SURVIVAL AND PROGNOSTIC FACTORS FOR GLIOBLASTOMA MULTIFORME: A RETROSPECTIVE SINGLE INSTITUTIONAL STUDY

Neurosurgery

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ABSTRACT

OBJECTIVE The purpose of the present retrospective analysis was to present and discuss clinical features (Patient specific and tumour specific) and various prognostic factors that predict the survival of the patients with Glioblastoma multiforme (GBM) and to compare the results with pre-existing literature. **MATERIALS & METHODS** A single institutional data of 221 patients of GBM was reviewed from 2014 to 2018. Data regarding patients' factor, tumour factor and survival analysis were collected and based on the above factor's survival outcome was calculated. **RESULTS** A total of 221 patients were analysed. 197 patients underwent resection and 24 patients underwent biopsy (Open or stereotactic). Patients had a mean age of 56.5 years at the time of diagnosis. Median survival in patients < 50 years was 9.21 months and > 50 years was 4.56 months. The overall survival was 4.27% for the entire cohort at the end of two years. **CONCLUSION** In patients with GBM overall survival and prognosis remains dismal. Standard treatment includes resection followed by chemo-radiation which has improved the overall survival outcome. However, the prognosis continues to remain poor.

KEYWORDS

Glioblastoma Multiforme, survival, prognostic factor, resection

INTRODUCTION

GBM is the most common primary CNS tumour across the world, with incidence of about 3 in 100000 newly diagnosed cases every year, accounting for > 51% of all Gliomas with approximately 13000 deaths in US every year^{1,2,3}. The term GBM was coined by Cushing's in nineteenth century.⁴

The exact aetiology of GBM is not known. There are multiple genetic disorders associated with GBM^{5,6,7,8}

Clinical manifestation depends on the size, location and the relation of the tumour to the adjoining structures. Clinically it can manifest as headaches, vomiting, with or without focal neurological deficits. Seizure is the presenting symptom in as many as 30%–50% of patients with high-grade glioma.^{9,10} Computerized tomography (CT) scan findings of GBM indicates hyperdense peripheral ring with hypodense central core with surrounding oedema (Fig 1).

The imaging modality of choice for GBM is a contrast-enhanced magnetic resonance imaging (MRI). GBM appear as a contrast-enhancing mass with a thick ring of enhancement with central necrosis (Fig 2). In butterfly gliomas there is trans-callosal spread of the tumour into the opposite hemisphere.¹¹ The median survival of patients after surgery and RT is less than one year. The overall survival at 2-years and 5-years is less than 10% and 2%, respectively^{12,13,14,15}

In the country like India where medical facilities are not easily accessible there could be delay in the diagnosis and majority of patients with GBM cannot afford post operative adjuvant treatment.

The purpose of the present retrospective analysis was to present and discuss clinical features (Patient specific and tumour specific) and various prognostic factors that predict the survival of the patients with GBM and to compare the results with literature.

Figure 1. NCCT head of a patient with GBM with surrounding edema

Fig 2. Pre-op and post-op contrast enhancing MRI showing extent of resection.

MATERIALS AND METHODS

A total of 221 patients of primary GBM who underwent intervention from 2014 to 2018 were included in the study. Case records of these cases were retrospectively analysed. 197 patients underwent craniotomy and maximum safe resection and 24 patients underwent biopsy. Detailed history of all patients was taken, clinical examination to look for pre-operative and post op neurological status, preoperative and post-operative imaging with intra-operative findings and biopsy report were taken. Clinical variables included patient-specific (age, gender, clinical features and performance status), tumour-specific (location, size, and extent of surgical resection / biopsy). In all the cases preoperative scan and immediate post operative scan was done to know the extent of resection.

RESULTS

All the patients underwent surgical intervention with an aim of maximum safe resection while preserving the eloquent areas of brain. If surgical resection was of high risk, then the patients underwent open or stereotactic biopsy for tissue diagnosis. Majority of the patients underwent gross total or maximum resection. Out of 221 cases, 197 patients underwent surgical resection and in 24 patients biopsy was done (Resection was not possible due to proximity to the vital areas or deep seated lesions).

