Journal on Oncology

www.journalononcology.org

Short Commentary

Open Access, Volume 2

Survival Benefit of Re-Irradiating recurrent glioma Patients with VMAT Technique

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Abstract

Patients who have been treated with re irradiation for recurrent glioma reported survival benefits. Limited data are available for the outcomes after fractionated re-irradiation of 45Gy. This study aims to investigate whether re-irradiation of recurrent glioma with 45Gy dose can increase the overall survival of patients. A retrospective analysis of 35 patients re-irradiated for high-grade glioma recurrence between 2015 and 2020 was performed. All included patients met the following criteria: a) histopathological confirmation of primary brain cancer at initial diagnosis; b) a history of initial primary radiation; c) histological and/or imaging modality confirmation of recurrence. Outcome metrics included overall survival, prognostic factors for survival, and treatment-related toxicity. After the end of re-irradiation the median overall survival was 11 months (95% confidence interval, 7-14 months). From the patients evaluated in the current study after the end of re-irradiation the progression free survival was 6 months (3.8-8 months) while after the end of first radiation was 13 months (8-17.9 months). Our findings suggest that re-irradiation might prolong survival rates.

Introduction

Patients who have been treated with re irradiation for recurrent glioma reported survival benefits [1,2]. Gliomas of Grade III and IV, based on the WHO classification, are generally treated according to the Stupp protocol [3]. The procedure of brain tumors classification is completed since June 2016 with the additional use of molecular testing [4]. After a total or subtotal resection a primary radiation dose of 60Gy in 30 fractions is indicated. For patients with glioblastoma of WHO Grade IV confirmed from molecular testing, a chemotherapy with Temozolomide is indicated simultaneously to radiotherapy while for maintenance a Temozolomide of 12 cycles is scheduled. Maintenance is suggested to be scheduled with Temozolomide of 6 cycles for patients with tumor of Grade III.

The median survival for patients with glioblastoma after following a primary radio chemotherapy is 12 months. For tumors of Grade III the prognosis depends on molecular and histopathological characteristics. After progression the optimal treatment for a pretreated glioma is yet unclear. Local re-irradiation has been established as a feasible option for recurrent glioma patients. Although re-irradiation is accompanied with the concern about the risks of toxicity and radio necrosis risk, many studies have shown that it is a safe option and may effectively increase the overall survival in selected patients [2]. However, the radiation dose and its fractionation it is still uncertain and is the subject of several ongoing trials. The fractionation of radiation dose might affect the effectiveness of re-irradiation in survival and quality of patient's life.

Manuscript Information: *Received: Sep 20, 2022; Accepted: Oct 19, 2022; Published: Oct 27, 2022*

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Citation: *Theodorou M, Peratikou A, Andreopoulos D, Polycarpou I. Survival Benefit of Re-Irradiating recurrent glioma Patients with VMAT Technique. J Oncology. 2022; 2(2): 1058.*

Methodology

Between 2012 and 2020, 35 patients with recurrent gliomas were re-irradiated with VMAT (volumetric modulated arc therapy). Nine patients were diagnosed with astrocytoma and twenty six patients with glioblastoma multiforme. Patient demographics are presented in Table 1. For first treatment patients received subtotal or total resection with adjuvant radiotherapy of 60Gy and 30 days in VMAT technique with simultaneous chemotherapy (Temozolomide). After recurrence, resection has been repeated followed by re-irradiation of 45Gy in 15 fractions (BED biological effective dose 56Gy) in VMAT technique. The median interval between the first radiotherapy and the re-irradiation was 6 months.

Table 1: Patient Demographics.

Characteristics	Number
Total Number of Patients	35
Sex	
Male	
Female	
Age	
Median 49 (range: 22-74)	
≤ 49	18
> 49	17
1st radiation dose	60 Gy
2nd radiation dose	45 Gy

For all the patients the following outcomes were assessed: 1) overall survival; 2) progression-free survival. Survival was evaluated using Kaplan-Meier analysis. Furthermore, the Karnofsky Performance Scale score (Yates et. al. 1980) was also used as another predictor of survival. Karnofsky Performance Scale score quantifies the patient abilities by measuring its level of activity and support needed. All statistical analyses were carried out using SPSS software. Overall Survival (OS) was defined as the time from the first radiation treatment or the re-irradiation to death.

