

# Treatment Outcome Of Gbm: A Retrospective Single Institutional Study

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## Abstract

**Background:** The most frequent malignant brain tumour is glioblastoma multiforme (GBM), with other CNS cancers accounting for 47.7% of all cases. The aim of the present study was to evaluate the effect of suggested predicting factors on survival of adult GBM patient. **Patients and methods:** This retrospective cohort analysis of adult GBM patients treated at clinical oncology, Zagazig University, Egypt. All demographic data, histopathological tumor types and grades were revised and adjusted according to WHO classification of CNS tumors (2016), surgical status, location, tumor morphology, treatment, outcome, recurrence, disease free survival and overall survival were collected and analyzed. **Results:** The median age of patients was 53 years (with predominance of males to females). 52.3% of patients was with a tumor size >5cm. most patients underwent initial surgery (79.3%) while remaining (20.7%) underwent a diagnostic biopsy due to no respectability. Extent of resection was assessed by post-operative MRI in 85 patients (76.6%) of whom 3 patients only underwent complete resection and 82 (73.9%) underwent partial resection. **Conclusion:** The prognosis of adult patients with GBM remain poor, however, surgical resection and adjuvant treatments improve overall survival. Age, surgical resection, size of residual tumor and adjuvant chemotherapy have been identified as prognostic indicators of overall survival. **Conclusion:** The prognosis of adult patients with GBM remain poor, however, surgical resection and adjuvant treatments improve overall survival, age, surgical resection, size of residual tumor and adjuvant chemotherapy have been identified as prognostic indicators of overall survival.

**Keywords:** Glioblastoma Multiforme; Outcome; Overall Survival; Disease Free Survival

## INTRODUCTION

Primary central nervous system tumors (CNS) are accounting for 1%:2% of all tumors (1). Glioblastoma multiforme (GBM) is the most common malignant brain tumor and other CNS tumors accounting for 47.7% of all cases. GBM has incidence of 3.21 per 100,000 population (2).

GBM accounts 50% of gliomas (3). It remains an incurable tumor with a median survival of only 15 months (4). Treatment of adult GBM is complex, initially consisting of maximally safe surgical resection followed by radiation therapy and concurrent Temozolamide chemotherapy (5).

Some Prognostic factors for adult GBM have been suggested including age, extent of surgery, Karnofsky performance status, tumor size and location (6).

The aim of our study is to evaluate the effect of suggested predicting factors on survival of adult GBM patients.

## PATIENTS AND METHODS

Our study is a retrospective cohort analysis included adult GBM patients treated at clinical oncology, Zagazig University, Egypt in the period between January 2013 and December 2021.

**Inclusion criteria:**

Patients who radiological and pathological diagnosed with GBM, age > 18 years and complete medical records.

**Exclusion criteria:**

Pediatrics below 18 years was excluded.

The data collected included: age, gender, tumor characteristics, extent of surgery, postoperative treatment and treatment after progression.

130 patients of GBM were collected in our study. The final analysis included 111 (85.4%). Nineteen patients were missed due to incomplete data or loss to follow up after initial diagnosis.

**Ethical Consideration:**

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Written informed consent of all the participants was obtained. The current study was approved by the Institutional Review Board (IRB) committee of Zagazig University (no. ZU-IRB # 6761/12-7-2021). This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical analysis:**

All data were collected, tabulated and statistically analyzed using Microsoft Office Excel 2010 for windows (Microsoft Cor., Redmond, WA, USA), SPSS 22.0 for windows (IBM Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software byba, Ostend, Belgium). Continuous variables were expressed as the mean ± SD & median (range), and the categorical variables were expressed as a number (percentage). Continuous data checked for normality by using Shapiro Walk test. Mann Whitney U test was used to compare two groups of non-normally distributed data. Percent of categorical variables were compared using Pearson’s Chi-square test. Trend of change in distribution of relative frequencies between ordinal data were compared using Chi-square test for trend. Progression Free Survival (PFS) was calculated as the time from date of start of treatment to date of progression or the most recent follow-up contact that patient was known as progression free. Overall Survival (OS) was calculated as the time from date of diagnosis to date of death or the most recent follow-up contact of patient. These time-to-event distributions were estimated using the method of Kaplan-Meier plot and compared using two-sided exact log-rank test. p-value < 0.05 was considered statistically significant.

