SURVIVAL OUTCOMES AMONG PATIENTS WITH HIGH-GRADE GLIOMA: A SINGLE INSTITUTION RETROSPECTIVE STUDY

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ABSTRACT

Background

The prognosis for glioma patients is poor, despite recent advances in diagnosis and treatment. Understanding Glioma's clinical characteristics and predictive factors is crucial for patient treatment and management.

Objectives

To assess the survival duration of HGG patients at a single facility and to discover clinical determinants of treatment outcome in HGG treated with a combined modality approach in Zhianawa Cancer Center.

Patients and Methods

This study included 133 patients with high-grade gliomas diagnosed between January 2015 and January 2020; these patients were referred to the Zhianawa Cancer Center. A retrospective analysis of the clinical data included survival outcomes, tumour characteristics, and demographic information. While the Cox regression model was used for the evaluation of multivariate data to look at the risk factors for mortality, on the other hand, survival data were analyzed using Kaplan-Meier curves with a log-rank test.

Results

In this particular patient cohort, grade IV glioma (83.9%), grade III glioma (16.1), and glioblastoma (81.4%) were the most common pathological types. A poor prognosis was associated with not using temozolomide, having a Karnofsky Performance Score (KPS) of less than 70%, and not receiving radiotherapy. Univariate analysis showed low KPS (70) to increase the risk of mortality. Patients who had radiotherapy with normal fractionation, concurrent chemotherapy, and radiotherapy adjuvant chemotherapy had the highest overall survival rates.

Conclusion

Mortality was significantly related to aging, absence of seizures, presence of motor alteration, pathological grade IV gliosarcoma, glioblastoma multiform, and non-standard radiation dose.

Keywords: *High-Grade Glioma, Glioblastoma, Clinical characteristics, Survival, Prognostic factors.*

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INTRODUCTION

The primary brain tumour that develops from the neuroepithelium that is the most prevalent and threatening is a glioma [1]. Primary malignant brain tumours have become more common over the past 30 years at 1-2% annually, with elderly individuals having the highest rates [2]. About 30% of all central nervous system (CNS) and 80% of malignant primary brain tumours are gliomas[3].

According to histology, Glioma is typically categorised into four grades: grades I and II are considered low-grade gliomas, whereas grades III and IV are considered high-grade gliomas (HGGs) [4]. Anaplastic oligodendroglioma (A.O.), anaplastic astrocytoma (A.A.), anaplastic oligoastrocytoma (AOA), and glioblastoma(GBM) are examples of HGGs from a histological standpoint[5].

Glioblastoma GBM is expected to rise significantly over the next 30 years in the United States, while the remaining gliomas will remain stable [6]. Studies show that the GBM has a slight male predominance (approximately a 1.4:1 male-to-female ratio) [7]. People in their fifth through seventh decades are more likely to develop glioblastoma [8]. Grade IV glioma is extremely detrimental; the median survival time is less than six months without any treatment [9]. Even with multimodal therapies, the median survival time for GBM patients is only about 15 months [10].

There is inconclusive proof that toxins, infections, head trauma, cell phone use, or environmental factors contribute to developing high-grade gliomas. Less than 5% of high-grade gliomas are caused by hereditary genetic syndromes, such as Li-Fraumeni cancer syndrome, linked to germline TP53 gene mutation, neurofibromatosis, and Turcot syndrome [11].

Depending on where in the brain the tumour is located, high-grade gliomas can present with different signs and symptoms. Due to their rapid growth, patients with glioblastomas exhibit focal neurologic deficits like hemiparesis, aphasia, and visual field defects. Throughout their illness, many patients experience or develop seizures; oligodendroglioma patients experience seizures more frequently than other patients. Additionally, behavioural changes and cognitive impairment may occur [12].

Since 2005, the recommended standard treatment has been maximal safe tumour resection followed by radiotherapy with concurrent (CCRT) and adjuvant (Adj) temozolomide (TMZ) [9, 13]. Tumour resection can lessen tumours' mass effect and help improve neurologic signs and symptoms. Gliomas frequently cannot be completely removed due to their infiltrative nature. In general, removing the enhancing portion of high-grade gliomas, especially glioblastomas, is advised. According to retrospective studies, the extent of resection is related to prognosis, with a significant survival benefit from a greater extent of resection [14].

