

## Original Article

### The Clinical Trend and Prognosis of Patients with Brain Glioma

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#### ABSTRACT

**Background and Objectives:** Gliomas are the most prevalent primary brain tumors. The purpose of this retrospective cohort study was evaluation of clinical trend and prognosis of patients with brain glioma and effective factors in prognosis.

**Materials and Methods:** Hundred and forty-five patients with supratentorial brain glioma, treated in Shahid Mostafa Khomeini & Hazrat-e-Rasool hospitals in Tehran, Iran from March 1999 to August 2005, were studied. Clinical, therapeutic and malignancy grade data were collected. The WHO classification was used for reporting malignancy grade. All patients were pursued until August 2005. Mann-Whitney, Kaplan-Meier, Cox Regression, and Chi-Square test were used for analysis.

**Results:** Median survival was 39.7 weeks for malignancy grade IV. One-year survival rates in malignancy grades of II, III, IV and all patients were 86%, 83%, 40% and 47%, respectively. In multivariate analysis, effective factors in prognosis of all patients above 60 were radiotherapy and malignancy grade IV; and in patients with malignant glioma were age of above 60 and radiotherapy; and in patients with low-grade glioma were motor deficits.

**Conclusions:** Survival rate decreases from malignancy grade II to IV and this reduction is evident in malignancy grade IV. Role of radiotherapy as an effective factor in prognosis in all patients and in malignant glioma is important.

**Keywords:** Glioma, Prognosis, Survival

#### Introduction

Brain tumors are the second most common cause of death due to neurological diseases after stroke (1). Gliomas are the most prevalent brain tumors and constitute 40-67 percent of early brain tumors (2). The incidence rate of glioma is 4

in 100000 men, and is less in women (3). In spite of advancements in treatment methods, the mean survival in malignant glioma is approximately one year, and the mean survival in low-grade gliomas is 5-10 years (4-9). According to the existent studies, radiotherapy, age, and Karnofsky Performance

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Scale (KPS) have the most effects in prognosis of glioblastoma multiform. In all gliomas, history, age, KPS, and radiotherapy have the most effects in survival (10).

Incidence of glioma in Asia and developing countries is less than US and other industrial countries (2, 3, 11, 12). Histopathological characteristics are very important in prognosis and clinical trend in brain glioma, but neurosurgeons in our country have confronted with patients that their clinical trends and prognoses do not have agreement with histopathological characteristics. For example, patients with higher malignancy grade had great longevity.

By considering the importance of problem and lack of similar studies in Iran, we evaluated effective factors in clinical trend and prognosis of brain glioma and survival time after surgery in different malignancy grades.

### Materials and Methods

In this retrospective cohort study, the population in study was all patients with supratentorial brain gliomas who had undergone surgical operation in Mostafa Khomeini and Hazrat-e-Rasool hospitals in Tehran, Iran from March 1999 to August 2005. Demographic data, clinical findings, treatment actions and radiography findings of patients with gliomas who had undergone a surgical operation, were recorded in Form No.1. The registry information terminated in death of the patients, but living patients were pursued until August 2005, so that all patients were evaluated for at least one year.

The slides with their diagnosis from the primary center were submitted to the other center, and two other pathologists reviewed them in a double blind approach. Gliomas were classified based on WHO system into four grades I to IV. Cases were excluded from the study if their diagnosis differed (more than one grade) between experts, or if we were not able to follow the cases (e.g., when the patients didn't refer due to severity of the disease, or they referred to other centers, or they had left the recorded address, or have cited wrong phone numbers).

We used Chi-Square and Mann-Whitney tests. Survival analysis was calculated by Kaplan-Meier model, and for comparison if variables we used Log-rank test and Cox-regression. Data were analyzed by SPSS 16.0 (SPSS Inc, Chicago) and SAS 6.0 (SAS

Institute Inc, Cary) Software.

## Results

### *Patient characteristics:*

Patients in the study were 145 persons. Male gender was dominant. More than one out of each five patients was over sixty years old. The mean age of patients was  $43.57 \pm 17.35$  (range 3- 77 years). The tumor grade was assessed in 127 (87%) patients with biopsy, and removed.

Glioma was diagnosed without grading in 14 patients (9.6%). Glioblastoma multiform constituted 40.7% of graded tumors. The most prevalent tumor location was frontal lobe (44.8%). Patient characteristics are shown in Table 1.