**RESULTS**

The median age of patients was 53 years (range; 19-85) with predominance of males to females (57.7% and 42.3% respectively). 52.3% of patients was with a tumor size > 5cm. most patients underwent initial surgery (79.3%) while remaining (20.7%) underwent a diagnostic biopsy due to no respectability. Extent of resection was assessed by post-operative MRI in 85 patients (76.6%) of whom 3 patients only underwent complete resection and 82 (73.9%) underwent partial resection (Table 1).

**Table (1): Clinicopathological characteristics, management, outcome and management of progression among the studied glioblastoma patients (N=111).**

Parameters	All studied patients (N=111)		Parameters	All studied patients (N=111)	
	No.	%		No.	%
<b><u>Sex</u></b>			<b><u>Radiotherapy dose</u></b>		
Male	64	57.7%	No	1	0.9%
Female	47	42.3%	40Gy	3	2.7%
<b><u>Age (years)</u></b>			60Gy	105	94.6%

Mean±SD	51±14.08		Missed	2	1.8%
Median (Range)	53 (19 – 85)		<b>Concurrent chemotherapy</b>		
≤40 years	27	24.3%	No	4	3.6%
>40-60 years	59	53.2%	Yes (Temodal)	106	95.5%
>60 years	25	22.5%	Missed	1	0.9%
<b>Residence</b>			<b>Adjuvant chemotherapy</b>		
Rural	94	84.7%	No	13	11.7%
Urban	17	15.3%	Yes (Temodal)	98	88.3%
<b>Clincial presentation</b>			<b>Number of CT cycles</b> (N=94)		
Headache	101	91%	1 cycle	1	1.1%
Seizures	8	7.2%	6 cycles	88	93.6%
Motor dysfunction	30	27%	12 cycles	5	5.3%
Dysarthria	2	1.8%	<b>Response to treatment</b>		
Visual deficits	5	4.5%	CR	1	0.9%
Sensory dysfunction	12	10.8%	PR	29	26.1%
Cranial nerve affection	1	0.9%	SD	60	54.1%
<b>Size of tumor</b>			PD	15	13.5%
≤5cm	53	47.7%	Missed	3	2.7%
>5cm	58	52.3%	N/A	3	2.7%
<b>Side of tumor</b>			<b>Follow-up duration</b>		
Left side	55	49.5%	(months)		
Right side	51	45.9%	Mean±SD	15.95±8.76	
Non-lateralized	2	1.8%	Median (Range)	12 (1 – 36)	
Multicentric	3	2.7%			
<b>Site of tumor</b>			<b>Progression</b> (N=108)		
Frontal lobe	24	21.6%	Absent	84	77.8%
Temporal lobe	25	22.5%	Present	24	22.2%
Parietal lobe	38	34.2%	<b>Treatment after progression</b> (N=24)		
Occipital lobe	14	12.6%	Chemotherapy	4	16.7%
Multiple brain lobes	3	2.7%	Surgery + Chemotherapy	3	12.5%
Thalamic	4	3.6%	Chemoradiation	2	8.3%
Corpus callosum	2	1.8%	Surgery + CCRT	1	4.2%
Ventricle	1	0.9%	Missed	14	58.3%
<b>Surgical resection</b>			<b>Chemotherapy regimen</b> (N=10)		
No	23	20.7%	PCV	4	40%
Yes	88	79.3%	Carbo + Vepside	4	40%
<b>Size of residual tumor</b>			TMZ	1	10%
No residual	3	2.7%	Multiple lines	1	10%
<3cm	15	13.5%	<b>Number of CT cycles</b> (N=10)		
3-5cm	64	57.7%	1 cycle	1	10%
>5cm	3	2.7%	3 cycles	6	60%
Missed	3	2.7%	6 cycles	3	30%
N/A	23	20.7%			
<b>Radiotherapy</b>			<b>Mortality</b>		
No	1	0.9%	Alive	58	52.3%
Yes	110	99.1%	Died	53	47.7%

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range).