Radiotherapy (R.T.) with a total dose of 60 Gy delivered in 30 to fractions for about six weeks is the standard treatment for glioblastoma [9, 15]. Radiation is typically applied to the gross tumour volume with a 2 to 3-cm margin to treat the infiltrating tumour. The innovative oral chemotherapy medication TMZ reportedly has a low incidence of side effects and can enter the brain. Adding temozolomide to radiation therapy increases glioblastoma patient survival [9].

The aim of this study was to assess the survival duration of HGG patients at a single facility and to discover clinical determinants of treatment outcome in HGG treated with a combined modality approach in Zhianawa Cancer Center.

PATIENTS AND METHODS

Patient selection, inclusion criteria, and exclusion criteria

We looked at the patient's age, gender, Karnofsky performance status (KPS), neurological condition, tumour characteristics, details of their treatment, and outcome. Based on the Radiation Therapy Oncology Group's (RTOG) and Recursive Partitioning Analysis (RPA), the KPS (Scale is a widely used method to assess the functional status of a patient, the Karnofsky index is between 100 and 0). was dichotomised at 70 (Cares for self but unable to carry on normal activity or to do active work). Age groups that we used for risk stratification in glioma patients using the Akaike information criterion (AIC) are 18–47 years old (young group), 48–63 years old (middle age group), and ≥ 64 years old (elderly group). In this study, R.T. dose prescription and fractionation were divided into three groups: normal fractionation (the patient receives 1.8–2 Grays per fraction, one fraction per day, five fractions per week, 25–35 fractions per treatment, 50–60 Gy in total), hypofractionation (the patient receives >2 Grays per fraction, one fraction per day, five fractions per week, 25–35 fractions per treatment, 50–60 Gy in total). 50–60 Gy total radiation) Moreover, extreme hypofractionation (the patient receives 5 Grays per fraction, the number of fractions per day is one, the number of fractions per week is five, the number of fractions per treatment is 5, Total dose is 25 Gy).

The present study was a retrospective study on 133 patients with high-grade Glioma. In our facility, these patients have been seen between January 2015 to January 2021 for radiation therapy. Kurdistan's Higher Council of Medical Specialties approved this research. Also, Our hospital's Institutional Review Board and Ethics Committee reviewed and approved the study.

Inclusion criteria were Patients with high-grade Glioma (grade III and IV) registered at Zhianawa cancer centre for radiation therapy treatment. The exclusion criteria were as follows: Patients less than 18 years old age, Brain stem glioma patients, and Patients who lost follow-up (lost information of age, sex, histopathology, radiotherapy status, or chemotherapy status)

Data collection and follow-up

Purposive or subjective non-random sampling. Patients who were registered for radiation treatment at the Zhianawa Cancer Center (Sulaimaniyah, Kurdistan/Iraq) during a period of our study design. According to our study's criteria, 133 patients have been collected. Clinical data were taken from the patient's medical records and analysed statistically. The data was anonymous, and permission had been acquired from the centre's administration. The patients' or their families' approval was obtained over the phone as opposed to getting written consent.

Statistical methods

Nominal and ordinal parameters were described with frequency analysis. Time for R.T. delay and survival durations in month parameters were described with means and standard deviation. R.T. delay parameter normality was tested with Kolmogorov-Smirnov Test. Since the distribution was abnormal, the Mann-Whitney U test was used for different analyses. All other nominal and ordinal parameter differences were tested with Fischer's Exact test and Chi-Square linear-by-linear association. Spearman's rho correlation was used for relationship analysis. Binary logistic regression and Cox regression were used for multivariate-level analysis. The median and mean overall survival among different groups were analysed using the Kaplan-Mier graph. In this study, a p-value of < 0.05 was considered significant,

RESULTS

The present study included a total of 133 participants with HGG. Twenty patients had missing data, so they were excluded from the analysis. Thus, 113 patients' data were included in the final study population for analysis. Comprehensive data on the patient's clinical data, tumour characteristics, and treatment details are provided in Table 1, with different analysis results between mortality groups.

There were 63(55.8%) men and 50 (44.2%) women, with a median age of 53.6 years. The average survival time for men and women was 14.4 and 15.8 months, respectively. 28.3% of patients were in the young group (18-47 years), 38.9% of patients were in the middle age group(48-63 years), and 32.7% of patients were elderly (64 years and over), the mean survival time for the three groups was 19.6,12.6 and 13.19 months, respectively. Most gliomas were found in the middle age group. Age distribution results were significantly different, showing that the age means of the death group were higher than the living group ($p<0.05$).

