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Assessment of Health-Related Quality of Life of Metastatic Brain Tumor Patients with Radiation-Induced Fatigue

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Abstract: Brain metastases (BMs) affect about 20% of cancer patients. Advances in treatments like radiation therapy (RT) have improved patient survival, but radiation-induced fatigue remains a significant issue, impacting the health-related quality of life (HRQOL) of patients. The present study aims to evaluate HRQOL in metastatic brain tumor patients experiencing RT-induced fatigue. A prospective observational study was conducted with 22 brain metastatic patients evaluated weekly during radiation therapy. The HRQOL was assessed by using Functional Assessment of Cancer Therapy- Fatigue (FACT-F) questionnaires. FACT-F has a noticeable impact on physical and emotional well-being, particularly during treatment, its effect on social well-being appears negligible. However, functional well-being is notably affected, with a significant proportion experiencing moderate to severe effects after treatment. The findings revealed that the Functional well-being of the majority of the patients was affected more when compared with other domains. Understanding these dynamics can aid in tailoring interventions to address specific aspects of well-being and improve the overall quality of life for brain metastasis patients. Radiation-induced fatigue had a great impact on the HRQOL of BM patients receiving radiation therapy.

Keywords: Brain Metastases, FACT-F, Health-Related Quality of Life, Fatigue

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Introduction

Metastatic brain tumors are characterized by the spread of cancer cells from primary tumors to the brain. Brain metastases incidence is increasing,

affecting 20 to 40% of all cancer patients (Soffietti *et al.*, 2002). The management of metastatic brain tumors often includes radiation therapy. The

primary goal of radiation therapy is to shrink tumors, alleviate symptoms, and improve overall survival rates and it plays an essential role in the treatment of metastatic tumors by utilizing high-energy radiation to target and destroy cancer cells. Radiation therapy commonly induces debilitating side effects, one of the most commonly reported side effects is radiation-induced fatigue (RIF). RIF is a specific type of fatigue experienced by individuals undergoing radiation therapy as part of cancer treatment which presents as an overwhelming sense of tiredness and exhaustion, persisting beyond the completion of treatment (Jones *et al.*, 2016). Nearly, 80% of cancer patients undergoing radiation experience fatigue to some degree (Mitchell *et al.*, 2014). The mechanisms underlying RIF are multifactorial, involving biological, psychological, and social factors. Radiation triggers inflammatory responses, disrupts neuroendocrine pathways, and induces oxidative stress, contributing to the development and persistence of fatigue (Hofman *et al.*, 2007). RIF not only impacts patients' daily functioning but also diminishes their health-related quality of life (HRQOL). Studies have demonstrated that RIF can persist for months to years post-treatment, affecting patients' physical, emotional, and social functioning (Huang *et al.*, 2020). The integration of HRQOL assessments in clinical practice is increasingly recognized as essential for optimizing supportive care interventions and enhancing patient-centered outcomes. Hence, we proposed to assess the health-related quality of life (HRQOL) of metastatic brain tumor patients with radiation-induced fatigue using the Functional Assessment of Cancer Therapy (FACT-F) questionnaire.

Materials and Methods

This prospective observational study was conducted at the Department of Radiation Oncology at Sri Ramachandra Institute of Higher Education and Research (Deemed to be University) from October 2023 to March 2024. Patients who came to regular visits to receive the radiation therapy after the completion of surgery and chemotherapy were consecutively selected.

The study was conducted among 22 patients as per the inclusion criteria after getting approval from the Institutional Ethics Committee (Reference number: CSP/23/APR/127/337). The study included BM patients undergoing radiation therapy at Sri Ramachandra Medical Centre and patients having symptoms of fatigue during the course of radiation therapy. Patients unwilling to give written informed consent, patients who do not have a history of histologically confirmed metastatic brain tumor, and patients who were unable to answer questionnaires were excluded from this study. The informed consent was obtained from the recruited patients. The demographic details were collected from the patient i.e., name, age, sex, chief complaints, past medical and medication history, physical examination, treatment details, and radiation therapy details. Then the subjects were allocated to complete the FACT-F questionnaire.

