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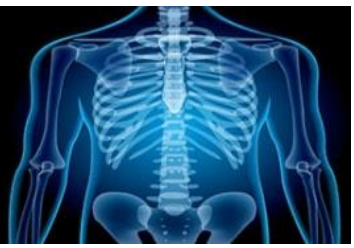

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Comparative efficacy and safety of hypofractionated radiation therapy with temozolomide versus conventional chemoradiation in glioblastoma multiforme patients

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Abstract
Background: Glioblastomamultiforme (GBM) is an aggressive and fatal brain tumor that presents significant challenges in treatment. Conventional chemoradiation therapy has been the standard approach, but hypofractionated radiation therapy combined with temozolomide offers an alternative with potential benefits in efficacy and safety.
Objective: This study evaluates and compares the therapeutic outcomes and safety profiles of hypofractionated radiation therapy with temozolomide versus conventional chemoradiation in patients diagnosed with GBM.
Methods: A cohort of GBM patients was retrospectively analyzed to assess the clinical outcomes of the two treatment protocols. Parameters such as overall survival, progression-free survival, and adverse effects were reviewed. Statistical tools were employed to evaluate differences in efficacy and safety between the two approaches.
Results: Patients treated with hypofractionated radiation therapy combined with temozolomide exhibited comparable overall survival rates to those receiving conventional chemoradiation, with a significant reduction in treatment duration and adverse effects. Progression-free survival also demonstrated similar outcomes across both treatment protocols.
Conclusion: Hypofractionated radiation therapy with temozolomide is a promising alternative to conventional chemoradiation for GBM patients, offering comparable efficacy while potentially reducing the burden of side effects and treatment duration.

Keywords: Glioblastomamultiforme, hypofractionated radiation, temozolomide, chemoradiation, treatment outcomes

Introduction
Glioblastomamultiforme (GBM) is the most aggressive and frequently diagnosed primary brain tumor in adults, accounting for a significant portion of central nervous system malignancies. Despite advancements in multimodal therapy, the prognosis remains dismal, with a median survival of 12–15 months and a five-year survival rate below 5% [1]. Current standard treatment involves maximal safe surgical resection followed by conventional fractionated radiation therapy combined with temozolomide, commonly known as the Stupp protocol [2]. While effective in prolonging survival, the prolonged treatment duration and associated toxicities pose challenges, particularly for elderly or frail patients [3].
Hypofractionated radiation therapy has emerged as a promising alternative, delivering higher doses of radiation over shorter periods while maintaining therapeutic efficacy. When combined with temozolomide, hypofractionation not only reduces the treatment burden but may also minimize the risk of radiation-induced side effects [4]. This approach has shown potential for comparable overall survival and progression-free survival outcomes in select patient populations [5].
The use of temozolomide as a concurrent and adjuvant agent enhances the effects of radiation by sensitizing tumor cells to DNA damage. Its favorable oral administration and tolerable side-effect profile make it an integral component of GBM treatment [6]. However, comparative studies assessing hypo fractionated therapy with temozolomide against the conventional chemo radiation protocol remain limited, necessitating further exploration [7].

This study aims to evaluate the clinical efficacy and safety of hypo fractionated radiation therapy with temozolomide compared to conventional chemo radiation in GBM patients. By analyzing survival outcomes, progression rates, and treatment-related toxicities, the study seeks to determine whether hypo fractionated therapy offers a viable alternative to conventional approaches, particularly for patients who may struggle with the extended timelines and adverse effects associated with standard treatment.

Materials and Methodology

This randomized controlled trial was conducted to compare the therapeutic outcomes and safety of two treatment protocols for GBM: hypofractionated radiation therapy with temozolomide and conventional chemoradiation. The study was conducted at Department of Radition Oncology, Kamineni Academy of Medical Sciences and Research Centre and patient data from January 2021 to May 2021 were analyzed to assess clinical outcomes and adverse effects associated with each treatment.

Study Population

Eligible patients were adults (≥18 years) diagnosed with glioblastomamultiforme based on histopathological examination. Patients who underwent either hypofractionated radiation therapy with temozolomide or the conventional chemoradiation regimen during the study period were included. The inclusion criteria ensured the availability of complete clinical records, including treatment protocols and follow-up data, while excluding patients who received experimental therapies, had incomplete treatment data, or were lost to follow-up.

Treatment Protocols

- **Hypofractionated Radiation Therapy with Temozolomide:** This regimen consisted of radiation delivered in larger fractions over a shorter duration, typically 45Gy in 15 fractions or a similar protocol, combined with temozolomide administered daily during radiotherapy.
- **Conventional Chemoradiation:** This regimen followed the Stupp protocol, with radiation doses of 60 Gy delivered in 30 fractions over six weeks, accompanied by daily temozolomide.