In this analysis, the most frequently reported symptom among our study patients was headaches (69.9%, n=79), followed by motor alteration (62.8%, n=71). In addition to these symptoms, vomiting, mental confusion, seizures, and altered vision each account for about (55%, n=48.7), (38%, n=33.6), (31%, n=35), and (29%, n=25.7) of cases, respectively. The seizure was significantly more common in the living group ($p<0.05$), whereas motor alteration was significantly more common in the death group ($p<0.05$).

The patients' KPS showed ≥70% in 70 (61.9%) patients and <70% in 43 (38.1%) patients; the mean survival time for the first and second groups was 17.17 and 11.91 months; There was a significant difference between the KPS of these two groups ($P = 0.013$).

WHO grade III patients comprised 18 (16.1%), while WHO grade IV patients accounted for 94 (83.9%) patients. Most patients (81.4%) had GBM grade IV, with the remaining 18.7% having variants of the HGG subtype. 30.5% of tumours had a size of less than 4 cm, 52.4% had a size of 4 to 6 cm, and 17.1% had a size of more than 6 cm. About 92.6% of tumours were unifocal, and just 8% were multicentric, all of which were in the death group.

Depending on the extent of the surgery, we divided the patients into four groups: biopsy (49 patients), subtotal resection (STR) (45 patients), Gross total resection(GTR) (15 patients), and four patients who underwent no surgery. The mean survival time for these four groups was 13.7, 16.1, 14.4, and 23.82 months, respectively (p=0.322).

TMZ-based chemotherapy was prescribed for 97 patients (85.7%) in either CCRT (18.6%) or Adj. (10.6%), Alternatively, CCRT+Adj (56.6%), with 14.2% of patients not receiving it. The patients received CCRT plus adj. CTX The overall survival rate was 18 months compared to others' 10.77, 13.9, and 9.4 months for not receiving TMZ, CCRT, and Adj, respectively.

Radiation therapy has a significant impact on HGG survival time. R.T. was given to 91.2% of the patients in this study. The majority of patients received normal fractionation (n=44/40, 4%), while the remaining 38% and 27% received hypofractionation and extreme hypofractionation, respectively. Hypofractionation and extreme hypofractionation were more common in the death group, with a statistically significant difference ($p<0.05$). The highest survival rate (19.642 months) was seen in patients with normal fractionation protocols, and this difference was statistically significant ($p<0.05$). The median time from diagnosis to radiation was roughly 3.87 months for the living group and 2.2 months for the death group. R.T. delay duration was significantly higher in the living group ($p<0.05$) Figure 1.

Only 15% of the participants in the study were alive at the time of the study, while the other 85% had passed away. The mean survival time for all patients was 15 (12.54-17.52) months, and the median survival time (MST) was 11.26 (95% CI 9.43-13.08) months. Table 2 provides the overall survival means of each subgroup.

Survival curves for the entire study population throughout the research are explained in Figure 2.

Tumour grade was significantly higher in the death group ($p<0.05$). The MST was 26 (95% CI 19-33) and 13 (95% CI 10.2-15.8) months for patients with grade III and IV gliomas, respectively. The survival curve of patients with grade III and IV gliomas is depicted in Figure 3. The log-rank test showed that patients with grade III glioma had a significantly longer survival time than grade IV glioma ($p<0.05$). Also, we analysed the survival curve of patients with each histological type; GBM was the most common pathology in the death group, and patients with anaplastic oligodendroglioma had the highest survival rate (32.462). The pathology difference was statistically significant ($p<0.05$) Figure 4.

Mortality was significantly correlated with age ($r=0.247$; $p<0.01$), seizure ($r=-0.200$; $p<0.05$), motor alteration ($r=0.189$; $p<0.05$), pathological type ($r=-0.252$; $p<0.01$), grade ($r=0.289$; $p<0.01$), radiation dose ($r=-0.298$; $p<0.01$) and R.T. delay duration ($r=-0.199$; 0.05) (Table 3).

Binary logistic regression analysis results showed that only R.T. delay significantly affected mortality ($p<0.05$).

All significant parameters at a univariate level were insignificant at a multivariate level ($p>0.05$) (Table 4). To understand the effect of R.T. delay duration, Cox Regression analysis was performed. Results showed that all significant parameters at the univariate level (Table 3) were insignificant at a multivariate level in the control of R.T. delay ($p>0.05$) (Table 5).

Table 1. Baseline characteristics and difference analysis results between mortality groups.