110 patients received radiotherapy. The radiotherapy was computerized tomography-based 3-dimensional radiotherapy .94.6% of patients received conventional fractionated radiotherapy (60Gy/30f

over 6 weeks) and 2.7% not completed sessions as they were deteriorated and died during sessions 93.6% of patients received adjuvant temozolamide for 6 cycles and 5.3% of them received 12 cycles as there is a good regressive course of tumor. Details of patients and treatment received (Table 1). The median of OS of patients developed progression was 10 months. Table 2 shows OS according to studied variables. Overall survival differed significantly according to age, surgical resection, size of residual tumor, adjuvant chemotherapy, best overall survival and progression. ( $p < 0.001, 0.003, < 0.001, < 0.001, > 0.001$  and  $0.011$  respectively). Survival didn't differ significantly with gender, size of tumor, site of tumor and radiotherapy. Survival significantly differed with treatment after progression. ( $p = 0.002$ ) (Table 3-5; Figure 1).

**Table (2): Relationship between clinicopathological characteristics and survival among the studied glioblastoma patients (N=111).**

Clinicopathological characteristics	All (N=111)	Alive (N=58)		Died (N=53)		p-value
		No.	%	No.	%	
<b><u>Sex</u></b>						
Male	64	33	51.6%	31	48.4%	0.865 <sup>a</sup>
Female	47	25	53.2%	22	46.8%	
<b><u>Age (years)</u></b>						
Mean±SD		45.81±13.47		56.67±12.55		<0.001 <sup>b</sup>
Median (Range)		48.50 (19 – 73)		58 (28 – 85)		
<b><u>Age group</u></b>						
≤40 years	27	19	70.4%	8	29.6%	0.001 <sup>c</sup>
>40-60 years	59	33	55.9%	26	44.1%	
>60 years	25	6	24%	19	76%	
<b><u>Residence</u></b>						
Rural	94	47	50%	47	50%	0.264 <sup>a</sup>
Urban	17	11	64.7%	6	35.3	
<b><u>Clinical presentation</u></b>						
Headache	101	57	56.4%	44	43.6%	0.006 <sup>a</sup>
Seizures	8	1	12.5%	7	87.5%	0.027 <sup>a</sup>
Motor dysfunction	30	14	46.7%	16	53.3%	0.473 <sup>a</sup>
Dysarthria	2	1	50%	1	50%	1.000 <sup>a</sup>
Visual deficits	5	4	80%	1	20%	0.366 <sup>a</sup>
Sensory dysfunction	12	4	33.3%	8	66.7%	0.165 <sup>a</sup>
Cranial nerve affection	1	0	0%	1	100%	0.477 <sup>a</sup>
<b><u>Size of tumor</u></b>						
≤5cm	53	25	47.2%	28	52.8%	0.308 <sup>c</sup>
>5cm	58	33	56.9%	25	43.1%	
<b><u>Side of tumor</u></b>						
Left side	55	31	56.4%	24	43.6%	0.297 <sup>a</sup>
Right side	51	26	51%	25	49%	
Non-lateralized	2	1	50%	1	50%	
Multicentric	3	0	0%	3	100%	
<b><u>Site of tumor</u></b>						
Frontal lobe	24	10	41.7%	14	58.3%	0.232 <sup>a</sup>
Temporal lobe	25	18	72%	7	28%	
Parietal lobe	38	19	50%	19	50%	
Occipital lobe	14	7	50%	7	50%	
Multiple brain lobes	3	0	0%	3	100%	
Thalamic	4	2	50%	2	50%	

<b>Corpus callosum</b>	<b>2</b>	<b>1</b>	<b>50%</b>	<b>1</b>	<b>50%</b>
<b>Ventricle</b>	<b>1</b>	<b>1</b>	<b>100%</b>	<b>0</b>	<b>0%</b>

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean  $\pm$  SD & median (range); a: Chi-square test; b: Mann Whitney U test; c: Chi-square test for trend; p-value<0.05 is significant.

