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Glioblastoma multiform prognosis beyond craniotomy and chemo irradiation

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SUMMARY

Glioblastoma Multiform (GBM) is a malignant glioma with aggressive behaviour and poor outcome. This study was done to assess the survival of GBM and to discover factors that can influence the survival. Retrospectively, from 2011 to 2021, a total of 50 individuals with histopathologically confirmed GBM and received adjuvant chemoradiation in Oncology Department were analyzed. The following data was collected: demographic profile (age and gender); Karnofsky Performance Status (KPS); gliomas site, surgery and treatment regimens. We could divided patients to two-groups according to age, fifty and below (19, 38%), and above fifty (31, 62%). Male to female ratio was 1.5:1. In relation to KPS, 30% were better score (≥90), 44% were have good score (70-80), and 26% were within poor score (<70). Parietal and temporal lobes were the most common parts involved by GBM. Most of patients underwent excisional biopsy in (38, 76%). All patients received the standard treatment included surgery and post-operative radiotherapy with or without concurrent and/or maintenance TMZ. The prognostic impact of various variables is described in table 2. In Logistic analysis, patients with age >50, and KPS<90 are worsen factors as compared to others. Otherwise, adjuvant therapy and lobe involvement were found to be independent prognostic factors GBM. In conclusion, older age and low performance status is a dependent prognostic factor for the clinical outcome of GBM. Multimodalities therapy may be not affected the prognosis or survival of GBM.

Key words: glioblastoma multiform, brain tumor, gliomas, chemo irradiation, crainotomy

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INTRODUCTION

Glioblastoma Multiform (GBM) is an aggressive primary brain glioma with poor outcome and prognosis. Approximately, it is account for 12% to 15% of all primary intracranial tumour and 60% to 75% of gliomas [1, 2]. Globally, brain tumours ranked in 20th level in the list of incidence of new cases of cancer. They were recorded 308,102 (1.6%) new cases of CNS tumours, with 251,329 (2.5%) deaths in 2020 [3]. Approximately, 68,000 new cases of high grade brain tumours diagnosed in the United States each year. Recently, gliomas account for nearly more than 80% of malignant brain tumours. According to WHO grade IV tumour is the most common primary malignant brain tumour [4]. Generally, it present in fifth or sixth decade of life and more prevalent in man than women [1]. Based on multidisciplinary approach, the standard management for GBM is resection followed by radiotherapy with concurrent chemotherapy with Temozolomide (TMZ), and then maintenance TMZ [3]. Several randomized trials showed that concomitant and adjuvant TMZ in addition to postoperative radiotherapy improved the survival of patients, and risen the median survival to 15 months [5-7].

Here, this study aimed to describe clinical features, treatment schedules and determine prognostic factors that impact survival in GBM.

METHODS

Retrospectively, we reviewed oncology records and histopathological reports of GBM patients from 2011 to 2021. The following data was collected: demographic profile (age and gender); Karnofsky Performance Status (KPS) [8]; gliomas site, surgery and treatment regimens. In general, data collected when frequently patients visited the outpatient clinic or during mobile interview with patients or relatives. Statistical analysis was done using SPSS 23.0 (IBM, NY, USA). Prognostic factors were determined by logistic analysis test. Any p-value below 0.05 indicates statistical significance.

RESULTS

The characteristics of the patients and management are summarized in Table 1. We could divided patients to two-groups according to age, fifty and below (19, 38%), and above fifty (31, 62%). Male to female ratio was 1.5:1. In relation to

Tab. 1. Patients and treatment characteristics

Characteristics		No.	%
Age	≤ 50	19	38
	>50	31	62
Gender	Male	30	60
	Female	20	40
KPS	≥ 90	15	30
	70-80	22	44
	<70	13	26
Lobe of tumor	Frontal	4	8
	Temporal	17	34
	Parietal	18	36
	Occipital	6	12
	Other	5	10
Surgery	Gross Total Resection (GTR)	5	10
	Subtotal Resection (STR)	7	14
	Biopsy	38	76
Adjuvant treatment	Concurrent chemo radiation and maintenance TMZ	28	56
	Radiotherapy and maintenance TMZ	12	24
	Radiotherapy only	10	20