	Alife (n=17)	Dead (n=96)	Total (n=113)	p-value
Gender, n (%)				
Male	7 (41.2)	56 (58.3)	63 (55.8)	**0.147[a]**
Female	10 (58.8)	40 (41.7)	50 (44.2)	
Age, n (%)				
18-47 ages	8 (47.1)	24 (25.0)	32 (28.3)	
48-63 ages	8 (47.1)	36 (37.5)	44 (38.9)	**0.009[b]**
64 years and over	1 (5.9)	36 (37.5)	37 (32.7)	
Seizure, n (%)	9 (52.9)	26 (27.1)	35 (31.0)	**0.036[a]**
Vomit, n (%)	6 (35.3)	23 (24.0)	29 (25.7)	**0.241[a]**

Table 1. Continued.

Headache, n (%)	12 (70.6)	67 (69.8)	79 (69.9)	**0.597[a]**
Mental confusion, n (%)	6 (35.3)	49 (51.0)	55 (48.7)	**0.175[a]**
The motor alteration, n (%)	7 (41.2)	64 (66.7)	71 (62.8)	**0.043[a]**
The visual alteration, n (%)	6 (35.3)	32 (33.3)	38 (33.6)	**0.539[a]**
KPS, n (%)				
Under 70	4 (23.5)	39 (40.6)	43 (38.1)	**0.142[a]**
70 and over	13 (76.5)	57 (59.4)	70 (61.9)	
Tumour size, n (%)				
Under 4 cm	4 (28.6)	21 (30.9)	25 (30.5)	
4-6 cm	5 (35.7)	38 (55.9)	43 (52.4)	**0.215[b]**
Over 6 cm	5 (35.7)	9 (13.2)	14 (17.1)	
Tumour type, n (%)				
Unifocal	17 (100.0)	87 (90.6)	104 (92.0)	**0.217[a]**
Multicentric	-	9 (9.4)	9 (8.0)	
Surgical approach, n (%)				
No	-	4 (4.2)	4 (3.5)	
Biopsy	5 (29.4)	44 (45.8)	49 (43.4)	**0.249[b]**
STR	10 (58.8)	35 (36.5)	45 (39.8)	
GTR	2 (11.8)	13 (13.5)	15 (13.3)	
Pathology type, n (%)				
GBM	10 (58.8)	82 (85.4)	92 (81.4)	
Gliosarcoma	-	2 (2.1)	2 (1.8)	**0.007[b]**
Anaplastic oligodendroglioma	3 (17.6)	6 (6.3)	9 (8.0)	
Anaplastic astrocytoma	4 (23.5)	5 (5.2)	9 (8.0)	
Not conclusive	-	1 (1.0)	1 (0.9)	
Grade, n (%)				
III	7 (41.2)	11 (11.6)	18 (16.1)	**0.006[a]**
IV	10 (58.8)	84 (88.4)	94 (83.9)	
TMZ, n (%)				
No	1 (5.9)	15 (15.6)	16 (14.2)	
CCRT	3 (17.6)	18 (18.8)	21 (18.6)	**0.146[b]**
Adj.	-	12 (12.5)	12 (10.6)	
CCRT + Adj.	13 (76.5)	51 (53.1)	64 (56.6)	
R.T., n (%)				
No	-	10 (10.4)	10 (8.8)	**0.182[a]**
Yes	17 (100.0)	86 (89.6)	103 (91.2)	
Radiation dose, n (%)				
Extreme hypofractation-2500/5	-	27 (29.3)	27 (24.8)	
Hypofractation-4000/5-15	5 (29.4)	33 (35.9)	38 (34.9)	**0.002[b]**
Normal fract.-5.000-6.000/25-30	12 (70.6)	32 (34.8)	44 (40.4)	
Survival DX to death, mean ± S.D.	-	15.03±12.45	15.03±12.45	**<0.05**
RT delay duration, mean ± S.D.	3.87±3.60	2.20±1.43	2.47±2.03	**0.045[c]**
Recent status, n (%)				
Death	-	87 (90.6)	87 (77.0)	
Death before R.T.	-	8 (8.3)	8 (7.1)	**<0.05**
Death during R.T.	-	1 (1.0)	1 (0.9)	
Live	17 (100.0)	-	15.0)	

a. Fischer's Exact Test, b. Chi-Square Linear-by-Linear association, c. Mann Whitney U Test.

Table 2. Overall survival means and differences between patient baseline groups.

