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Clinical outcome of patients with glioblastoma multiforme: Single center experience

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ABSTRACT

Glioblastoma multiforme (GBM) is the most common and fatal brain tumor in adults. Prognosis remains dismal and median overall survival rarely exceeds 12 months. In this study, we evaluated the demographic and clinical features of Turkish glioblastoma patients from single institute to identify the important prognostic factors which might be related with patient outcomes in this population, retrospectively. Demographic data, clinicopathological data and treatment parameters (i.e. extent of surgical resection, radiotherapy and use of chemotherapy) were obtained from medical records. SPSS version 22 was used for all statistical analyses. The median progression-free survival and overall survival was 9,9 and 13,7 months; respectively. The group of patients with the highest mean overall survival had a tumor at the fronto-temporal region, followed by frontal localization. In univariate analysis, age, concurrent chemoradiotherapy and adjuvant temozolomide use were all predictors for both PFS and OS. However, in multivariate analysis, age and concurrent radiotherapy were significant predictors of survival. Patients receiving cyberknife after recurrence had longer OS. We retrospectively evaluated glioblastoma patients from single institute, the results supported previously reported factors that influence survival time in glioblastoma.

1. Introduction

Glioblastoma multiforme (GBM) is the most common malignant brain tumor in adults. Prognosis is dismal and the median overall survival is around 12 months despite advances in treatment modalities.[1] The standard therapy is a combined modality approach which consists of maximal safe surgical resection of primary tumor, and subsequently radiotherapy with concomitant and adjuvant temozolomide.[2-4] Advances in surgery and radiotherapy techniques and the addition of chemotherapy to treatment resulted in better local control, and also prolongation of survival in recent years. However; the disease almost always recur and long-term survival rarely occurs. Treatment options are limited after disease recurrence. New approaches include antiangiogenic therapy, immunotherapy, targeted molecular therapy, gene therapy, and radiation-enhancement therapies and under investigation in various clinical trials.[5]

Clinical factors such as age at presentation, tumor location, Karnofsky performance status, the extent of surgery and histopathological factors are important prognostic factors for GBM.[6] In this study, we retrospectively analysed the clinical and demographic features of Turkish glioblastoma patients from single institute to identify the important prognostic factors which might be related with patient outcomes in this population.

2. Methods

This retrospective, single-center study was achieved in the radiation oncology and medical oncology departments at Samsun Training Hospital. Patients who were diagnosed between January 2012 to December 2016 were enrolled the study. Local Ethics Committee approved the study.

Demographic data, clinicopathological data and treatment parameters (i.e. extent of surgical resection, radiotherapy and use of chemotherapy) were obtained from medical records. Data on patient death was obtained from the National Registry of Death System, Turkey.

2.1. Statistical analysis

Progression-free survival (PFS) was determined as the duration between initial surgery and progressive disease or death. Overall

survival (OS) was described as the time from the diagnosis date to death, or to the last follow-up for surviving patients. Statistical evaluations was performed using Statistical Package for Social Sciences for Windows version 23 [SPSS Inc; Chicago, IL, USA] software package. Kaplan-Meier curves were used to calculate the overall survival OS and PFS. Log-rank test was used for univariate analyses. Multivariate linear regression analyse was made to evaluate independent variables for overall survival. A p value less than 0.05 was considered statistically significant.

3. Results

A total of 99 patients diagnosed with GBM are included in the present study: 50 (50.5%) males and 49 (49.5%) females. Median age of patients were 57 and median tumor diameter was 40 mm. Tumor and treatment characteristics are described in Table 1.

Most of the patients had received concurrent chemo-radiotherapy after operation. The majority of patients (n = 70/99) received subsequent temozolomide, and 70% of patients completed their chemotherapy regimen (see Table 2).

Patients received first, second and third line treatment after recurrence, 45,5%, 18,2%, 8,1%; respectively. Cyberknife stereotactic radiotherapy was the most preferred first-line treatment regimen after disease progression. Patients mostly received irinotecan and bevacizumab chemotherapy in second line setting. Only a few patients could able to take a third line treatment as a result of patient's overall clinical worse condition.

The median follow up time was 12 months (3–55 months). The median progression free survival (PFS) was 9,9 months (Fig. 1). PFS was not statistically different according to gender, localization and operation type. Concurrent chemoradiotherapy resulted with a longer PFS compared with radiotherapy alone. Patients who received adjuvant temozolamide had longer PFS than patients who did not take temozolamide (11,9 vs 8,3 months).