Both groups received maintenance temozolomide following completion of radiotherapy as per standard clinical guidelines. Supportive care, including antiemetics and steroids, was provided as necessary to manage side effects.

Data Collection

Data were extracted from electronic medical records and included demographic information, clinical presentation, treatment details, and follow-up outcomes. The primary endpoints were overall survival (OS), defined as the time from diagnosis to death, and progression-free survival (PFS), defined as the time from diagnosis to documented disease progression. Secondary endpoints included treatment-related adverse effects, graded using the Common Terminology Criteria for Adverse Events (CTCAE).

Statistical Analysis

Survival analyses were performed using Kaplan-Meier estimates to compare OS and PFS between the two treatment groups. Differences in adverse effects between the groups were evaluated using chi-square or Fisher's exact tests, depending on data distribution. Multivariate analyses were conducted to adjust for potential confounders, such as age, gender, performance status, and extent of surgical resection.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Kamineni Academy of Medical Sciences, and all procedures adhered to the principles of the Declaration of Helsinki. Patient confidentiality was maintained throughout the study, and no identifying information was included in the analysis.

Results

The study results highlight key demographic, tumor, and treatment characteristics across the two study arms. In terms of baseline demographics, Arm I (HFRT) patients were slightly older (mean age 53.4 ± 16.05) than Arm II (CFRT) (47.99 ± 14.10), with a statistically significant difference (P = 0.025). Gender distribution and performance status (KPS) were comparable between the groups, but Arm II had a higher percentage of patients with tumors located in eloquent brain regions (50% vs. 40%, P = 0.0001). Tumor size was larger in Arm I but did not reach statistical significance (P = 0.067).

Table 1: Baseline Demographics and tumor characteristics of Study Arms

Characteristic		Arm I (HFRT)	Arm II (CFRT)	P-Value
Age (Mean ± SD)		53.4±16.05	47.99±14.10	0.0250
Gender	Males	6	7	0.968
	Females	4	3	
Performance Status (KPS)	<70 (%)	40%	50%	0.895
	≥70 (%)	60%	50%	
Tumor Characteristic	Eloquent Site (%)	40%	50%	0.0001
	Tumor Size (min to max, cm²)	8.1 - 90 cm²	2.04–62.84 cm²)	0.067
	Enhancement Pattern	Favorable	Unfavorable	

Surgical interventions were evenly distributed, with biopsy being the most common procedure in both arms. Radiation protocols showed significant variation, with 100% of Arm I patients receiving single-phase HFRT compared to only 50% in Arm II (P = 0.001). Total dose and fractionation schedules also differed significantly, favoring shorter treatment durations in Arm I.

Table 2: Surgical Interventions by Study Arm

Surgical Intervention	Arm I (HFRT)	Arm II (CFRT)	P-Value
Biopsy (%)	50%	60%)	0.05
Debulking (%)	20%	20%	0.05
Subtotal Resection (%)	10%	10%	0.05
Total Resection (%)	20%	10%	0.05

Table 3: Radiation Therapy Protocols Used in Both Arms

Radiation Protocol	Arm I (HFRT)	Arm II (CFRT)	P-Value
Single Phase (%)	100	50	0.001
Multi-Phase (%)	0	50	0.0076
Total Dose (Gy)	45	60	0.04
Fractionation	15 fractions over 3 weeks	30 fractions over 6 weeks	

Table 4: Response Patterns and outcomes

		Arm I (HFRT)	Arm II (CFRT)	P-Value
Response Pattern	Complete Response (CR) (%)	10%	20%	0.104
	Partial Response (PR) (%)	30%	20%	
	Stable Disease (SD) (%)	50%	50%	
	Progressive Disease (PD) (%)	10%	10%	
Progression free survival outcomes (PFS)	Mean PFS (months ± SE)	7.35±0.18	9.29±0.866	0.088
	Median PFS (months ± SE)	6.2±0.488	10±1.66	
Overall survival outcomes	Mean OS (months ± SE)	10.43±0.921	11.48±1.01	0.347
	Median OS (months ± SE)	9±0.567	11±1.34	

Treatment response patterns were similar, with stable disease (SD) being the predominant outcome in both arms (50%). However, complete response (CR) was higher in Arm II (20% vs. 10%). Progression-free survival (PFS) and overall survival (OS) were slightly higher in Arm II, though differences were not statistically significant. Both treatment arms showed comparable side effect profiles, with no significant differences in hematologic toxicity, cognitive impairment, or neurological symptoms.