	Mean	Std. Deviation	P-value
Gender, n (%)			
Male	14.47	11.331	**0.976[a]**
Female	15.82	13.981	
Age, n (%)			
18-47 ages	19.68	17.934	
48-63 ages	12.60	8.491	**0.627[b]**
64 years and over	14.37	10.769	
KPS, n (%)			
Under 70	11.91	10.680	**0.013[a]**
70 and over	17.17	13.197	
Tumour size, n (%)			
Under 4 cm	14.14	10.123	
4-6 cm	17.23	14.130	**0.792[b]**
Over 6 cm	17.07	14.795	
Tumour type, n (%)			
Unifocal	15.67	12.783	**0.108[a]**
Multicentric	8.90	6.145	
Surgical approach, n (%)			
No	23.82	19.659	
Biopsy	13.70	13.118	**0.322[b]**
STR	16.01	12.466	
GTR	14.24	6.166	
Pathology type, n (%)			
GBM	13.77	10.184	
Gliosarcoma	7.17	1.358	
Anaplastic oligodendroglioma	32.46	26.923	**0.342[b]**
Anaplastic astrocytoma	18.52	11.779	
Not conclusive	12.31	.	
Grade, n (%)			
III	26.13	21.701	**0.071[a]**
IV	13.61	10.113	
TMZ, n (%)			
No	10.77	15.257	
CCRT	13.92	14.127	**0.003[b]**
Adj.	9.40	3.482	
CCRT + Adj.	18.01	11.677	
RT, n (%)			
No	4.61	6.236	**0.000[a]**
Yes	16.25	12.444	
Radiation dose, n (%)			
Extreme hypofractation-2500/5	10.47	8.565	
Hypofractation-4000/5-15	15.83	9.595	**0.013[b]**
Normal fact.-5.000-6.000/25-30	19.64	16.024	

a Mann Whitney U Test, b. Kruskal Wallis Test. SD: Standard Deviation.

Table 3. Spearman's rho correlation analysis between mortality and research parameters.

Mortality	Value of coefficient Rs	P-value
Gender	-0.123	**0.193**
Age	0.247**	**0.008**
Seizure	-0.200*	**0.034**
Vomit	-0.093	**0.328**
Headache	-0.006	**0.948**
Mental confusion	0.113	**0.235**
Motor alteration	0.189*	**0.045**
Visual alteration	-0.015	**0.876**
KPS	-0.126	**0.184**
Tumor size	-0.126	**0.259**
Tumor type	0.124	**0.191**
Surgical approach	-0.122	**0.199**
Pathological type	-0.252**	**0.007**
Grade	0.289**	**0.002**
TMZ	-0.152	**0.108**
RT	-0.131	**0.166**
Radiation dose	-0.298**	**0.002**
RT delay duration	-0.199*	**0.044**

$*p<0.05$ $**p<0.05$

Table 4. Binary logistic regression analysis for significantly correlated parameters with mortality

	B	S.E.	Wald	DF	p-value	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Age (Years)			2,135	2	0,344			
(48-63	-1,639	1,264	1,681	1	0,195	0,194	0,016	2,314
64 and above	-1,712	1,183	2,095	1	0,148	0,181	0,018	1,833
Seizure	0,761	0,688	1,223	1	0,269	2,141	0,555	8,252
Motor alteration	0,019	0,743	0,001	1	0,979	1,020	0,238	4,377
Surgical approach			3,528	3	0,317			
Surgical approach(Biopsy)	17,502	20311,593	0,000	1	0,999	3,992E7	0,000	.
Surgical approach(STR)	0,558	1,148	0,236	1	0,627	1,746	0,184	16,558
Surgical approach(GTR)	-,962	1,020	0,890	1	0,346	0,382	0,052	2,820
Pathological type			1,668	4	0,797			
Pathological type(GBM)	0,420	41007,123	0,000	1	1,000	1,522	0,000	.
Pathological type(Gliosarcoma)	20,165	49836,010	0,000	1	1,000	5,724E8	0,000	.
Pathological type(Anaplastic oligodendroglioma)	-,485	41007,123	0,000	1	1,000	0,616	0,000	.
Pathological type(Anaplastic astrocytoma)	-0,612	41007,123	0,000	1	1,000	0,542	0,000	.
Radiation dose			1,038	2	0,595			
Radiation dose(Hypofractation)	18,977	8131,061	0,000	1	0,998	1,745E8	0,000	.
Radiation dose(Normal fraction)	0,802	0,787	1,038	1	0,308	2,230	0,477	10,427
RT Delay	-0,332	0,149	4,971	1	0,026	0,718	0,536	0,961
Constant	3,054	41007,123	0,000	1	1,000	21,204		

-2 Log Likelihood: 61.872; Cox & Snell R2: 0.256; Nagelkerke R2: 0.432
B: Variables with positive coefficients, S.E.: Standard error, Wald: Coefficient test.
CI: confidence interval. Exp(B): Exponential value of B (hazard ratio). DF: Degrees of freedom.