**Table (3): Relationship between management and survival among the studied glioblastoma patients (N=111).**

<b>Management</b>	<b>All (N=111)</b>	<b>Alive (N=58)</b>		<b>Died (N=53)</b>		<b>p-value</b>
		<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	
<b><u>Surgical resection</u></b>						
No	23	7	30.4%	16	69.6%	0.019 <sup>a</sup>
Yes	88	51	58%	37	42%	
<b><u>Size of residual tumor</u></b>						
No residual	3	3	100%	0	0%	0.037 <sup>a</sup>
<3cm	15	9	60%	6	40%	
3-5cm	64	37	57%	27	42.2%	
>5cm	3	0	0%	3	100%	
Missed	3	2	66.7%	1	33.3%	
N/A	23	7	30.4%	16	69.6%	
<b><u>Radiotherapy</u></b>						
No	1	0	0%	1	100%	0.477 <sup>a</sup>
Yes	110	58	52.7%	52	47.3%	
<b><u>Radiotherapy dose</u></b>						
No	1	0	0%	1	100%	0.074 <sup>a</sup>
40Gy	3	0	0%	3	100%	
60Gy	105	58	55.2%	47	44.8%	
Missed	2	0	0%	2	100%	
<b><u>Concurrent chemotherapy</u></b>						
No	4	0	0%	4	100%	0.057 <sup>a</sup>
Yes (Temodal)	106	58	54.7%	48	45.3%	
Missed	1	0	0%	1	100%	
<b><u>Adjuvant chemotherapy</u></b>						
No	13	0	0%	13	100%	<0.001 <sup>a</sup>
Yes (Temodal)	98	58	59.2%	40	40.8%	
<b><u>Number of CT cycles</u></b>						
	(N=94)					
1 cycle	1	0	0%	1	100%	0.253 <sup>a</sup>
6 cycles	88	56	63.6%	32	36.4%	
12 cycles	5	2	40%	3	60%	

Categorical variables were expressed as number (percentage); a: Chi-square test; p-value<0.05 is significant.

**Table (4): Relationship between outcome of treatment/progression after treatment & its management and survival among the studied glioblastoma patients (N=111).**

<b>Outcome of treatment</b>	<b>All (N=111)</b>	<b>Alive (N=58)</b>		<b>Died (N=53)</b>		<b>p-value</b>
		<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	
<b><u>Response to treatment</u></b>						
CR	1	1	100%	0	0%	<0.001 <sup>a</sup>
PR	29	22	75.9%	7	24.1%	
SD	60	32	53.3%	28	46.7%	
PD	15	0	0%	15	100%	

Missed	3	0	0%	3	100%	
N/A	3	3	100%	0	0%	
<b>Progression</b>	(N=108)	(N=55)		(N=53)		
Absent	84	51	60.7%	33	39.3%	<0.001 <sup>a</sup>
Present	24	4	16.7%	20	83.3%	
<b>Treatment after progression</b>	(N=24)	(N=4)		(N=20)		
Chemotherapy	4	0	0%	4	100%	0.002 <sup>a</sup>
Surgery + Chemotherapy	3	3	100%	0	0%	
Chemoradiation	2	0	0%	2	100%	
Surgery + CCRT	1	0	0%	1	100%	
Missed	14	1	7.1%	13	92.9%	
<b>Chemotherapy regimen</b>	(N=10)	(N=3)		(N=7)		
PCV	4	3	75%	1	25%	0.093 <sup>a</sup>
Carbo + Vepside	4	0	0%	4	100%	
TMZ	1	0	0%	1	100%	
Multiple lines	1	0	0%	1	100%	
<b>Number of CT cycles</b>	(N=10)	(N=3)		(N=7)		
1 cycle	1	0	0%	1	100%	0.788 <sup>a</sup>
3 cycles	6	2	33.3%	4	66.7%	
6 cycles	3	1	33.3%	2	66.7%	