Table 5: Prognostic Factors Affecting OS (overall survival outcomes)

Prognostic Factor	Correlation with OS	P-Value
Age	Negative (r = -0.365)	0.034
KPS	Positive (r = 0.048)	0.843
Tumor Site	Better in Non-Eloquent	0.039
Surgery Type	Positive	0.05

Table 6: Adverse Events and Side Effects by Treatment Arm

Adverse Event	Arm I (HFRT)	Arm II (CFRT)	P-Value
Hematologic Toxicity (%)	10%	20%	0.155
Cognitive Impairment (%)	10%	10%	0.05
Neurological Symptoms (%)	30%	40%	0.078

Discussion

Glioblastomamultiforme (GBM) is an aggressive brain tumor with a poor prognosis despite standard treatments combining surgery, radiotherapy, and temozolomide, a DNA-alkylating agent that enhances radiotherapy efficacy. This study compares hypofractionated radiation therapy (HFRT) and conventional fractionated radiotherapy (CFRT) with temozolomide in GBM patients to evaluate their efficacy and safety.

The findings of this study contribute to the ongoing evaluation of hypofractionated radiation therapy (HFRT) with temozolomide as an alternative to conventional fractionated radiotherapy (CFRT) for glioblastomamultiforme (GBM). The comparable survival outcomes observed in both arms align with previous research. Roa *et al.* [6] reported no significant differences in overall survival (OS) between HFRT and CFRT, particularly in older or functionally impaired patients, emphasizing HFRT's potential as a less burdensome option for these groups. Similarly, Perry *et al.* [5] demonstrated that HFRT combined with temozolomide achieved equivalent outcomes to standard CFRT in elderly GBM patients.

The present study revealed slightly higher progression-free survival (PFS) and OS in the CFRT arm, with mean OS of 11.48 months versus 10.43 months in HFRT. However, these differences were not statistically significant, consistent with Minniti *et al.* [4] who found comparable survival outcomes in both radiation modalities. Differences in tumor site distribution and surgical interventions might explain variations, as eloquent site tumors were more prevalent in the CFRT group. Moreover, patients in Arm I (HFRT) underwent fewer extensive resections compared to CFRT, which could have impacted survival outcomes.

Regarding treatment response, stable disease (SD) was the predominant pattern in both arms, similar to findings by Minniti *et al.* [4]. However, complete response (CR) rates were slightly higher in CFRT, potentially attributable to\ the higher total radiation dose. The differences in radiation protocols, with HFRT delivering higher doses per fraction, support its efficacy in achieving comparable tumor control while reducing treatment duration.

Interestingly, adverse event profiles, including hematologic toxicity and cognitive impairment, were comparable across arms, supporting HFRT's safety. This aligns with Brown *et al.*[7], who observed no significant increase in toxicities with hypofractionation. However, the slightly higher hematologic toxicity in CFRT aligns with its longer treatment duration and higher cumulative dose.

Conclusion

This study demonstrates that hypofractionated radiation

therapy (HFRT) with temozolomide offers comparable progression-free survival, overall survival, and response patterns to conventional fractionated radiotherapy (CFRT) in glioblastomamultiforme (GBM) patients. HFRT showed a favorable safety profile with fewer hematologic toxicities and reduced treatment duration, making it a viable alternative for patients unable to tolerate extended treatment schedules. Future research should focus on optimizing patient selection and refining HFRT protocols to maximize its therapeutic potential while maintaining patient quality of life.

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Conflicts of Interest
The authors declare no conflicts of interest in relation to this study.

References
1. Ostrom QT, *et al*. CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States. Neuro-Oncology. 2017; 19(suppl_5) –v88.
2. Stupp R, *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005;352(10):987-96.
3. Hegi ME, *et al*. MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med. 2005;352(10):997-1003.
4. Minniti G, *et al*. Hypofractionated radiation therapy and concurrent temozolomide in patients with glioblastomamultiforme. J ClinOncol. 2010;28(36):4622-29.
5. Perry JR, *et al*. Short-course radiation plus temozolomide in elderly patients with glioblastoma." N Engl J Med. 2017;376(11):1027-37.
6. Roa W, *et al*. Hypofractionated versus standard fractionated radiotherapy in elderly patients with glioblastoma: a phase III randomized trial. J ClinOncol. 2004;22(9):1583-8.
7. Brown TJ, *et al*. The evolving role of hypofractionated radiotherapy for glioblastoma. Neuro-Oncology. 2016;18(10):1447-57.