Table 5. Cox Regression analysis results for mortality with R.T. delay time-dependent parameter

	B	S.E.	Wald	DF	p-value	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
Age			0,280	2	,869			
48-63	-0,155	0,329	0,221	1	0,638	0,857	0,450	1,632
64 and above	-0,131	0,295	0,196	1	0,658	0,878	0,493	1,564
Seizure	0,439	0,279	2,479	1	0,115	1,551	0,898	2,680
Motor alteration	0,070	0,306	0,052	1	0,820	1,072	0,589	1,953
Surgical approach			2,747	3	0,432			
Surgical approach(Biopsy)	0,765	0,770	0,986	1	0,321	2,149	0,475	9,727
Surgical approach(STR)	-0,250	0,374	0,447	1	0,504	0,779	0,374	1,622
Surgical approach(GTR)	-0,187	0,351	0,284	1	0,594	0,830	0,417	1,649
Pathological type			7,186	4	0,126			
Pathological type(GBM)	0,987	1,062	0,864	1	0,353	2,683	0,335	21,502
Pathological type(Gliosarcoma)	1,806	1,345	1,801	1	0,180	6,084	0,436	84,970
Pathological type(Anaplastic oligodendroglioma)	0,158	1,180	0,018	1	0,894	1,171	0,116	11,835
Pathological type(Anaplastic astrocytoma)	0,151	1,175	0,017	1	0,898	1,163	0,116	11,643
Radiation dose			4,332	2	0,115			
Radiation dose(Hypofractation)	0,433	0,348	1,543	1	0,214	1,541	0,779	3,050
Radiation dose(Normal fraction)	-0,256	0,300	0,727	1	0,394	0,774	0,430	1,394

-2 Log-Likelihood: 631.189; p>0.072

B: Variables with positive coefficients, S.E.: Standard error, Wald: Coefficient test.

CI: confidence interval. Exp(B): Exponential value of B (hazard ratio). DF: Degrees of freedom.

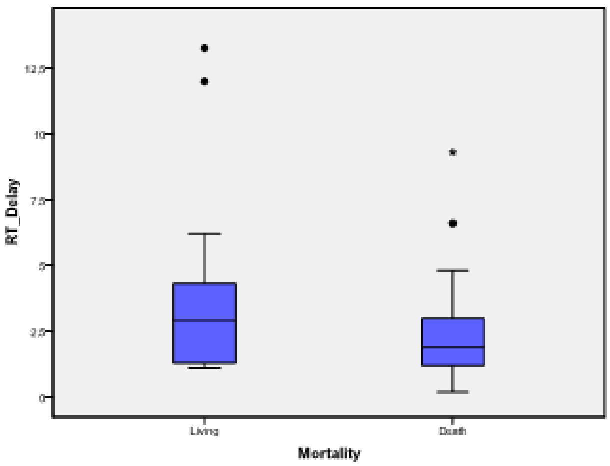

Figure 1. R.T. delay means and distributions between mortality Groups.

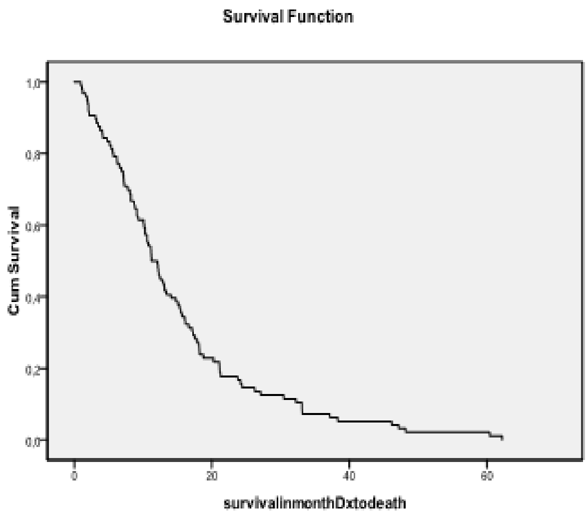

Figure 2. Survival curves for the entire study population throughout the research.