**Table1.** Patients and tumors characteristics

<b>Patients characteristics</b>	<b>Number (%)</b>
<b>gender</b>	
Male	102 (70.3)
Female	43(29.7)
<b>Age(year)</b>	
<40	63(43.4)
40-60	51(35.2)
>60	31(21.4)
<b>Tumor location</b>	
Frontal lobe	65(44.8)
Temporal lobe	33(22.8)
Parietal lobe	17(11.7)
Occipital lobe	14(9.7)
Other cases* or unknown	16(11)
<b>Tumor site</b>	
Left	68(46.9)
Right	67(46.2)
Bilateral	3(2.1)
Central	4(2.8)
Other sites** or unknown	3(2)
<b>Tumor malignancy grade</b>	
1	1(0.7)
2	37(25.5)
3	30(20.7)
4(GBM)	59(40.7)
Without diagnosis of glioma	14(9.6)
	4(2.7)
<b>Without biopsy</b>	

\* Other cases included 8 cases with Corpus Callosum tumor, 4 cases with thalamus tumor, 2 cases with multiple tumors and 1 case with median brain tumor.

\*\* Other sites included two cases with multiple tumors.

**Therapeutic management of patients:**

Hundred and thirty-one patients (90.3%) had craniotomy, and 10 patients (6.9%) had only biopsy. Four patients (2.8%) had no surgery. Ninety-six patients (66%) had radiation therapy, and chemotherapy had been done in 18 patients (12.4%).

**Clinical characteristics of patients:**

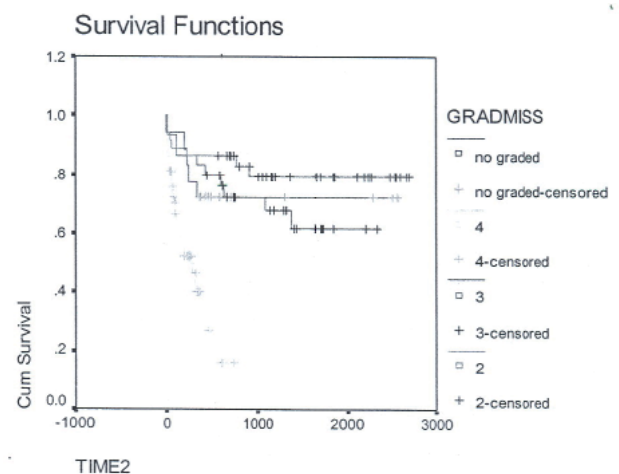
The most prevalent signs and symptoms of patients in the study were increased intracranial pressure, headache, neurotic- motor defect, and seizure (Table 2).

**Table 2:** Frequency of signs and symptoms before the surgical operation in patients with Brain Glioma

Signs and Symptoms	Number (person)	Percent (%)
increase of intracranial pressure	96	66.2
headache	85	58.6
neurotic- motor defect	77	53.1
seizure	59	40.7
Cranial nerves disorder	40	27.6
Superior neurotic- motor damage	40	27.6
Decrease of alertness level	32	22.1
Psychic disorder	32	22.1
Walking disorder	27	18.6
Speaking disorder	22	15.2
Disorder of sphincter	16	11
Sensory disorder	15	10.3
Basic ganglionic and diencephalon disorder	6	4.1

**Follow-up and survival:**

Median survivals of all patients were not calculable, and mean survival was 52.8 months ( $\pm 2SD= 45.5-60.1$  months, range 0-89.5 months). Annual survival rate was 67%. Forty-seven patients (39.6%) died, and 87 patients (60.4%) were alive at the end of follow up. Median survival was 39.7 weeks ( $\pm 2SD= 15.3-64.1$  weeks) for malignancy grade IV; Mean survival was 43.4 weeks ( $\pm 2SD= 32.6-54.2$  weeks, ranges: 0 -104.3 weeks); annual survival rate was 40%; thirty-five patients (59.3%) died and 24 patients (40.7%) were alive at the end of follow-up. Median survival was not calculated for patients with malignancy grade II, III, and all patients. However, annual survival rate in those patients was 86%, 83% and 67% respectively (Fig. 1).



**Fig. 1:** Curve of survival rates of patients based on different grades of tumor malignancy

**Effective factors in prognosis:**

Correlations between 22 variables including the age, malignancy grade, relapse, radiotherapy, seizure, neuromotor defects and gender with survival was assessed by Log-rank test (univariate analysis). Correlation among all variables and survival was meaningful except the gender (Table 3).