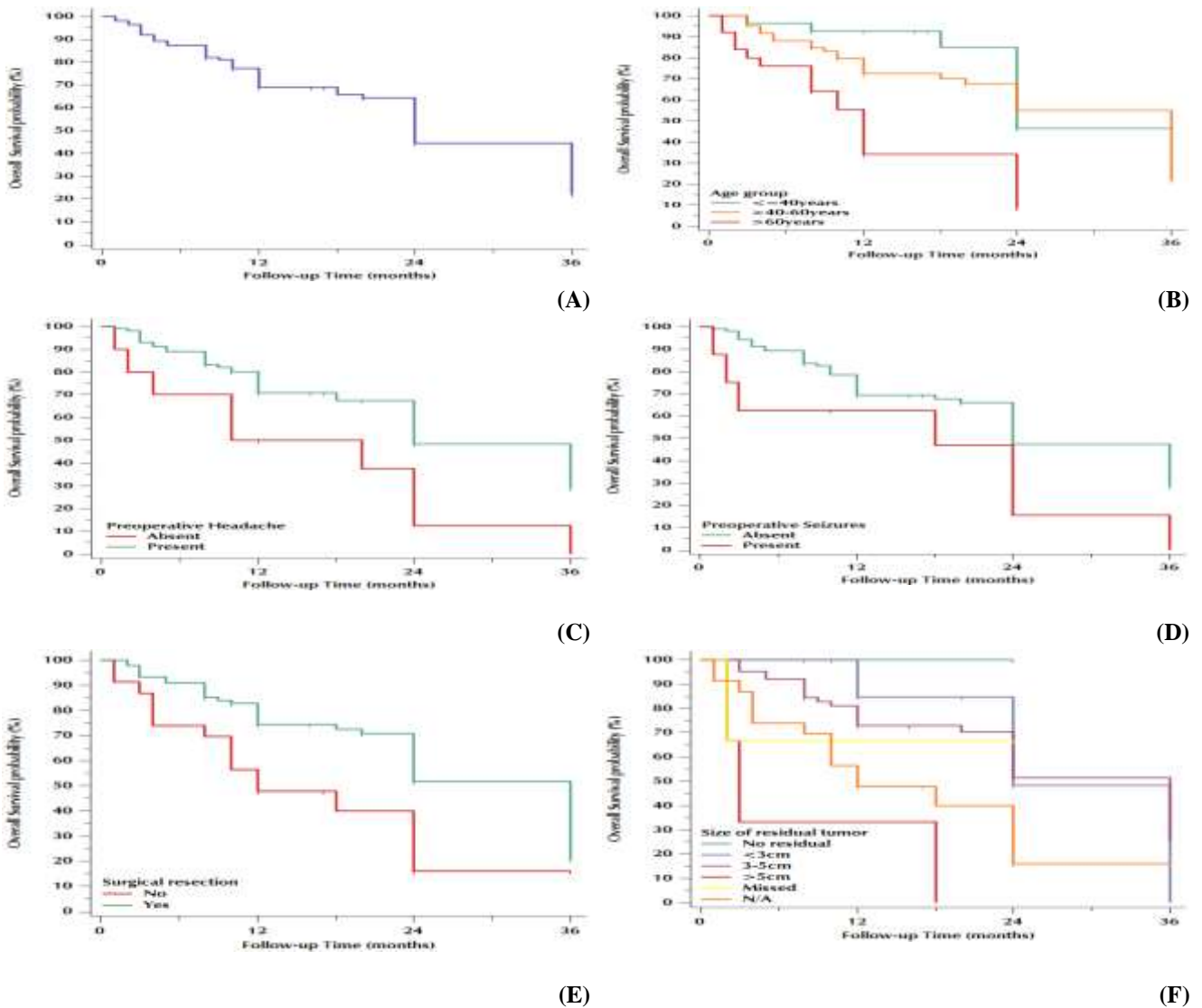
Categorical variables were expressed as number (percentage); a: Chi-square test; p-value<0.05 is significant.

