Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/21157
DOI URL: http://dx.doi.org/10.21474/IJAR01/21157

RESEARCH ARTICLE

GLIOBLASTOMA AND HYPOFRACTIONATED RADIOTHERAPY: A SUITABLE OPTION FOR VULNERABLE PATIENTS

S. Smiti, R. Laraichi, A. Lachgar, K. Nouni, H.El Kacemi, T. Kebdani and K. Hassouni
1. Radiation Therapy Department, National Institute of Cancer, University Mohamed 5, Rabat, Morocco.

Manuscript Info

Manuscript History
Received: 12 April 2025
Final Accepted: 15 May 2025
Published: June 2025

Key words:-
Glioblastoma, Hypo Fractionated Regimen, Overall Survival, Progression-Free Survival

Abstract

Glioblastoma is the most common primary brain tumor. This disease is caracterised by poor diagnosis. The survival depends on multiples criteria as age and general conditions. The treatment is based on surgery or radiation therapy . For eldery patients or patient with low performance status « PS » <2, hypofractionated regimen was proposed. Two hypofractionated radiotherapy regimens were compared. The objective of the study is to analysize the efficiency of this therapeutic regimen. This study shows that hypofractionated treatment produces results in terms of global survival and progression-free survival, which are not statically significant compared with the normofractionated regimen. The hypofractionated regimen is a therapeutic alternative for patients not suitable for normofractionated treatment.

"© 2025 by the Author(s). Published by IJAR under CC BY 4.0. Unrestricted use allowed with credit to the author."

Introduction:-

Glioblastoma is the most common primary brain tumor. The median age of incidence is 65 years. Its prognosis is poor, with an average survival estimated at 9 to 15 months, which depends on the patient's general condition, age, and certain molecular biology data. However, overall survival remains limited.

The objective of this study is to analyze the effectiveness of the hypofractionated regimen in subjects aged 65 years or older , or in cases of impaired performance status, that is, greater than or equal to 2, in order to extract guidelines to be applied in clinical routine.

Materials and Methods:-

This study was carried out in the radiotherapy department of the national Institute of Cancer in Rabat,for the period between January 1st, 2023 and December 31th, 2023, over a period of one year, having included patients followed for glioblastoma treated by radiotherapy according to a hypofractionated regimen. Two protocols were proposed, either 40.05 Gy in 15 fractions or 25 Gy in 5 fractions. The external radiation therapy was delivred without chemotherapy. And were excluded patients treated for other brain tumors.

Results:-

The primary endpoint of the study was overall survival, secondary endpoints were progression-free survival. In 2023, two hypofractionated radiotherapy regimens were compared in elderly people or those with low PS. Inclusion criteria were age greater than 65 years or performance status greater than or equal to 2. Patients were assigned to two groups during the study, one group receiving radiotherapy at a dose of 40.05 Gy in 15 fractions of 2.67 Gy per

Corresponding Author:- S. Smiti
Address:- Radiation Therapy Department, National Institute of Cancer, University Mohamed 5, Rabat, Morocco.

fraction, five fractions per week, and one group receiving radiotherapy with a total dose of 25 Gy in 5 fractions of 5 Gy, five fractions per week.

The number of patients included in the study was 13 patients, who were put on a hypofractionated regimen against 42 on a normofractionated regimen and with concomitant chemotherapy +/- adjuvant. 58% of patients were over 65 years. As for general condition, 63 % of patients had a low performance status less than 2, highlighted in table 1.
A total of 13 patients were included in the study. Ten patients received 40.05 Gy in 15 fractions, compared to 3 with the 25 Gy in 5 fractions protocol.

The study finds that the median overall survival time was 6.6 months (95% CI: 6.58; 6.62) for patients who received 40.05 Gy in 15 fractions versus 6.3 months(95% CI: 6.27; 6.32) for patients who received 25 Gy in 5 fractions without statistically significant difference (p = 0.93). Progression-free survival times were 4.5 and 3.6 months, respectively, with no statistically significant difference (p = 0.68), and no significant difference between the different sub-groups according to performance status. On the other hand, for patients who received the normo-fractionated regimen with associated chemotherapy, the median overall survival time was 6.92 months and for progression-free survival 5.2 months with a statistically significant difference (p= 0.011), highlighted in figure 1.