Overall survival was 13,7 in the whole study population; 12,3 months in women and 15,1 months in men (p; 0.4)(Fig. 2). Patients with secondary tumors (progression from low-grade diffuse astrocytoma or anaplastic astrocytoma) lived longer than primary glioblastomas but the difference was not statistically significant

Table 1
Tumor and treatment characteristics.

Tumor site	Temporal	28 (28.3%)
	Parietal	16 (16.2%)
	Frontal	15 (15.2%)
	Frontoparietal	12 (12.1%)
	Parietooccipital	10 (10.1%)
	Frontotemporal	7 (7.1%)
	Occipital	4 (4%)
	Other	7 (7%)
Primary/secondary	Primary	92 (92.9%)
	Secondary	5 (5.1%)
	Unknown	2 (2%)
Hemisphere	Right	41 (41.4%)
	Left	53 (53.5%)
	Midline	4 (4.1%)
	Unknown	1 (1%)
Operation type	Total	53 (53.5%)
	Subtotal	35 (35.4%)
	Biopsy	7 (7.1%)
	Unknown	4 (4%)
Adjuvant treatment	Chemoradiotherapy	88 (88.9%)
	Radiotherapy	5 (5.1%)
	No treatment	4 (4%)
	Unknown	2 (2%)
Temozolamide	Yes	70 (70.7%)
	No	14 (14.1%)
	Unknown	15 (15.2%)

Table 2
Treatments in recurrence.

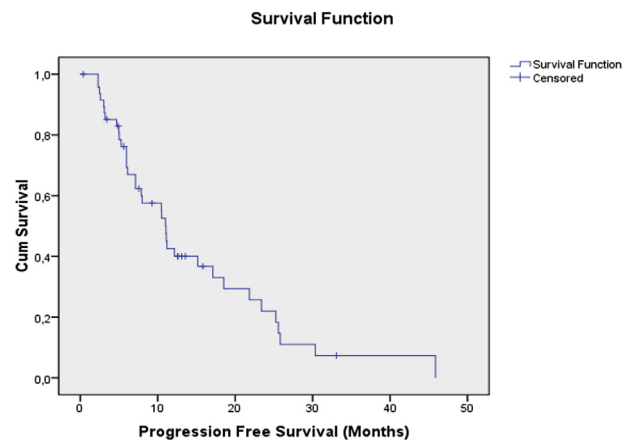| First line		45
	Cyberknife	22 (48,9%)
	Operation	16 (35,6%)
	Irınotecan + bevacizumab	5 (11,1%)
	Temozolomide	2 (4,4%)
Second line		18
	Irınotecan+bevacizumab	10 (55.6%)
	Cyberknife	4 (22.2%)
	Temozolomide	3 (16.7%)
	Chemoradiotherapy	1 (5.6%)
Third line		8
	Cyberknife	4 (50%)
	Irınotecan + bevacizumab	2 (25%)
	Temozolomide	2 (25%)

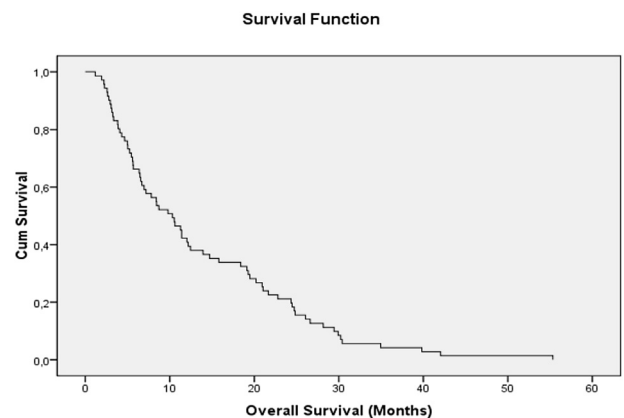**Fig. 1.** Progression free survival for study population.

Fig. 2. Overall survival for study population.

(13,3 vs 23,9 months; p:0,25).

Overall survival was different according to tumor localization. The group of patients with the highest mean overall survival had a tumor at frontotemporal region (20,3 months), followed by frontal localization (17,4 months). Left sided and right sided tumors had similar overall survival (p; 0,19). Univariate and multivariate analysis showed that patients receiving cyberknife after recurrence had longer OS.

In univariate analysis, age, concurrent chemoradiotherapy and adjuvant temozolomide use were all predictors for both PFS and OS. However, in multivariate analysis, age and concurrent radiotherapy were significant predictive factors for survival (Table 3 and Table 4).