.379–8.415

OS, overall survival; ECOG, eastern cooperative oncology group; HR, hazard ratio.

Table 3 The multivariate stepwise regression hazards model analysis of prognostic factors for progression free survival in 223 patients with glioblastoma multiforme.

Prognostic factors (Patients No.)	*P* value	Hazard ratio (HR)	95% CI
Radiation dose			
Incomplete or palliative dose (31)			
>40 Gy and <54 Gy (124)			
⩾54 Gy and ⩽60 Gy (68)	<0.001	0.960	0.962–0.979
Extent of surgical resection			
Biopsy (131)			
Incomplete resection (77)			
Complete resection (15)	0.003	0.690	0.543–0.878
Chemotherapy			
Nitrosourea-based (102)			
Temozolomide (21)			
No chemotherapy (110)	<0.001	1.622	1.382–1.904

ECOG, eastern cooperative oncology group; HR, hazard ratio.

Table 4 Multivariate stepwise regression hazards model analysis of prognostic factors for overall survival in 223 patients with glioblastoma multiforme.

Prognostic factors (Patients No.)	*P* value	Hazard ratio (HR)	95% CI
Radiation dose			
Incomplete or palliative dose (31)			
>40 Gy and <54 Gy (124)			
⩾54 Gy and ⩽60 Gy (68)	<0.001	0.957	0.939–0.976
Extent of surgical resection			
Biopsy (131)			
Incomplete resection (77)			
Complete resection (15)	0.002	0.690	0.543–0.877
Chemotherapy			
Nitrosourea-based (102)			
Temozolomide (21)			
No chemotherapy (110)	<0.001	1.652	1.407–1.940

ECOG, eastern cooperative oncology group; HR, hazard ratio.

On univariate analysis of prognostic factors for progression free survival, age ($P = 0.001$), tumor size ($P = 0.018$), performance status ($P < 0.001$), the extent of surgical resection ($P = 0.010$), dose of radiation ($P < 0.001$), and adjuvant chemotherapy ($P < 0.001$) were prognostic factors. In addition, we found a significant improvement for progression free survival ($P = 0.021$) and overall survival ($P = 0.010$) for patients who were treated after 2005 compared to those treated before 2005. However, sex, tumor location and radiotherapy techniques were found not to be prognostic factors for progression free survival (Table 1).

Similarly, on univariate analysis of prognostic factors for overall survival, age ($P = 0.003$), tumor size ($P < 0.013$), performance status ($P < 0.001$), the extent of surgical resection ($P = 0.009$), dose of radiation ($P < 0.001$), and adjuvant chemotherapy ($P < 0.001$) were prognostic factors. (Figs. 1–4) However, sex, tumor location and radiotherapy techniques were found not to be prognostic factors for progression free survival (Table 2).

On multivariate stepwise regression hazards model analysis of prognostic factors for progression free survival, adjuvant chemotherapy [HR = 1.622; 95% CI = 1.382–1.904; ($P = <0.001$)], radiation dose [HR = 0.960; 95% CI = 0.962–0.979; ($P = <0.001$)], and the extent of surgical resection [HR = 0.690; 95% CI = 0.543–0.878; ($P = 0.003$)] were independent prognostic factors for progression free survival (Table 3).

Likewise, multivariate stepwise regression hazards model analysis of prognostic factors for overall survival revealed that adjuvant chemotherapy [HR = 1.652; 95% CI = 1.407–1.940; ($P = <0.001$)], radiation dose [HR = 0.957; 95% CI = 0.939–0976; ($P = <0.001$)], and the extent of surgical resection [HR = 0.690; 95% CI = 0.543–0.877; ($P = 0.002$)] had retained statistical significance for overall survival (Table 4).

Discussion

Glioblastoma multiforme is the most aggressive primary central nervous system (CNS) neoplasm. The incidence of GBM does not depend on geographic or ethnical factors. These neoplasms usually occur in the sixth and seventh decades of life [1,4]. In the present study, the median age of our patients was 53 years, which was consistent with the results of the literature review in which the average median age of 7726 patients in the reported series was 62 years [5–31]. (Table 5).

In almost all reported series in the literature review, men represent a higher proportion of GBM sufferers than women, with a mean male/female ratio of 1.4 (range from 1.0 to 1.9) in 8 studies including 4933 patients [10,12,18,22–25,31] (Table 5). In the present study this ratio was 1.7 which was consistent with the reported series.