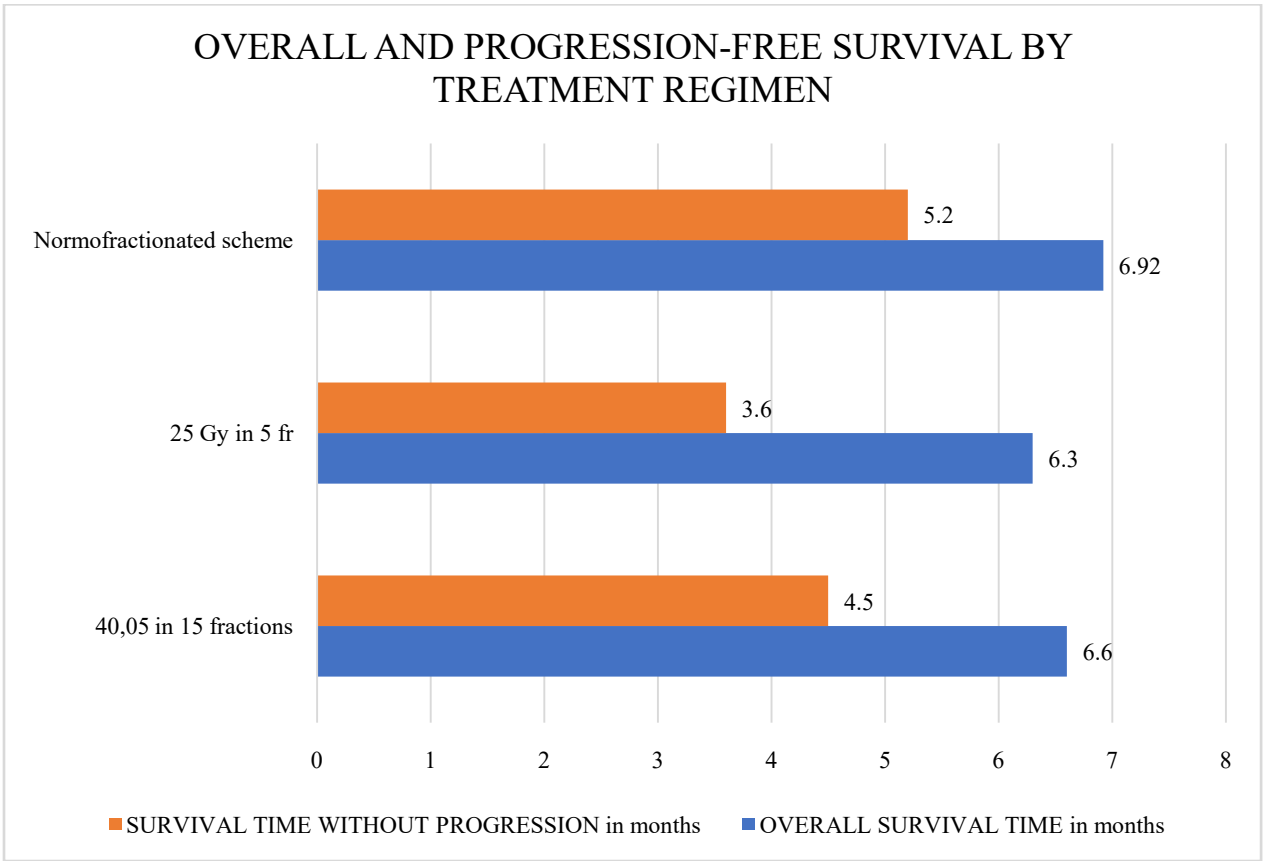

Figure 1:- Overall survive and progression-free survival by regimen of radiation therapy normo and hypo fractionated.

Table 1:- Characteristics of study patients.

Age	
More than 65 years old	58%
Less than 65 years old	42%
Gender	
Male	68%
Female	32%
Status Performance	
<2	63%
>2	37%
Regimen	
Hypo fractionated 40.05 Gy in 15 fractions	10
Hypo fractionated 25 Gy in 5 fractions	3
Concomitant Chemotherapy	None

Discussion:-

Elderly patients are often less tolerant of high doses of radiotherapy and chemotherapy than younger patients [1]. Hypofractionated radiotherapy offers a number of advantages, not least the rapidity of its therapeutic effect [2,3]. Reducing the number of sessions also makes it possible to limit the constraints associated with travel, which may improve patients' quality of life. However, moderate hypofractionation may lead to an increase in late toxicities, as the dose per fraction increases [4,5]. A study by Roa et al. in 2004 compared hypofractionated radiotherapy with normofractionated radiotherapy [6]. The primary objective of the study was overall survival, while secondary objectives included the proportion of patients alive at 6 months, quality of life and use of corticosteroids. The inclusion criteria were patients over 60 years, with a Karnofsky index greater than 50%; this index is presented in Table 2, while a comparison with the ECOG performance score is shown in Table 3.