Tab. 2. Prognostic factors in the Logistic analysis

Characteristics		**P value**
Age	>50	0.02
Gender	M *vs*. F	0.73
KPS	≥ 90	<0.0001
	70-80	
	<70	
Lobe of tumor	Frontal	0.06
	Temporal	
	Parietal	
	Occipital	
Resection	GTR	0.2
	STR	
	Biopsy	
Adjuvant treatment	Concurrent chemoradiation and maintenance TMZ	0.08
	Concurrent chemoradiation	
	Radiotherapy and maintenance TMZ	
	Radiotherapy only	

KPS, 30% were better score (≥90), 44% were have good score (70-80), and 26% were within fair score (<70). Parietal and temporal lobes were the most common parts involved by GBM in 34% and 36% respectively. Frontal lobe was the lowest one. Most of patients underwent excisional biopsy in (38, 76%). All patients received the standard treatment included surgery and post-operative radiotherapy 60 Gy in 30 fractions with or without concurrent and/or maintenance TMZ.

The prognostic impact of various variables is described in Table 2. In Logistic analysis using, patients with age >50, and KPS<90, worse factors as compared to others. Otherwise, adjuvant therapy and lobe involvement were found to be independent prognostic factors GBM.

DISCUSSION

Many studies revealed that the prognosis of GBM has not showed much improvement over the last few decades. The established standard treatment for GBM consist of maximal safe resection margins followed by radiotherapy with or without concurrent and adjuvant TMZ [3]. A total gross resection is not always possible due to the tumour infiltration into the surrounding brain parenchyma which may lead to dysfunction, therefor; radiotherapy has to be delivered to take care of the residual masses. GBM survival is poor; therefor determine prognostic factors affecting this survival in native patients are necessary. All patients underwent craniotomy and adjuvant treatment.

The patients baseline characteristics were similar to other reviewed studies with M:F ratio of 1.5:1 and the median age of patients in this study is 50 years old. This difference from US patients due to the lower life expectancy of the Iraqi population [9].

There is no difference in prognosis between men and women. The findings were in line with several studies [10-12]. However, other series showed better survival in women compared to men [13-15]. An experimental *in vivo* study on rats with GBM Expressing Estrogen Receptor-β (ERβ) demonstrate an increase of cytotoxic effect compared to GBM without ERβ expression. Overexpression of ERβ will drop the proliferation of cancer cells and suppress the growth of GBM with improvement the response of therapy due to the effect of the reproductive hormone on GBM [16].

Age and performance status are the most important variables affecting patients prognosis in GBM. Curran et al, agree with our data and found a better prognosis in patients who were <50 years old and KPS of 90-100 [17].

Recently, GBM studies consistently stated that the older the age of the patient when diagnosed with GBM, the poorer prognosis and survival [10-15, 18, 19]. Besides the different biological nature of GBM in older patients, poorer prognosis may be caused by a reduction to tolerate medication in older patients [20]. Also, low KPS often associated with the patient's inability in tolerating an overly aggressive treatment and increased morbidity [21].

This study showed that most of patients underwent biopsy only, which is an impaction on prognosis and survival of GBM, since poorer survival associated with residual tumour size [22-26]. However, the lower the size and volume, the better the survival and prognosis of GBM patients.

This study showed no statistically difference in the prognosis from the administration of adjuvant treatment. However, there is a trend toward better prognosis in the group that received concurrent chemo radiation and adjuvant TMZ, which supported by several randomized trials that benefit where recorded in patients who received adjuvant concurrent chemo radiation and adjuvant TMZ compared to patients who treated by adjuvant radiation only [6, 27-29].

A randomized study by Kocher and his colleagues showed no difference of survival in patients who received concurrent chemo radiation without adjuvant TMZ compared to patients who received adjuvant radiation only [30].

In current study, GBM involving the parietal and temporal lobes showed no significant poorer prognosis. Kumar et al, found poorer survivability in GBM involving the parietal lobe, corpus callosum, and brainstem [18]. The study by Awad et al, Tian et al. and Wee et al. also reported poor survival in patients with GBM located in the periventricular, brainstem, corpus callosum and basal ganglia [12, 14, 31]. However, several other studies showed that tumour location does not affect survival [32-34].

CONCLUSION

Older age and low performance status is a dependent prognostic factor for the clinical outcome of GBM. Multimodalities therapy may be not affected the prognosis or survival of GBM.

COMPETING INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICAL APPROVAL

The study was conducted following the protocol of the Ethical Committee and written informed consent was obtained from all the participants.

AUTHORS CONTRIBUTION

All the authors participate in the design, collection and analysis of the data of the research.

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