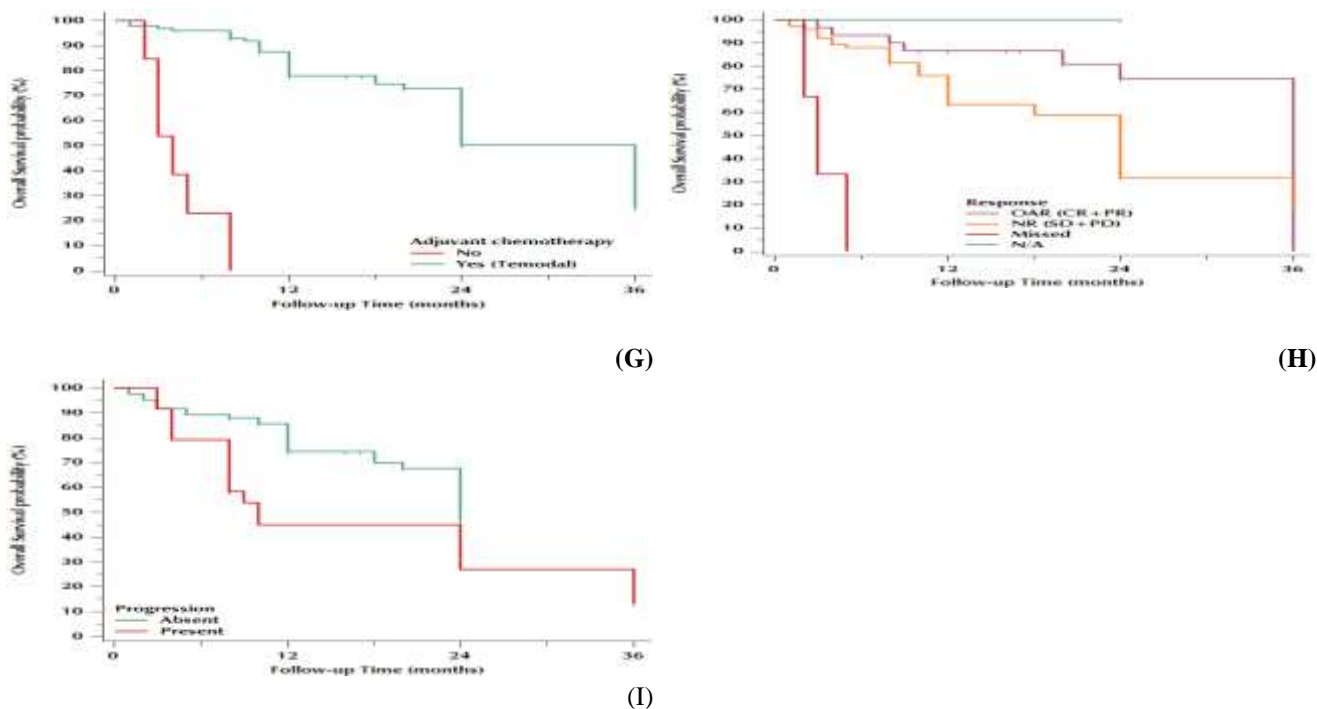
**Table (5): Overall Survival among the studied glioblastoma patients (N=111).**

	N	Overall Survival (OS)					p-value <sup>d</sup>
		Median	(95%CI) (months)	1-year	2-year	3-year	
<b>All patients</b>	<b>111</b>	<b>24</b>	<b>(21.76 – 26.23)</b>	<b>68.8%</b>	<b>44.4%</b>	<b>22.2%</b>	<b>-----</b>
<b>Sex</b>							
Male	64	24	(18.60 – 29.39)	71.6%	46.2%	23.1%	0.604
Female	47	24	(14.38 – 33.62)	64.9%	41.8%	20.9%	
<b>Age group</b>							
≤40 years	27	24		92.6%	46.3%	46.3%	<0.001
>40-60 years	59	36	(27.16 – 44.83)	72.5%	55.1%	22%	
>60 years	25	12	(10.21 – 13.78)	34.1%	8.5%	-----	
<b>Headache</b>							
Absent	10	10	(0 – 25.25)	50%	12.5%	0%	0.008
Present	101	24	(18.46 – 29.53)	70.7%	48.4%	29%	
<b>Seizures</b>							
Absent	103	24	(19.05 – 28.94)	69.4%	47.5%	28.5%	0.035
Present	8	18	(1.62 – 34.37)	62.5%	15.6%	0%	
<b>Size of tumor</b>							
≤5cm	53	24	(22 – 26)	76.6%	39.8%	10%	0.782
>5cm	58	NR		61.8%	51.5%	51.5%	
<b>Surgical resection</b>							
No	23	12	(2.20 – 21.79)	47.8%	15.9%	15.9%	0.003
Yes	88	36	(28.74 – 43.25)	74.5%	51.6%	20.6%	
<b>Size of residual tumor</b>							
No residual	3	NR		100%	100%	-----	<0.001
<3cm	15	24	(24 – 36)	84.6%	48.4%	0%	
3-5cm	64	36	(24 – 36)	73%	51.4%	25.7%	
>5cm	3	3	(2 – 18)	33.3%	0%	0%	