Table 2:- Karnosky Performance status [7]

KARNOFSKY PERFORMANCE STATUS SCALE
KPS scale

Able to carry on normal activity and to work; no special care needed.	**100**	**Normal no complaints; no evidence of disease.**
	90	**Able to carry on normal activity; minor signs or symptoms of disease.**
	80	**Normal activity with effort; some signs or symptoms of disease.**
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	**70**	**Cares for self; unable to carry on normal activity or to do active work.**
	60	**Requires occasional assistance, but is able to care for most of his personal needs.**
	50	**Requires considerable assistance and frequent medical care.**
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	**40**	**Disabled; requires special care and assistance.**
	30	**Severely disabled; hospital admission is indicated although death not imminent.**
	20	**Very sick; hospital admission necessary; active supportive treatment necessary.**
	10	**Moribund; fatal processes progressing rapidly.**
	0	**Dead**

Comparing the ECOG Performance Status and the Karnofsky Performance Status Scales

The ECOG (Eastern Cooperative Oncology Group) and Karnofsky performance scales are two tools commonly used to assess a patient's level of functional impairment, compare the effectiveness of treatments and estimate prognosis. The Karnofsky index, ranging from 100 to 0, was introduced in 1949 in a medical textbook, while the first elements of the ECOG scale appeared in the scientific literature in 1960. There are several correspondences between the two scales, one of the most widely used of which is shown in the table below.

Table 3:- The table below displays one commonly used comparison. [8].

ECOG PERFORMANCE STATUS	KARNOFSKY PERFORMANCE STATUS
0—Fully active, able to carry on all pre-disease performance without restriction	100—Normal, no complaints; no evidence of disease 90—Able to carry on normal activity; minor signs or symptoms of disease
1—Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80—Normal activity with effort, some signs or symptoms of disease 70—Cares for self but unable to carry on normal activity or to do active work
2—Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours	60—Requires occasional assistance but is able to care for most of personal needs 50—Requires considerable assistance and frequent medical care
3—Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours	40—Disabled; requires special care and assistance 30—Severely disabled; hospitalization is indicated although death not imminent
4—Completely disabled; cannot carry on any selfcare; totally confined to bed or chair	20—Very ill; hospitalization and active supportive care necessary 10—Moribund
5—Dead	0—Dead

In the study, patients received either normofractionated radiotherapy of 60 Gy in 30 fractions of 2 Gy, or hypofractionated radiotherapy of 40.05 Gy in 15 fractions of 2.67 Gy, with five sessions per week in both groups. The results showed that among the 100 patients included, overall survival was 5.1 months in the normofractionated group compared with 5.6 months in the hypofractionated group, with no significant difference between the two arms ($p = 0.57$).

With regard to secondary endpoints, no significant difference was observed in terms of 6-month survival or quality of life. However, patients in the hypofractionated group had a reduced need for corticosteroid therapy ($p = 0.02$). In 2017, another study evaluated two hypofractionated radiotherapy protocols in patients aged over 65 [9].
The analysis was carried out, using data from a phase III trial conducted by the International Atomic Energy Agency (IAEA). This was a multicentre, international, randomised, prospective, non-inferiority trial [10], carried out after the data have been used. Inclusion criteria included an age greater than 65 years and a Karnofsky index greater than 50%.

The patients included in the IAEA study were divided into two groups: the first received radiotherapy of 40.05 Gy in 15 fractions of 2.67 Gy, with five sessions per week; the second received a protocol of 25 Gy in five fractions of 5 Gy, also with five weekly sessions, concentrated over one week of treatment. The primary objective of the study was overall survival, while secondary endpoints included progression-free survival, quality of life and toxicity.

In addition, the 2017 study by Perry et al. compared hypofractionated radiotherapy alone with hypofractionated radiotherapy plus temozolomide concurrently and then adjuvantly in a phase III trial in patients over 65 years of age with good general condition [11].
Patients were randomly assigned to one of two treatment arms: the first received exclusive hypofractionated radiotherapy at a dose of 40.05 Gy, administered in 15 fractions over five sessions per week; the second received radiochemotherapy using the same radiotherapy regimen, combined with concomitant chemotherapy with temozolomide at a dose of 75 mg/m²/day, followed by 12 adjuvant cycles at a dose of 150-200 mg/m².