FACT-F (Version 4) Questionnaire

The FACT-F (Version 4) contains 5 domains which include physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB), and fatigue sub-scale (FS). The recall period used is "over the last week." The scaled items focus on physical sensations; embarrassment; interference with activities at home; clothing selection; impact on social activities; difficulty participating in a sport; preventing work or school attendance; causing a problem with relationships among close friends, relatives, or a partner; sexual difficulties; and impact of treatment on life and lifestyle. The level of fatigue is measured on a four-point Likert scale (0 = not at all fatigued to 4 = very much fatigued).

Statistical analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp). To describe the data descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables and the mean and Standard deviation were used for

Table 1: Demographic characteristics of the patients

Patient Demographics	Number	Percentage (%)
Age		
18-20	2	9.1
21-30	2	9.1
31-40	1	4.5
41-50	4	18.2
51-60	7	31.8
61-70	5	22.7
71-80	1	4.5
Gender		
Male	14	63.6
Female	8	36.4
Marital Status		
Married	17	77.3
Unmarried	4	18.2
Widowed	1	4.5
Socioeconomic Status		
Upper Class	2	9.1
Upper middle	10	45.5
Lower middle	7	31.8
Upper lower	2	9.1
Lower	1	4.5
Education status		
Literate	14	63.6
Illiterate	8	36.4
Co-morbid conditions		
DM	5	22.7
DM & HTN	1	4.5
Seizure	2	9.1
Bronchial Asthma	1	4.5
DM & HTN & CAD	1	4.5
DM & HTN & Hypothyroidism	1	4.5
RT Techniques		
IMRT	5	22.7
3D-CRT	12	54.6
2D	5	22.7

continuous variables. To find the significant difference between the bivariate samples in Paired groups, the Friedmann test was used. In all the above statistical tools the probability value <0.05 was considered statistically significant.

Results

Table 1 represents the baseline characteristics of patients. The majority of the patients were in the age group of 51-60 years and the maximum percentage of patients were male. The marital status of the majority of the patients 77.3% were married, 18.2% were unmarried and 4.5%

widower were observed. The socioeconomic status of maximum patients was 45.5%, upper middle class. The majority of the patients 63.6% were illiterate. Co-morbid conditions observed among patients were diabetes mellitus (22.7%), seizure (9.1%), bronchial asthma (4.5%), diabetes mellitus with hypertension (4.5%), diabetes mellitus with hypertension and CAD (4.5%), diabetes mellitus with hypertension and hypothyroidism (4.5%) and had no co-morbidities (50%). RT techniques: 2D (22.7%), IMRT (Intensity-modulated radiation therapy) (22.7%), 3DCRT (conformal radiation therapy)

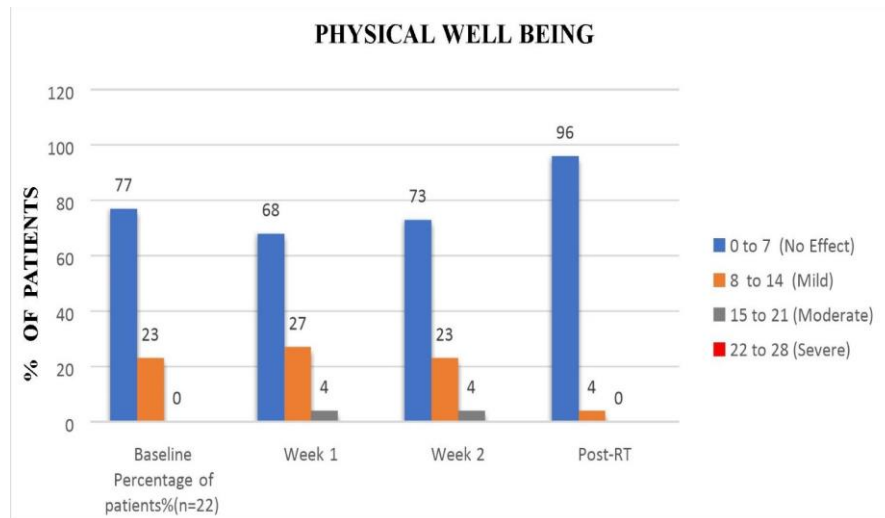


Fig. 1: Physical well-being for BM Patients.