Missed	3	NR		66.7%	66.7%	-----	
N/A	23	12	(2.20 – 21.79)	47.8%	15.9%	15.9%	
<b>Adjuvant CT</b>							
No	13	4	(2.85 – 5.14)	0%	0%	0%	<0.001
Yes (Temodal)	98	36	(28.94 – 43.05)	78%	50.3%	25.2%	
<b>Best overall response</b>							
OAR (CR+PR)	30	36		86.5%	74.6%	0%	<0.001
NR (SD+PD)	75	24	(18 – NR)	63.4%	31.7%	19%	
Missed	3	3	(2 – 5)	0%	0%	0%	
N/A	3	NR		100%	100%	-----	
<b>Progression</b>							
Absent	84	24		74.5%	46.7%	-----	0.011
Present	24	10	(6.99 – 13)	44.9%	26.9%	13.5%	

Categorical variables were expressed as number or percentage; Continuous variables were expressed as median (95% CI); 95% CI: 95% Confidence Interval; d: Log-rank test; p-value<0.05 is significant.





**Figure (1): Kaplan Meier plot for Overall Survival (OS):** (A) for all studied Glioblastoma patients (N=111); (B) Stratified by age group; (C) Stratified by preoperative headache; (D) Stratified by preoperative seizures; (E) Stratified by surgical resection; (F) Stratified by size of residual tumor; (G) Stratified by adjuvant chemotherapy; (H) Stratified by response to treatment; (I) Stratified by progression.

## DISCUSSION:

Glioblastoma multiform (GBM) is challenging to cure because of tumor heterogeneity. While certain tumour cells might respond well to certain therapy, others might not respond at all. Because of this, the treatment plan for GBM may incorporate a number of techniques. Surgery, radiation therapy, chemotherapy, and combination treatment are all multimodal techniques that are used to treat GBM (2,3).

In our study the median age of patients a diagnosis was 53 years and this is lower than results from Tunisia (54 years) and higher than results from Ain shams university ,Cairo(52 years) and Iran (7,8). Extent of resection was significantly affected by overall survive and this comes in disagreement with results from Denmark (9).

The rate of patient underwent gross total resection was only 2.7% which is much less than the 53% reported by Fekete et al and less than from results from ain shams university , cairo .this due to the large tumor size among patients (52.3%) which was >5 cm (10).

Patients between (40-60 years) had better OS of 36 months comparing to older patients with OS of 12 months and this is higher than results from Ain shams university and Li et al .(11).

This due to the ability of youngerpatients to tolerate the multimodality treatment of GBM. Patients with headache and patients who presented by seizures survived better .this comes in agreement with results from Canada (12).

Median OS of all patients was 24 months this is higher than results from sohag university ,may be due to lower median age at diagnosis and higher rate of patients recieved post.operative radiotherapy and adjuvant temozolamide (13).

Patients underwent surgical excision had a median OS of 36 months compared to 12 months of those underwent biopsy. This comes in disagreement with results from,Ain shams .

Patients didn,t not receive adjuvant temozolamid had shown significantly lower survival and poorer prognosis than those received adjuvant chemotherapy temozolamide and this comes in agreement with results from Iran (14).

Overall survival rates for 1,2 and 3 year(s) were (68.8%,44.4% and 22.25 respectively ) is lower than in comparison to results from **Ehsan et al (15)**.

## CONCLUSION:

The prognosis of adult patients with GBM remain poor, however, surgical resection and adjuvant treatments improve overall survival ., age ,surgical resection, size of residual tumor and adjuvant chemotherapy have been identified as prognostic indicators of overall survival .

**Conflict of interest:** The authors declare no conflict of interest.

**Author contribution:** Authors contributed equally in the study.

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