Glioblastoma multiforme are diffusely infiltrative tumors; consequently, surgical curative resection is rarely possible for this neoplasm [1]. Optimal safe resection is an essential goal in the initial management of patients with GBM, and the extent of surgical resection must be balanced against the risk of neurologic dysfunction. A variety of preoperative neuroimaging and intraoperative mapping and neuromonitoring have been incorporated into the patient management to achieve these goals [2,32,33]. At present most neurosurgical operating rooms are specially designed and equipped with computerized tomography (CT) or magnetic resonance imaging (MRI) scanners to guide the real time resection. Currently, modern intraoperative neurosurgical techniques are used to facilitate the optimal tumor resection while minimizing normal brain damage [32]. There is no consensus regarding the definition of complete brain tumor resection in the literature. Many authors used the terms of "complete" [8,24,34], "total" [11,35,36], "gross total" [5,26,37] or "more than 98% tumor" resection [2,32] according to the postsurgical residual disease.

In the literature review, the mean rate of complete (total gross) resection was 33% (range 10–63%) in 11 reports including 3078 patients. In addition, the mean rate of biopsy alone was 20% (range 1–56%) in 15 reports including 7836 patients [8,12,16,23,24,28,34–41]. Fig. 5 represents the relative distribution of the extent of surgical resection among 3078 patients with glioblastoma multiforme in 11 reported series in the literature [8,16,24,28,34–40].

In the present study, the rate of complete tumor resection (defined as resection of more than 98% of the tumor) was significantly lower (7% vs. 33%) than that of the mean value in the reported series [8,16,24,28,34–40], and the rate of biopsy alone was relatively higher (26% vs. 20%) than that of the mean value in the reported series [12,16,17,23,36,38,40,41].

Table 5 Characteristics and treatment outcomes of 28 major reported series of glioblastoma multiforme.

Authors [Ref.]	No. of patients	Mean age	M/F ratio	Median OS (month)	Median PFS (month)	1-year OS (%)	2-year OS (%)	3-year OS (%)
Caloglu [5]	78	–	–	9.8	–	–	–	–
Chaichana [6]	129	73	–	7.9	–	–	–	–
Chaichana [7]	393	–	–	11.9	–	–	–	–
Ewelt [8]	103	70.8	–	5.1	3.2	–	–	–
Fazeny-Dorner [9]	357	–	–	9.4	–	–	–	–
Filippini [10]	676	58	1.6	13.6	6.0	57	16	7
Gamburg, [11]	114	–	–	6	–	–	–	–
Grossman [12]	219	55	1.2	11.1	–	44.5	–	–
Hall [13]	21	38	–	8	–	–	–	–
Helseth [14]	516	63.7	–	9.9	–	–	–	–
Jeremic [15]	175	–	–	14	–	–	–	–
Lai [16]	1375	72	–	8.9	–	–	–	–
Li [18]	116	–	1.9	16.9	9.1	–	–	–
Li [17]	192	53	–	15.7	–	62.5	25.5	–
Lin [19]	69	–	–	12	–	–	–	–
Ma [20]	205	–	–	12	–	52	17	–
McGirt [21]	306	54	–	12.8	–	–	20	10
Odrazka [22]	85	58	1	10.1	–	41	5	–
Paszat [23]	3279	61	1.44	7	–	29.4	11.1	7.4
Piroth [24]	110	61.4	1	8.7	4.8	28	5	–
Scoccianti [41]	1059	–	–	9.5	–	–	24.8	–
Scott [25]	206	75	1.2	4.5	–	–	–	–
Shinoda [26]	82	–	–	13	–	53.7	14.6	–
Shrieve [27]	78	–	–	19.9	–	88.5	35.9	–
Stark [28]	267	61	1.2	7	–	–	–	–
Tait [29]	625	–	–	6.3	–	–	–	–
Tramacere [30]	75	–	–	14.7	–	69.3	38.4	14.7
Wasserfallen [31]	46	52	1.5	15.8	–	–	–	–
Present study	223	51	1.72	11	6	45.9	7.7	3.1
Total	11,179	62	1.43	9.2	5.9	41.3	15.7	7.7

M/F, male/female; PFS, Progression free survival; OS, overall survival.

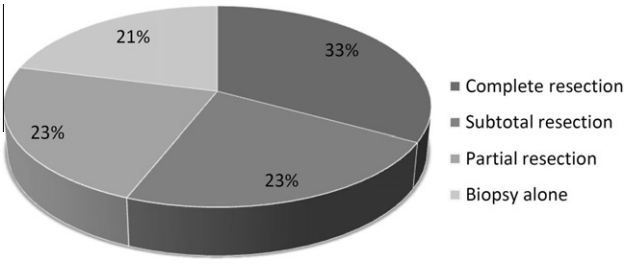

Figure 5 Relative distribution of the extent of surgical resection among 3078 patients with glioblastoma multiforme in the literature. [8,16,24,28,34–40].