The primary endpoint was overall survival, while secondary endpoints included progression-free survival, treatment tolerance and quality of life. The results showed a significant improvement in overall survival and progression-free survival in the radiochemotherapy group: 9.3 months versus 7.6 months for overall survival ($p<0.001$), and 5.3 months versus 3.9 months for progression-free survival ($p<0.001$). These differences were statistically significant in favour of the protocol combining chemotherapy with hypofractionated radiotherapy.
In our study, patients received hypofractionated radiotherapy without concomitant or adjuvant chemotherapy. The median overall survival was 6.6 months for patients treated with 40.05 Gy in 15 fractions, compared with 6.3 months for those treated with 25 Gy in 5 fractions. There was no statistically significant difference in the probability of survival at 6 months ($p = 0.93$). Similarly, the median progression-free survival was 4.5 and 3.6 months respectively, with no significant difference ($p = 0.68$).

In comparison, a normofractionated regimen combined with chemotherapy resulted in a median overall survival of 6.92 months and a progression-free survival of 5.2 months, with a statistically significant difference ($p = 0.011$).
Our results are therefore consistent with the literature, confirming the value of the hypofractionated regimen, while highlighting the benefit of combining it with chemotherapy.

Conclusion:-

Hypofractionated radiotherapy can be proposed as a therapeutic strategy for patients aged over 65 or in poor general condition, particularly when prolonged treatment or combined chemotherapy is not an option. In our study, the two hypofractionated treatment protocols showed similar results, with no statistically significant difference between them. However, a significant difference was observed when they were compared with the normofractionated regimen combined with concomitant and adjuvant chemotherapy.

These results give clinicians the possibility of adapting the choice of hypofractionated protocol according to the patient's profile, with a view to optimising survival and quality of life. Nevertheless, this study also raises important questions about the place of chemotherapy, and opens the way to its possible integration, even in patients considered fragile.

References:-

[1] Laperriere N, Weller M, Stupp R, Perry JR, Brandes AA, Wick W, et al. Optimal management of elderly patients with glioblastoma. Cancer Treat Rev 2013;39:350–7,http://dx.doi.org/10.1016/j.ctrv.2012.05.008.
[2] Cihoric N, Crowe S, Eychmüller S, Aebersold DM, Ghadjar P. Clinically significant bleeding in incurable cancer patients: effectiveness of hemostatic radiotherapy. Radiat Oncol 2012;7:132,http://dx.doi.org/10.1186/1748-717X-7-132
[3] Bourgier C, Charissoux M, Boisselier P, Ducteil A, Azria D. What type of hypofractionated radiotherapy of primary tumors in palliative care? Cancer Radiother 2015;19:442–5,http://dx.doi.org/10.1016/j.canrad.2015.06.009.
[4] Donato V, Valeriani M, Zurlo A. Short course radiation therapy for elderly cancer patients. Evidence from the literature review. Crit Rev Oncol Hematol 2003;45:305–11.
[5] Nahum AE. The radiobiology of hypofractionation. Clin Oncol (R Coll Radiol) 2015;27:260–9,http://dx.doi.org/10.1016/j.clon.2015.02.001.
[6] Roa W, Brasher PMA, Bauman G, Anthes M, Bruera E, Chan A, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized clinical trial. J Clin Oncol 2004;22:1583–8,http://dx.doi.org/10.1200/JCO.2004.06.082.
[7] Karnofsky et al. Cancer. 1948;1(4):634-56

[9] Guedes de Castro D, Matiello J, Roa W, Ghosh S, Kepka L, Kumar N, et al. Survival outcomes with short-course radiation therapy in elderly patients with glioblastoma: data from a randomized phase 3 trial. Int J Radiat Oncol Biol Phys 2017;98:931–8,http://dx.doi.org/10.1016/j.ijrobp.2017.03.037.
[10] Roa W, Kepka L, Kumar N, Sinaika V, Matiello J, Lomidze D, et al. International atomic energy agency randomized phase III study of radiation therapy in elderly and/or frail patients with newly diagnosed glioblastoma multiforme. J Clin Oncol 2015;33:4145–50,http://dx.doi.org/10.1200/JCO.2015.62.6606.
[11] Perry JR, Laperriere N, O'Callaghan CJ, Brandes AA, Menten J, Phillips C, et al. Short-course radiation plus temozolomide in elderly patients with glioblastoma. N Engl J Med 2017;376:1027–37, ,http://dx.doi.org/10.1056/NEJMoa1611977.
Webographie
[8] https://ecog-acrin.org/resources/ecog-performance-status/