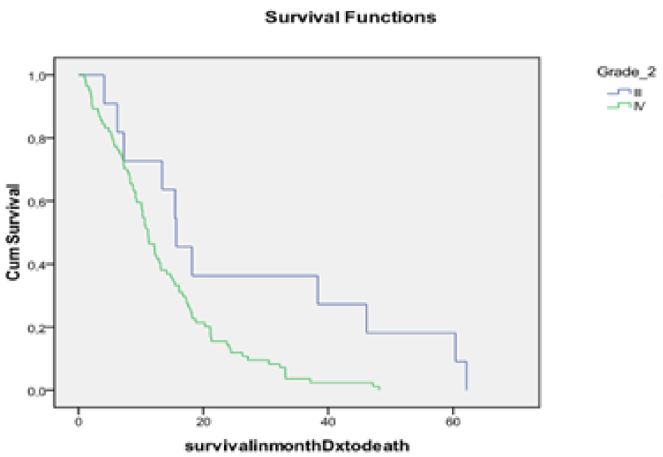

Figure 3. A comparison of survival times among patients with Grade III or IV glioma. Patients with Grade III glioma had a significantly longer survival time than Grade IV glioma (P<0.5)

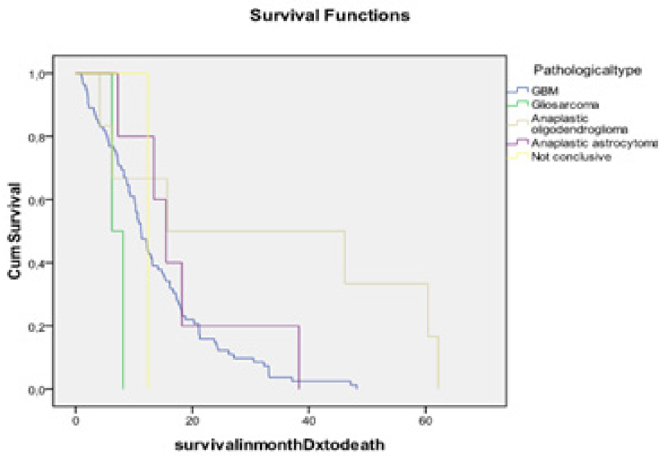

Figure 4. A comparison of survival times among tumour histology. Tumour histology did impact on survival of these patients (p<0.05)

DISCUSSION

This study, Determine the major clinical and pathological prognostic factors related to the outcome of HGG patients. The independent prognostic factors for HGG patients included age, KPS, the extent of surgical resection, histopathology, grade, radiotherapy status, and chemotherapy status. The patient's fundamental clinical traits and pathological parameters were combined for better clinical application. A particular patient's postoperative risk and prognosis could be estimated using the visual nomogram based on the seven clinicopathological factors. Accurate prognosis prediction facilitates efficient doctor-patient communication and provides extra direction for patients to receive individualised care. These seven parameters are extremely important as they are typical and frequently used pathological indices and clinical characteristics of patients.

Currently, important molecular markers like IDH status and 1p/19q status, as well as the WHO histological classification, are primarily used to assess the prognosis of glioma patients [16]. The IDH status may be a good indicator of prognosis in glioma patients. The majority of studies considered it a good prognostic factor[17]. Due to the difficulty of performing this kind of test in our region and the fact that most of our patients needed a molecular marker profile, we did not include a molecular marker parameter in our analysis.

There are many studies about clinical predictors for survival in patients with HGG. Most studies have reported that age, KPS, and tumour grade were independent important prognostic factors [18]. Data from the Glioma Outcome Project showed that resection rather than biopsy, age under 60, and KPS greater than 70 were all significantly correlated with better outcomes (Laws et al.) [19].

Barnholtz-Sloan et al . found that the global incidence of malignant CNS tumours was highest in male patients and adults older than 40, while benign tumours were more common in female patients[20]. In the Western Province of Saudi Arabia, the mean age at diagnosis of all CNS tumours in males and females was 38 years. In the United States, the mean age is 59 years. In the United Arab Emirates, the mean age is 33.4 years[21]. In our study, men predominated, and the mean age was 53.61 years, similar to the average in Western countries. Compared to other Middle Eastern studies, these findings are different.

Age is a reliable predictor of outcome and treatment response in all patients with Glioma, according to many studies [22, 23]; our study yielded comparable findings in this regard because the mean age of the dead group was higher than the living group, We had 37 patients who were 64 years old or older, and 36 of them had passed away. Glioma patients with advanced age have a particularly poor prognosis [24, 22]. According to clinical practice patterns, surgical resection, radiotherapy, and chemotherapy are used less frequently as people age increase [25,23]. The prognosis of glioma patients is also thought to be significantly influenced by a patient's age. To provide individualised treatment for glioma patients and improve outcomes, age should be taken into account.