**Table 3:** Variables relevant to survival

Variable		Number	Log-Rank test (p)
<b>Gender</b>	Male	102	NS
	Female	43	
<b>neurotic- motor defect</b>	Yes	77	0.0024
	No	68	
<b>Tumor malignancy grade</b>	2	37	<0.0001
	3	30	
	4	59	
<b>Age</b>	<40	63	<0.0001
	40 -60	51	
	>60	31	
<b>Radiotherapy</b>	Done	96	<0.0001
	Not done	49	
<b>Relapse</b>	Yes	69	<0.0049
	No	76	
<b>Seizure history</b>	Yes	59	<0.0001
	No	86	

In simultaneous efficacy survey, it was shown that radiotherapy, age, malignancy grade, gender, relapse, seizure and neuromotor defect were effective on survival (multivariate analysis). The efficacy of three assessed factors out of above-mentioned seven variables was meaningful in the presence of other

variables, and they were considered as independent effective factors on prognosis (Table 4). These include age older than 60 years, radiotherapy in patients with malignant glioma (malignancy grade III, IV), and malignancy grade IV. Neuromotor defect was an independent effective factor on only prognosis.

**Table 4:** Effective and independent factors on prognosis in all patients

Effective factor on prognosis	Statistic Index	Estimate	Standard Error	P Value	Odd Ratio
<b>Malignancy grade</b>	2			0.132	
	3	0.593	0.544	0.276	1.809
	4	1.099	0.550	0.046	3.002
<b>Age</b>	<40			0.098	
	40 -60	0.536	0.406	0.187	1.709
	>60	0.991	0.459	0.031	2.693
<b>Radiotherapy</b>		2.695	0.422	<0.001	14.811
<b>Gender</b>		0.235	0.328	0.475	1.264
<b>Relapse</b>		0.609	0.370	0.100	1.839
<b>Seizure</b>		0.301	0.439	0.493	1.351
<b>Neuromotor defect</b>		0.430	0.336	0.200	1.538

## Discussion

In our retrospective cohort, clinical trends and prognosis in 145 patients with supratentorial brain glioma and different malignancy grades were studied. In this study, survival time in different malignancy grades had an ascending trend, that is, it approved results of the past studies (4, 9, 13). In our study, median survival time in malignancy grade IV was 39.7 weeks and mean survival time was 43.4 weeks, that is, it agreed with median survival in patients with grade IV tumor who had surgery and radiotherapy in the past studies, in whom median survival was 39 weeks (13). In Rosenthal Study (14), median survival in grade IV glioma was 29.6 weeks, which is less than our findings. Upper mean age in our patients and less microscopic evaluation in that study is probable reasons of this difference. Percentage of radiotherapy of patients in the two studies was near each other.

Grade IV median survival in Ozbek (15) and Stark (16) studies were more than our study. Higher percentage of microscopic examination and radiotherapy in the two studies (15, 16) justify this difference. In patients with malignancy grade III, mean survival was 54.8 months and median survival was not computable, that is less than the previous studies (13). In Devaux study (17) median survival in malignancy grade III was reported 21.9 months because surgeons approached to biopsy more than in our study. Total mean survival was 52.8 months in our study, and median was not computable. In Rosenthal study (14), median survival was 9.2 months, and 5-years survival rate was reported 19%.

The effectiveness of seven factors was studied in our study: malignancy grade, age, radiotherapy, neuromotor defect, relapse, seizure history before diagnosis, and gender. All of these factors except gender were meaningfully effective in survival based on Log-rank analysis. Cox-regression multivariate analysis was used for estimation of simultaneous factors effective in prognosis. Malignancy grade, radiotherapy, and age were identified to be independent effective factors in prognosis. Role of the radiotherapy was greater in our study. Results of our study was in accordance with previous studies (15, 16, 18, 19).

In Lutterbach study (20) age, KPS number, and central tumor location were identified as independent effective factors in prognosis. In Seylian and Anvary study (21) age of more than 50 years was indentified only in univariate analysis, and the effect was not stable in multivariate analysis. In patients with low

malignancy grades, neuromotor defect had a negative effect in prognosis. In the past studies (22-24), neuromotor defect had negative effect in prognosis too, but in the Seylian and Anvary studies neuromotor defect did not show adequate effect in survival (21). In Rosenthal study (14) and our study frontal and then temporal lobes were the most common tumor locations in patients with Glioma and glioblastoma multiforme, but multilobar and then temporal lobes were reported as the most common site (16).

The seizure incidence rate in patients with brain tumor was 35% in the past studies and 40.7% in our study.

The headache rate in patients with brain tumor as the initial symptom was 20% in the past studied (25) and 58.6% in our study.

We had no long survival in patients with glioblastoma. Our study had very limitations similar to other retrospective cohort studies, such as bias, geographic dispersion of patients, change of phone numbers or recorded address, and inability of patients for referring to hospitals.

## Conclusion

In spite of advancements in treatment of brain tumors, the present study demonstrates that survival rate in patients with GBM was low. With respect to the fact that age and malignancy grade do not change with intervention, extended radiotherapy after surgical operations can be adequate for increasing survival of patients with glioma.

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