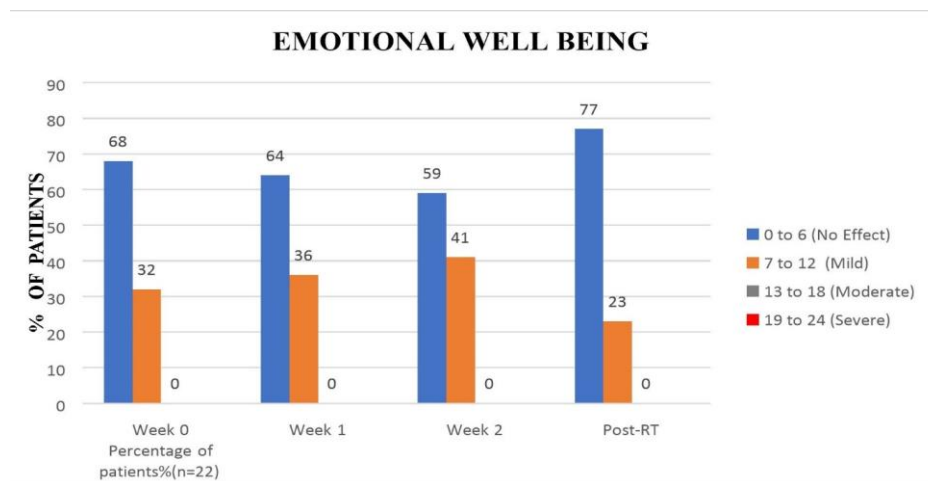


Fig. 2: Emotional well-being for BM Patients.

(54.6%).

Fact-F questionnaire

The presented data provides the impact of FACT-F (Functional Assessment of Cancer Therapy) on the well-being of patients with brain metastases across various dimensions. Figure 1 illustrates its effect on physical well-being, showing a peak of 27% reporting mild effects at week 1, 4% experiencing moderate effects at week 1 and 2. Notably, 96% reported no impact after termination of radiation therapy. Figure 2 outlines emotional well-being, with 41% reporting mild effects at week 2 and 77% reporting no effect after termination of radiation therapy. Figure 3

indicates no significant impact on social well-being throughout the treatment process. Figure 4 details the influence of fatigue on functional well-being, with 73% experiencing mild effects at week 1, 32% reporting moderate effects after termination of radiation therapy, and 64% noting severe effects at week 2. Figure 5 illustrates the effects on fatigue subscale, with 64% experiencing mild effects at week 2 and 36% reporting moderate effects at week 2. Table 2 shows comparison of PWB, SWB, EWB and FS with post RT.

Overall, the data suggests that FACT-F has a noticeable impact on physical and emotional well-

