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EVALUATION OF RESPONSE TO HYPO-FRACTIONATED RADIATION IN ELDERLY PATIENTS OF GLIOBLASTOMA MULTIFORME IN OUR POPULATION

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Abstract:

Objectives: To evaluate the response of elderly patients diagnosed with glioblastoma Multiforme (GBM) to hypo-fractionated radiation therapy in our population.
Materials and Methods: After ethical approval, 49 patients were enrolled and underwent surgical resection followed by early postoperative MRI to assess residual disease (GTR/STR). Hypofractionated radiotherapy was started within 4–6 weeks with concurrent temozolomide, and patients were monitored weekly, followed by clinical and MRI evaluation at 3 and 6 months to assess tumor response and recurrence. Data were collected via a structured questionnaire and analyzed using SPSS Version 25.
Results: The mean age was 69.61 ± 5.79 years, with most patients aged 60–70 years, and the mean interval to radiotherapy was 5.46 ± 1.02 weeks. Most participants were male (69.4%), and subtotal resection was more common (59.2%). Tumor response showed 18.4% complete and 34.7% partial responses, with recurrence in 30.6%. No significant association was found between tumor response and age, gender, ECOG status, or extent of resection ($p>0.05$), while residual disease showed a significant association ($p=0.02$).
Conclusion: It was concluded that Hypofractionated radiotherapy with concurrent temozolomide is a feasible and effective option for elderly GBM patients, showing good short-term tumor response and disease control. Residual disease significantly affected outcomes, while other factors showed no significant association. Overall, it provides a practical alternative to conventional schedules with better compliance, though larger long-term studies are needed.

Keywords: Glioblastoma Multiforme, hypo-fractionated radiation, ECOG status.

INTRODUCTION:

The most prevalent and aggressive primary malignant brain tumor in adults is glioblastoma multiforme (GBM), which makes up around 15% of all intracranial neoplasms.(1) It has a dismal prognosis, widespread penetration into neighboring brain tissue, and fast proliferation.(2) Despite improvements in chemotherapy, radiation, and surgical methods, the median survival time for GBM patients is still roughly 12 to 15 months. Due to longer life expectancies, GBM is becoming more common in the elderly, who bear a disproportionately heavy load. (3)
However, older patients frequently exhibit decreased tolerance to harsh therapy, more comorbidities, and a worse pe rformance status treatment

related toxicities in this age group are often linked to standard treatment, which consists of maximal safe surgical resection follow ed by six weeks of conventionally fractionated radiation with concurrent and adjuvant temozolomide.
This has led to the investigation of different therapeutic strategies that strike a compromise between tolerance and efficacy.
For older GBM patients, hypo-
fractionated radiation therapy has shown promise since it administers more doses each fraction over a shorter total treatment durati on.(4) Numerous studies have shown that hypo-
fractionated and conventional radiation have similar survival rates, with the added advantages of less treatment load and better pat ient compliance. This approach, when combined with temozolomide, may provide a practical and efficient therapy alternative that is suited to the requirements of aged patients.(5) Patients older than 40 years of age and 15 years of age can follow a hypo-fractionated regimen with TMZ for three weeks.(6) Management is made more difficult in low- and middle-income nations by issues such delayed presentation, restricted access to sophisticated care, and budgetary limitations. In order to develop evidence-based, context-appropriate treatment procedures that enhance both survival and quality of life, it is crucial to assess how our local elderly GBM population responds to hypo-fractionated radiation.
In order to optimize care for this vulnerable and frequently underrepresented patient group, this study attempts to assess the response of older individuals with glioblastoma multiforme (GBM) to hypo-fractionated radiation therapy in our community. The current study will show how hypo-fractionated radiation regimens can effectively treat older patients and those with poor performance status, resulting in fewer hospital visits and lower overall costs. Furthermore, this strategy might lessen the workload for radiotherapy departments, enabling more effective resource distribution for patients with better prognoses.

Objective: To evaluate the response of elderly patients diagnosed with glioblastoma Multiforme (GBM) to hypo-fractionated radiation therapy in our population.

MATERIALS AND METHODS:

Study Design: Cross sectional study
Study setting: Department of Radiation Oncology, Combined Military Hospital, Rawalpindi.
Duration of the study: Duration of the study was 6 month (from June 2025 to Dec 2025).
Sampling Technique: Non-probability Consecutive sampling
SAMPLE SIZE: The sample size for this study was calculated using the WHO Sample Size Calculator version 1.1. With a confidence level of 95% and an anticipated population proportion of 0.1 (10%), the required sample size is estimated to be 49 patients.