Results

Figure 1 shows the progression free survival for patients after first radiation and after re-irradiation. After the end of re-irradiation the progression free survival was 6 months (3.8-8 months) while after the end of first radiation was 13 months (8-17.9 months). The overall survival after combining radiation with re-irradiation is also presented in Figure 1. A combination of radiation and re-irradiation achieved a median overall survival of 42 months (95% confidence interval, 29-54 months). Figure 2 shows the patient survival after the end of re-irradiation. After the end of re-irradiation the median overall survival was 11 months (95% confidence interval, 7-14 months).

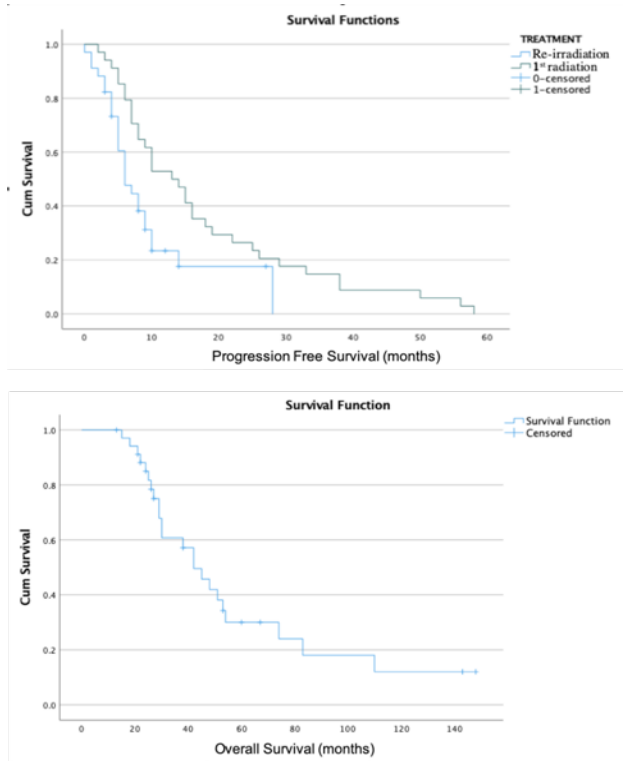

Figure 1: Kaplan-Meier curves showing progression free survival for patients after 1st radiation and after 2nd radiation (re-irradiation) and the overall survival after combining radiation and re-irradiation.

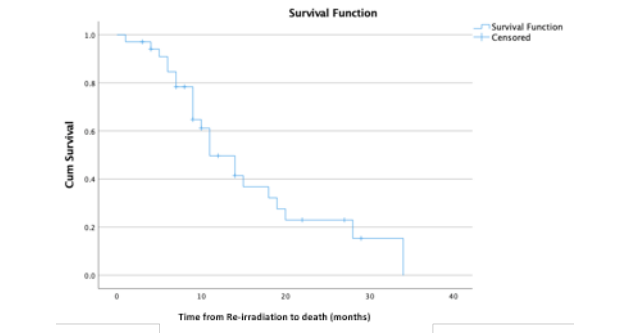

Figure 2: Kaplan-Meier curve showing survival from re-irradiation.

Discussion

Recurrent Glioblastoma WHO IV is associated with a median overall survival of less than a year [5] and the majority of patients have profound tumor-related symptoms. The results of this study suggest that re-irradiation may prolong the overall survival. This is in agreement with the results found by Fetcko et al. [6] who reported in a systematic review that in high-grade gliomas a median overall survival is 20.19 months (9-65 months) and progression free survival is 5.42 months (3-16 months). The small number of sample used in the current study might limit the evidence of our findings.

Conclusion

Re-irradiation of recurrent glioma patients with VMAT technique might prolong survival rates.

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