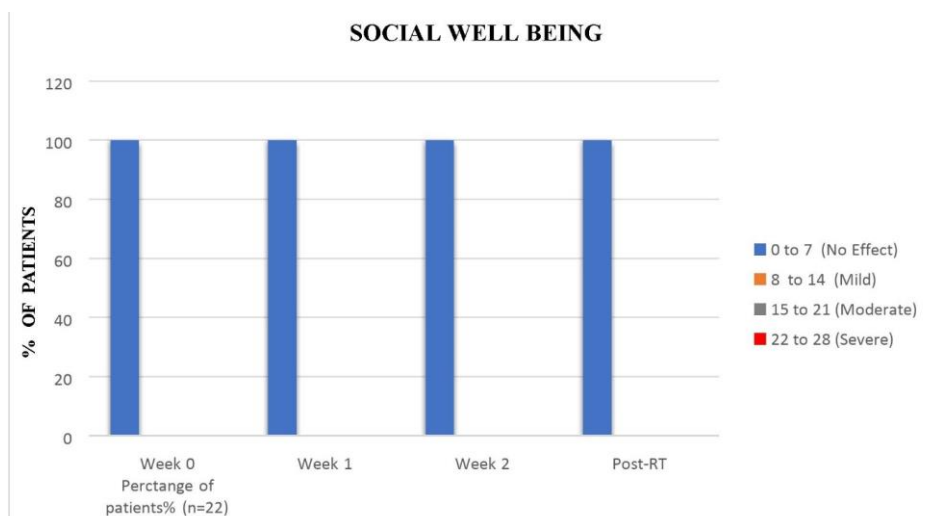


Fig. 3: Social well-being for BM Patients

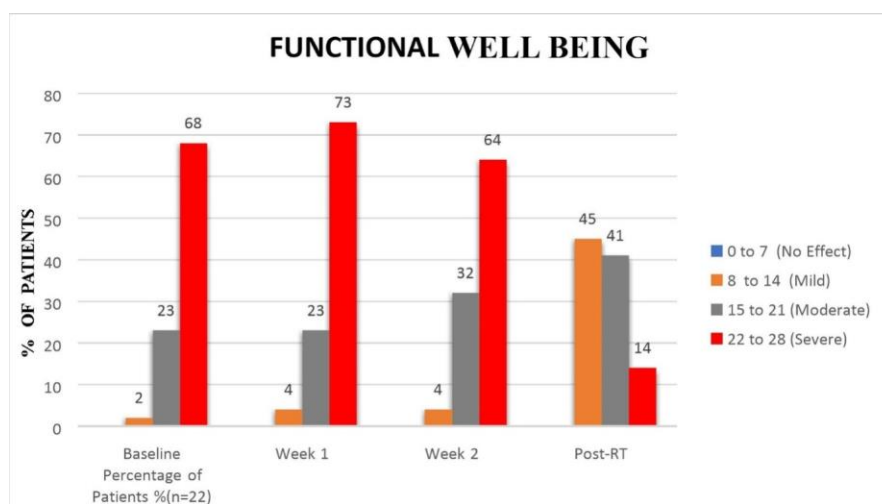


Fig. 4: Functional well-being for BM Patients.

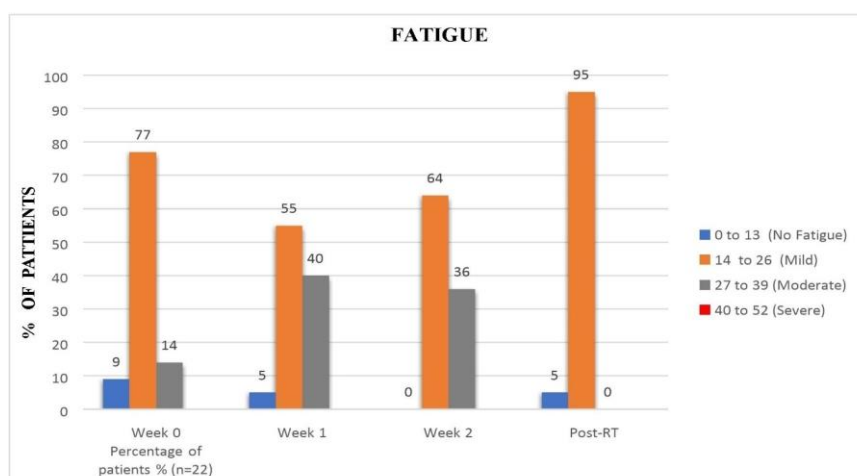


Fig. 5: Fatigue sub-scale for BM Patients.

Table 2: Comparison of PWB, SWB, EWB, FWB and FS with Post RT

S.No.	FACT-F	Mean±SD				P-Value
		W -0	W-1	W-2	POST-RT	
1	PWB	4.91±3.7	6.50±4.0	6.95±3.79	3.50±2.69	0.004
2	SWB	20.5±0.0	20.4±0.36	20.42±0.36	20.5±0.00	1.432
3	EWB	6.05±2.0	5.95±1.89	6.32±1.89	5.23±1.60	0.008
4	FWB	23.3±4.4	23.5±4.38	23.1±4.43	15.82±5.72	0.002
5	FS	11.9±3.4	14.0±4.82	15.0±4.04	10.5±2.04	0.049

being, particularly during treatment, its effect on social well-being appears negligible. However, functional well-being is notably affected, with a significant proportion experiencing moderate to severe effects after treatment. Understanding these dynamics can aid in tailoring interventions to address specific aspects of well-being and improve the overall quality of life for brain metastasis patients.