Selection criteria:

Inclusion criteria:
- Patients with histologically confirmed diagnosis of glioblastoma multiforme.
- Both genders.
- Patients having age more than 60 years (ECOG PS 0,1,2,3)
- Patients having ability to undergo MRI evaluation.

Exclusion criteria:
- Patients with prior cranial radiotherapy.
- Patients with other active malignancies.
- Biopsy not done and histopathology is not available.
- Patients who have other multiple co-morbids (cardiac and pulmonary issues).

Methods:
Following approval from the ethical committees of CMH and CPSP, patients meeting the selection criteria were enrolled in the study after obtaining written informed consent. A total of 49 patients were included. All patients underwent surgical resection performed by a neurosurgeon, with decisions based on tumor location, disease extent, ECOG performance status, patient age, and comorbidities. Postoperative contrast-enhanced MRI (CEMRI) of the brain was performed within 24–48 hours to assess residual disease. Persistent contrast enhancement was considered residual tumor; Gross Total Resection (GTR) was defined as the absence of contrast enhancement, while persistent enhancement was categorized as Subtotal Resection (STR).
Hypo-fractionated radiotherapy was initiated within 4–6 weeks after surgery. Patients were positioned supine with arms at their sides, and immobilization was achieved using a 5- or 9-point thermoplastic mask during CT simulation on the Aquilion LB CT Simulator. Treatment planning was performed using Eclipse Version 16.1, and postoperative CEMRI was co-registered with planning CT to delineate target volumes. The enhancing residual tumor and surgical cavity were contoured with a 2 cm margin and appropriate anatomical cropping, while organs at risk, including the brainstem, eyes, lenses, and optic nerves, were also contoured. Concurrent chemotherapy included temozolomide (75 mg/m² daily) during radiotherapy along with dexamethasone (6–12 mg daily), a proton pump inhibitor, and antiepileptic drugs as required. Dexamethasone was gradually tapered weekly after radiotherapy.
Patients were clinically evaluated weekly during radiotherapy with physical examination and laboratory investigations including complete blood counts, serum electrolytes, renal function tests, and liver function tests. Three weeks after radiotherapy, patients were assessed for adjuvant temozolomide therapy. Follow-up included clinical evaluation and MRI brain at 3 and 6 months. Tumor

response was assessed on MRI, and disease recurrence was defined as progressive enhancement of residual tumor or appearance of new lesions on follow-up imaging.

RESULTS: The mean age of the study participants was 69.61 ± 5.79 years, with the majority belonging to the 60–70 years age group (71.4%), followed by 71–80 years (24.5%) and those older than 80 years (4.1%). The mean time interval between surgery and initiation of radiotherapy was 5.46 ± 1.02 weeks. Regarding laboratory parameters, the mean hemoglobin level was 11.61 ± 1.15 g/dL, total leukocyte count was 7.48 ± 0.93 ×10⁹/L, and platelet count was 261.57 ± 11.7 ×10⁹/L. The mean serum creatinine level was 0.9 ± 0.2 mg/dL, while the mean alanine aminotransferase (ALT) level was 32 ± 10 U/L (Table 1). The majority of participants were male (69.4%), while females constituted 30.6% of the study population. Regarding the extent of resection, 40.8% of patients underwent gross total resection (GTR), whereas 59.2% had subtotal resection (STR). In terms of ECOG performance status, 44.9% of patients were in the 0–1 category, 38.8% in category 2, and 16.3% in category 3. Residual disease was present in 57.1% of patients and absent in 42.9%. Assessment of tumor response revealed that 18.4% achieved complete response, 34.7% had partial response, 24.5% demonstrated stable disease, and 22.4% showed progressive disease. Furthermore, recurrence was observed in 30.6% of patients, while 69.4% had no evidence of recurrence (Table 2). There was no statistically significant association between extent of resection and tumor response (p = 0.64). Among patients who underwent gross total resection (GTR), 25.0% achieved complete response, 35.0% had partial response, 25.0% showed stable disease, and 15.0% developed progressive disease. In comparison, among those with subtotal resection (STR), 13.8% achieved complete response, 34.5% had partial response, 24.1% had stable disease, and 27.6% showed progressive disease (Table 3). There was no statistically significant association between age groups and tumor response (p = 0.23). Among patients aged 60–70 years, 22.9% achieved complete response, 31.4% partial response, 28.6% had stable disease, and 17.1% showed progressive disease, while varied distributions were observed in older age groups. Similarly, gender did not show a significant association with tumor response, with comparable response patterns observed in both males and females. ECOG performance status was also not significantly associated with tumor response (p = 0.38), although patients with poorer performance status (ECOG 3) demonstrated a higher proportion of progressive disease. In contrast, the presence of residual disease showed a statistically significant association with tumor response (p = 0.02), with patients having no residual disease demonstrating higher rates of stable disease and lower rates of progression compared to those with residual disease (Table 4).