The absence of novel preoperative neuroimaging [such as PET scan and magnetic resonance spectroscopy (MRS)] and intraoperative mapping and neuromonitoring particularly before 2005 were our limitation resource causing our lower rate of complete resection compared to most reported series. It may also be due to the different definition of the extent of surgical resection among the reported series.

Postoperative adjuvant radiotherapy is a principal element in the treatment of patients with GBM [2]. External beam radiotherapy is usually recommended to start within 2–4 weeks following surgical resection or biopsy. A total dose of 60 Gy is often delivered using involved portals and conventional fractionation (daily fractions of 2 Gy, five fractions per day) [2,16,36]. In the present study, the vast majority (86%) of patients were treated with a curative intent, however; only 31% received the optimal or acceptable radiation dose. It was mainly due to poor patients' compliance, poor performance status, and our limited resource before 2000. Before 2000, we had no linear accelerator and patients were treated with cobalt 60 teletherapy. Therefore, for avoiding the toxicities of optimal radiation dose (60 Gy), most patients received up to 54 Gy.

Adjuvant chemotherapy plays an important role in the management of patients with GBM [2,10]. Before 1999, nitrosourea-based combinations were the most commonly used chemotherapeutic agents in GBM, among which carmustine and lomustine were the most active agents. However, by adding these agents to combined surgery and postoperative radiotherapy, no significant improvements in terms of response rates and overall survival were observed [2,42]. Since 1999 and by introducing temozolomide a modest improvement in median survival was seen. At present, concurrent chemoradiation followed by sequential adjuvant temozolomide is recommended for patients with GBM [2,9,43,44].

In the present study, chemotherapy was considered for 108 (48.5%) eligible patients with acceptable performance status and without significant comorbidity since 1998. However, due to the lack of medical insurance coverage for this drug, patients' low economic status and other limited resources, most

cases did not receive temozolomide. Therefore, only 21 (9.5%) patients received adjuvant temozolomide.

Glioblastoma multiforme is a highly aggressive tumor, median survival is usually less than 12 months and long-term survival is exceptional [23,45]. In the present study, the median progression-free survival was 6 months which was in agreement with 5.9 months for 1201 patients in the literature [8,10,18,24]. Correspondingly, the median overall survival of our patients was 11 months which was comparable with 9.2 months for 11,152 patients in the literature [5–31,41].

1-, 2- and 3-year overall response rates were 41.5 (in 5197 patients) [10,12,17,20,22–24,26,27,30], 15.6% (in 6343 patients) [10,17,20–23,26,27,30,41], and 7.7% (in 4532 patients) [10,21,23,30] respectively in the literature. In the present study, these rates were 45.9%, 7.7% and 3.1% respectively, among which 2- and 3-year overall response rates were lower than that in the literature.

In almost all reported series in the literature, we found young age, good performance status and safe optimal resection to be the well-known good prognostic factors in patients with GBM [2,5,7,8,10,11,14–18,22,24–31,38,40,41,46,47]. In the present study, we found radiation dose, extent of surgical resection, and adjuvant chemotherapy to be independent prognostic factors for overall survival. These results were consistent with the results of other reported series in the literature in which adjuvant radiotherapy particularly with higher doses ($\geqslant$60 Gy); and adjuvant chemotherapy particularly concurrent chemoradiation with temozolomide were favorable prognostic factors for overall survival [2–5,8–10,12–18,20,22–24,27–29,31,33,36–41,47–54].

Mutations of tumor suppressor genes, particularly p53 and amplifications of oncogenes especially EGFR gene amplification play an important role in the pathogenesis and progression of GBM. These molecular genetic alterations are important targets for use in the early detection of these neoplasms. Consequently, molecular analysis and profiling approach using immunohistochemistry would provide novel diagnostic and prognostic perceptions in the biology of GBM [55,56]. In this series, there were no data regarding molecular markers, and these markers are not routinely checked in our patients with GBM.

Conclusion

According to the findings of the present study and review of the literature, GBM is a highly violent tumor; tends to have early relapse and short-term survival. Multimodality therapy including safe optimal surgical resection combined by adjuvant radiotherapy or concurrent chemoradiation and sequential chemotherapy is recommended for all patients with this fatal neoplasm. Despite modest improvement in the overall survival of patients with GBM in the recent decade, the outcome remains poor. Therefore, the need for more effective novel treatments in this neoplasm is urgently needed. This study emphasizes that the current standard of care is not feasible everywhere in the world largely due to cost. Research into economically viable treatments is needed. In addition, our results emphasize that the current standard of care is not that great, since survival is still similar even when most patients do not get it.

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