The clinical characteristics of all the GBM cases are summarized in Table 1. The mean age for presentation was 56.5 years, with most patients presenting in their fifth decade of life. The mean age for resection group was 54.5 years and for biopsy group was 61.5 years. The male patients made up 55% of the cohort, with female patients accounting for the remaining 45%. The performance score like

Karnofsky performance score (KPS) was used to assess functional status of the patient at different time points. The majority of patients were independent with regard to their functional status, with a median KPS score of 70 (range 20–90). There was an overall improvement in the KPS Score four weeks post procedure in the surgical resection group (From 56.6% to 71.5%). However, only two patients showed improvement in the biopsy group (58.4 to 66.6%). The significant improvement in the KPS score had a significant impact on the patient survival. Headache and vomiting were the most common presenting symptoms in both the groups i.e., resection and biopsy 57% and 49.3%, respectively.

TABLE 1

TOTAL NUMBER OF PATIENTS (n=221)			
Characteristics	All Cases	Resection cases	Biopsy cases
1. No of cases	221	197(89.1%)	24(10.9%)
2. Mean age at diagnosis in yrs (Range)	56.5(23-79)	54.5(25-79)	61.5(23-76)
3. Sex			
Male	122(55.2%)	109(55.4%)	13(54.2%)
Female	99 (44.8%)	88(44.6%)	11(45.8%)
4. Median KPS at diagnosis			
Before Surgery	96(43.4%)	86(43.6%)	10(41.6%)
< 70	125(56.6%)	111(56.4%)	14(58.4%)
> 70	63(28.5%)	55 (27.9%)	08(33.3%)
After Surgery(04 weeks)			
< 70	158(71.5%)	142(72.1%)	16(66.6%)
> 70			
5 Symptoms at presentation			
Headache	126(57%)	112(56.9%)	14(58.3%)
Vomiting	109(49.3%)	97(49.2%)	12(50%)
Motor Weakness	70(31.7%)	62(31.5%)	15(62.5%)

Tumour-specific characteristics of GBM are summarized in Table 2. Right side was more commonly involved than the left. The most common lobes for GBM were Frontal / Frontoparietal (41.1%) followed by parietal (23.1%) and temporal lobes (16.8%). The tumours with size > 4 cm constituted the majority (77%) with < 4 cm constituting 23 % of the total number. Gross total resection of the tumour was done in 145 patients (65.61%) with maximum resection in 52 patients (23.5%). Biopsy was done in 24 (10.9%) patients.

TABLE 2

Characteristics	All Cases
1. Tumor Location	
Right side	117(52.9%)
Left side	89 (40.3%)
Midline	15 (6.8%)
2. Lobar Distribution	
Frontal/Frontoparietal	91(41.1%)
Parietal	51(23.1%)
Temporal	37 (16.8%)
Occipital	16 (7.3%)
Others	26 (11.7%)
3. Size	
> 4 cm	170(76.9%)
< 4 cm	51 (23.1%)
4. Extent of surgery	
Gross total resection	145(65.6%)
Maximum Resection	52 (23.5%)
Early Biopsy	24 (10.9%)

The survival duration was calculated from the date of diagnosis to the date of death or the date of last contact. The overall survival was 4.27% of the overall cohort at the end of two years. Median survival was maximum for 20-30 years of age group and decreases with increasing age (Graph 1).

Age, Gender, symptoms, tumour location, preoperative performance status (KPS), extent of surgical resection and post op adjuvant therapy had significant impact on survival.

The survival analysis is summarised in Table 3. Patients with age < 50

years and > 50 years had an average of 9.21 and 5.43 months survival respectively, with overall two years survival of 10.44 % and 4.56% respectively. Females had a better median survival and two years survival as compared to males (9.76 months, 10.25% Vs 8.45 months, 7.67%). There was no significant difference in the median survival with the clinical symptoms (7.14 months Vs 7.74 months), however the two years percentage survival was better in the patients who were asymptomatic with features of raised ICP (8.08% Vs 6.84 %). Patients had better median and two years survival on the left side of the lesion as compared to the right or at the midline lesion (9.73 months, 10.87% vs 8.85 months, 7.38% vs 4.43 months, 0%). Patients with preoperative KPS Score > 70 had median and two years survival better than patients with pre operative KPS < 70 respectively (9.36 months, 10.34% vs 6.73 months, 5.27%). The patient who underwent resection had significant survival benefits than the patients who underwent biopsy (9.62 months, 11.84% vs 6.45 months, 5.38%). Patients with post op adjuvant therapy had better survival benefits (11.75 months, 11.94% vs 5.62 months, 6.28%).