Table 1: Baseline Characteristics and Laboratory Parameters of Study Participants (n = 49)

Variables	
Age (Years)	69.61± 5.79
Age Groups	
60-70 Years	35(71.4%)
71-80 Years	12(24.5%)
>80 Years	2(4.1%)
Time interval between surgery and radiotherapy (weeks)	5.46±1.02
Laboratory values	
Hemoglobin (g/dL)	11.61±1.15
Total Leukocyte Count (×10⁹/L)	7.48±0.93
Platelet Count (×10⁹/L)	261.57±11.7
Serum Creatinine (mg/dL)	0.9 ± 0.2
ALT (U/L)	32 ± 10

Table 2: Clinical and Treatment Characteristics of Study Participants (n = 49)

Variables	
Gender	
Male	34(69.4%)
Female	158(30.6%)
Extent of Resection	
Gross Total Resection (GTR)	20(40.8%)
Subtotal Resection (STR)	29(59.2%)
ECOG performance status	
0–1	22(44.9%)

2	19(38.8%)
3	8(16.3%)
Residual disease	
YES	28(57.1%)
NO	21 42.9%)
Tumor response	
Complete Response	9(18.4%)
Partial Response	17(34.7%)
Stable Disease	12(24.5%)
Progressive Disease	11(22.4%)
Recurrence status	
YES	15(30.6%)
NO	34(69.4%)

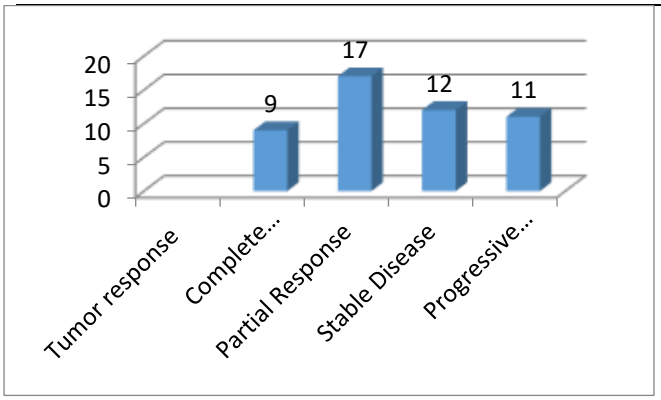

Fig 1: Frequency of patients on the basis of Tumor response.

Table 3: Association of Tumor Response with Extent of Resection (n = 49)

Variables	**Tumor Response**				p-value
Extent of Resection	Complete Response	Partial Response	Stable Disease	Progressive Disease	
GTR	5(25.0%)	7(35.0%)	5(25.0%)	3(15.0%)	0.64
STR	4(13.8%)	10(34.5%)	7(24.1%)	8(27.6%)	

Table 4: Stratification of Tumor Response with Demographic and Clinical Variables (n = 49)

Variables	**Tumor Response**				p-value
	Complete Response	Partial Response	Stable Disease	Progressive Disease	
Age Groups	8(22.9%)	11(31.4%)	10(28.6%)	6(17.1%)	
60-70 Years	0(0.0%)	6(50.0%)	2(16.7%)	4(33.3%)	0.23
71-80 Years	1(50.0%)	0(0.0%)	0(0.0%)	1(50.0%)	
>80 Years	9(18.4%)	17(34.7%)	12(24.5%)	11(22.4%)	
Gender					
Male	7(20.6%)	12(35.3%)	7(20.6%)	8(23.5%)	
Female	2(13.3%)	5(33.3%)	5(33.3%)	3(20.0%)	
ECOG performance status					
0–1	6(27.3%)	8(36.4%)	5(22.7%)	3(13.6%)	0.38
2	2(10.5%)	7(36.8%)	6(31.6%)	4(21.1%)	
3	1(12.5%)	2(25.0%)	1(12.5%)	4(50.0%)	
Residual disease					
YES	4(14.3%)	12(42.9%)	3(10.7%)	9(32.1%)	0.02
NO	5(23.8%)	5(23.8%)	9(42.9%)	2(9.5%)	