According to our analysis, low KPS is a standalone risk factor for glioma patient mortality following treatment as well as for long-term survival. in patients were KPS<70 and ≥70. Overall survival was 11.9 and 17.17 months, respectively. This result aligns with numerous studies that demonstrate KPS is a promising prognostic indicator in glioma patients. For instance, it was found that patients with KPS > 70 lived longer than those with KPS 70[26].

In our population, those with seizures are significantly more likely to survive than those with motor alterations. However, there is no conclusive evidence currently linking these two clinical manifestations to prognostic factors.

The relationship between the glioma resection and the patient's prognosis remains unclear. Given the invasive nature of the tumour and the absence of distinct tumour borders, gross total resection is thought impossible [18, 27, 28]. According to Lacroix et al., resection of 98% or more of the tumour volume was associated with a significant survival benefit (median survival of 13 months), as opposed to resections of less than 98%. (median survival 8.8 months) [18]. According to McGirt et al., the median survival following maximal, near to total, and subtotal resection was 13, 11, and 8 months, respectively [28]; an investigation by Sanai et al. Compared to our data, most patients (n = 49, 43.4%) underwent biopsies, and those who underwent gross total resection were (n = 15, 13.3%). As a result, the median survival time for patients who underwent biopsies was 13.7 months and for those who underwent GTR was 14.24 months.

Glioma patients' treatment plans must include postoperative adjuvant radiotherapy [29]. External beam radiotherapy is usually recommended to start within 2–4 weeks following surgical resection or biopsy. Several studies revealed that radiotherapy significantly improves survival for glioma patients and is a significant prognostic factor in their prognosis [26, 27, 28]. The finding of our study further highlights the significance of this treatment modality that patients who did not receive radiation therapy in the most recent years (2015–2021) had even worse survival outcomes. Our data population included about 40.4% of patients who received normal fractionation, and the mean overall survival was 19.64 months, which was higher than the survival rates of the other two groups (p=0.013). Most of these patients were grade III patients with KPS levels greater than 70The average time it took for R.T. to start the following diagnosis, was 2.5 months, with a standard deviation of +/-2. Since our centre has a large waiting list for R.T., which may affect survival outcomes, we discovered that patients with longer R.T. delays lived longer. This is because these patients had good KPS and could wait for R.T. Multivariate analyses showed the impact of R.T. delay duration.

Chemotherapy also can significantly improve a patient's prognosis for HGG [30]. The National Comprehensive Cancer Network (NCCN) guidelines also suggest radiotherapy and chemotherapy as standard treatment modalities for HGG patients[31], which is also supported by our findings. In about 64% of patients, Temozolomide (TMZ) was given concurrently with radiotherapy (CCRT), then adjuvant TMZ; with a p-value of 0.003, this group had a higher overall survival rate than other lines.

The histopathology and tumour grade impact the natural history of HGG. It has been universally accepted that Grade IV glioma has a worse prognosis than Grade III glioma [32]. The previous studies have shown that the median survival time (MST) of patients with Grade III and Grade IV glioma, on average, were 2-5 years and <2 years, respectively [33, 21]. The MST of Grade III and Grade IV gliomas in Thailand was reported to be 20 and 9 months, respectively [34]. According to the second research published in Thailand, patients with HGG had an average survival duration of 20 months [35]. The current study also revealed considerable variations in patients with grades III and IV in terms of overall survival; the median overall survival for these patients was 15.7 months and 11.16 months, respectively. Additionally, the tumour grade was found to be a predictor of good survival in our analysis, Anaplastic oligodendroglioma grade III patients in this study had the highest survival rate (32 months), and this difference was statistically significant (p 0.05), which is similar to previous research.

For all patients, The median survival time is 12 months. The overall survival at 12,18, and 24 months were 27%, 17%, and 13%, respectively; compared to earlier reports, our overall survival rates were low, suggesting that this type of tumour requires more attention.

In conclusion, this retrospective analysis at a single institute demonstrates that patients with HGG had a short survival time. Based on a univariant analysis, the clinical predictors of patient survival were found. Age, KPS, surgical extent, pathological type and grade, radiation status, and chemotherapy status were independent prognostic factors for HGG patients. A better outcome was independently correlated with younger patients, a good performance status at diagnosis, the extent of resection, radiotherapy and chemotherapy.

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