TABLE 3

TOTAL NUMBER OF PATIENTS (N=221)			
VARIABLE	Number of patients	Median survival (Months)	Two years survival (%)
1 Age			
< 50 Years	60 (27.1%)	9.21	10.44
> 50 Years	161 (72.9%)	5.43	4.56
2 Gender			
Male	122(55.2%)	8.45	7.67
Female	99(44.8%)	9.76	10.25
3 Headache & vomiting			
Yes	109 (49.3%)	7.14	6.84
No	112(50.7%)	7.74	8.08
4 Tumor Location			
Right	117(52.9%)	8.85	7.38
Left	89 (40.3%)	9.73	10.87
Midline (Genu)	15 (6.8%)	4.43	0
5 KPS			
< 70	96(43.4%)	6.73	5.27
> 70	125(56.6%)	9.36	10.34
6 Extent of surgery			
Resection	197(89.1%)	9.62	11.84
Biopsy	24 (10.9%)	6.45	5.38
7 Use of chemo-radiation			
a. YES	158(71.5%)	11.75	11.94
b. NO	63 (28.5%)	5.62	6.28

DISCUSSION

The prognosis of GBM has not changed in the recent past. Treatment of the choice is surgery followed by the adjuvant therapy¹⁶. Complete resection is not possible due to infiltration of the tumour in the surrounding brain parenchyma and its location near the eloquent areas or in the deep seated lesions. Hence, the adjuvant therapy plays an important role,¹⁷ however in spite of the adjuvant therapy overall survival remains poor.

In GBM, various factors like clinical status, tumour factors, KPS score, extent of resection and post op adjuvant therapy effects the outcome. Hence, it is important to analyse each of the factors and their impact on the outcome.

The median age of our patient was 56.5 years which was almost the same as seen in stupps study¹⁸. However, in other studies the median age was found to be 64 years^{19, 20} which was higher in our study. The

higher percentage of Primary GBM in men compared with women has been reported in some literature, with male to female ratio ranging from 1.0 to 1.9. This is consistent with what was found in our study where there was a male preponderance and male to female ratio was 1.2. The performance status (KPS) showed significant improvement post resection and post biopsy. Neurological symptoms varied depending on the location of tumour and size. Various studies showed that headache is the most common initial presenting symptom and is associated with elevated intracranial pressure with one-third of patients with GBM present with nausea, vomiting and headache and the eloquent area tumor causing motor weakness.^{23,24,25} These results were found to be consistent with our study. In our study, tumour location was more on right side with majority of them located in frontal or frontoparietal lobe followed by parietal and temporal lobe. These results were also consistent with similar results found in other studies^{26,27,28}. 66 % of the patients had gross total resection with 23 % patient with maximum safe resection and 11% patient underwent early biopsy.

The median survival (Months) and two years survival percentage for age groups < 50 years and >50 years when collaborated with other studies showed 10.44 % survival in <50 yrs age group which was less than the survival in other studies in the same group²⁹. In our study the female gender had better survival rates. Not much literature is presently available regarding impact of gender on survival in patients with GBM. Our study revealed a correlation between female sex and improved survival rates in patients with GBM. In our study the patients with left sided tumour had better survival rate. Many studies findings show that higher KPS at presentation correlates with improved outcome^{30,31} which was consistent with our study, showing KPS > 70 had a better survival rate (10.34%) linked to the young age of presentation. The overall survival rate was better in resection group than biopsy group, with an overall two years survival of 11.84% in resection group. Many studies showed gross total resection and maximum safe resection of the tumour had more impact on overall survival than the tumor decompression^{32,33}.

The patients who underwent post op adjuvant therapy had a better outcome with overall median survival of 11.75 months and two years survival of 11.94% as compared to 5.62 months and 6.28% who were not subjected to adjuvant therapy.

Surgery is the principal component of standard care. The surgery can help in reducing the tumour volume resulting in improvement of the neurological status. The extent of surgical resection depends on the site and eloquence of the brain area involved. GBM is locally invasive tumour that cannot be cure completely by surgery with relapse occurring in approximately 80% of cases usually within 2-3 cm of the margin of the original lesion³⁴.

CONCLUSION

GBS are highly malignant tumor which are difficult to eradicate and carry a poor prognosis. In our study the factors such as age, gender, preoperative performance status and extent of resection followed by adjuvant treatment had a significant impact on the survival outcome which was comparable with other studies.

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