Discussion: Due to decreased physiological reserve, increased treatment-related toxicity, and frequent comorbidities, glioblastoma multiforme (GBM) continues to be the most aggressive primary brain tumor in adults, with particularly dismal prognosis in the older population. In this study, we assessed how older GBM patients responded to concurrent temozolomide and hypofractionated radiation, with an emphasis on treatment response, recurrence patterns, and related clinical variables. The main objective of the present study was to evaluate the response of elderly patients diagnosed with glioblastoma Multiforme (GBM) to hypo-fractionated radiation therapy in our population. In our study, a minority of patients showed stable or progressing disease, whereas a respectable percentage of patients experienced complete or partial remission after hypofractionated radiation. These results corroborate the findings of earlier trials that showed hypofractionated schedules were not inferior to standard fractionation in a subset of patients, suggesting that shorter radiation regimens can still offer significant tumor control in older individuals. In this age group, hypofractionation is very helpful since it shortens treatment duration, increases compliance, and lowers hospital stays without appreciably sacrificing effectiveness. In a study it was stated that Response assessment on MRI at 3 months post-treatment showed 18(25.7%) patients had regression, 20(28.6%) were stable, and 22(31.4%) had a progressive primary tumor. Radiotherapy remains a key component in the management of glioblastoma multiforme (GBM); however, conventional fractionation schedules are often prolonged and may result in early treatment discontinuation.(7, 8) In contrast, hypofractionated radiotherapy has been introduced as a shorter treatment approach, and retrospective evidence suggests that it provides comparable survival outcomes in elderly patients with GBM. Several studies have supported its effectiveness: Roa et al.(9) demonstrated that a 40 Gy in 15 fractions regimen provided comparable survival to conventional 60 Gy schedules in elderly GBM patients, while maintaining better tolerability. Similarly, the Nordic trial (Malmström et al.) reported that hypofractionated radiotherapy and temozolomide-based regimens achieved survival outcomes equivalent to standard therapy in patients older than 60 years, particularly in those with poor performance status. Perry et al.(10) further showed that the addition of temozolomide to short-course radiotherapy significantly improved overall survival compared to radiotherapy alone in elderly and frail patients. Collectively, these studies support the use of hypofractionated radiotherapy as an effective treatment approach with acceptable response rates in the elderly GBM population.

The mean age of our study population was in the late sixties, which is consistent with the known higher incidence of GBM in older age groups. Most patients had a performance status of ECOG 0–2, indicating that selected elderly patients were still functionally suitable for active treatment. This age cut-off has been a matter of debate, particularly because the median age at diagnosis of glioblastoma multiforme (GBM) is approximately 65 years across different populations.(11-13) In addition, several studies have demonstrated a progressive decline in treatment outcomes with increasing age (14), indicating that standard therapeutic regimens may be less appropriate or less well tolerated in the elderly population.

Similar studies have shown that careful patient selection based on performance status plays a crucial role in determining tolerance and outcomes of combined chemoradiotherapy in elderly GBM patients. Although patients with gross complete resection tended to have better outcomes, we found no statistically significant correlation between the extent of surgical resection and tumor response. Given that maximal cytoreduction lowers tumor burden and increases the benefit of adjuvant therapy, this trend makes biological sense. However, tumor location and surgical risk frequently restrict the practicality of full resection in older patients, which may account for the lack of high significance.

Poorer tumor response was significantly correlated with the prevalence of residual disease. Patients without residual disease showed improved disease control and reduced rates of progression, underscoring the significance of maximal safe resection of older patients wherever possible. This is consistent with previous research highlighting residual tumor burden as a critical predictor of GBM outcomes.

Age groups, gender, and ECOG performance status did not significantly correlate with tumor response. This could be the result of the older cohort's restricted variability and comparatively small sample size. Nonetheless, there was a tendency for patients with higher ECOG scores to respond worse, which is in line with the widespread knowledge that treatment tolerance and survival outcomes are influenced by functional status.

Even following combined modality treatment, a significant percentage of patients experienced recurrence during follow-up, demonstrating the aggressive nature of GBM. Despite this, a considerable proportion of patients experienced partial response or disease stabilization, suggesting that concurrent temozolomide and hypofractionated radiation therapy can offer satisfactory short-term disease control in this high-risk group.

CONCLUSION: Hypofractionated radiotherapy, combined with concurrent temozolomide, appears to be a feasible and effective treatment approach for elderly patients with glioblastoma multiforme. In this study, a considerable proportion of patients achieved complete or partial tumor response, while acceptable disease control was observed during short-term follow-up. Residual disease emerged as a significant factor influencing treatment response, whereas age, gender, ECOG performance status, and extent of resection showed no statistically significant association. Overall, hypofractionated radiotherapy offers a practical alternative to conventional prolonged schedules, improving treatment compliance without compromising efficacy in a high-risk elderly population. Further large-scale studies with longer follow-up are recommended to better define long-term survival benefits and optimize treatment strategies.

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