Discussion

This study was carried out to assess the impact of fatigue on BM patients undergoing radiation therapy using the FACT- F questionnaire. In this study, the mean age group of patients was 56 years. These results were per the study conducted by Paolo Tralongo *et al.* (2003). The findings showed that fatigue is a regular occurrence in older people, may last longer than in younger people, may result in functional reliance, and may significantly affect older people's quality of life and care (Paolo Tralongo *et al.*, 2003). In this study, an average daily dose of 2 Gy was received by patients (minimum dose- 48Gy maximum dose - 60 Gy). This study found that male patients had poor QOL. These results were controversial with the study conducted by Bernhard Holzner *et al.* (2001) who have reported that women reported significantly lower QOL than men in the areas of physical and emotional well-being.

The present study found that 5.23% of patients were unmarried and 4.5% patients were widows. These results were following the study

conducted by Hjermsstad *et al.* (1998). Due to a decrease in socio-emotional support, people who have lost their partners were in a less stable social and emotional environment. (Hjermsstad *et al.*, 1998). In the present study, 63.6% were literate. These results are in accordance with the study conducted by Georg Kemmler *et al.* (2001) who reported that educated people are likely to have good QOL. In the foregoing study the maximum number of patients who were irradiated with IGRT was 31.8%. These results were in accordance with the study conducted by Claudia Scaringi *et al.* (2018). Radiation technologies such as IMRT (Intensity-modulated radiation therapy) and IGRT (Image-guided radiation therapy) enable more accurate delivery of treatment, allowing for escalated doses and modified fractionation schedules. These advancements can enhance tumor control while minimizing radiation exposure to surrounding healthy tissues, thereby reducing the potential for long-term treatment side effects (Claudia Scaringi *et al.*, 2018).

The present study found that there are 2 most common comorbidities among brain metastasis patients which included diabetes mellitus with hypertension(4.5%), and diabetes mellitus (22.7%), These results were comparable with the study conducted by Houben *et al.* (2004), The findings indicated that individuals with brain tumor who are older than 45 had a greater prevalence of hypertension and cerebrovascular illness (Houben *et al.*, 2004). Another study by Jeong *et al.* (2023) suggested that tumor

metabolism interacts with a number of the pathophysiologic features of type 2 diabetes. Clinical and experimental data suggest that hyperglycemia, hyperinsulinemia, and a chronic inflammatory state linked to diabetes are related to increased cancer risk and mortality (Jeong *et al.*, 2023).

The current study found that patients had moderate fatigue in week 2 and severe fatigue from week 3 to week 6 and after terminating radiotherapy showed mild fatigue. These results are in accordance with the study conducted by Smets *et al.* (1998) who found similar results in patients feeling tired every two weeks. The findings show that fatigue gradually increased throughout radiation therapy and decreased when treatment was finished. After radiation, fatigue scores were significantly but only modestly higher than those before treatment (Smets *et al.*, 1998).

The present study found that HRQOL emotional well-being of brain metastasis patients was low in weeks 4, 5, 6 when compared to other domains and improved after terminating radiotherapy. These results are in accordance with the study conducted by Verhaak *et al.* (2019) with BM reporting significantly lower emotional well-being and social well-being is significantly higher compared to the general population.

Conclusion

The finding of the present study indicated that Fatigue had a greater impact on the HRQOL of Brain metastasis patients receiving radiotherapy. The present study revealed that the Functional well-being of the majority of the patients was severely affected when compared with other domains.

Ethical Statement

The study was conducted by using Functional Assessment of Cancer Therapy (FACT-F) questionnaire and no animal was killed so there is no need of Ethical approval.

Author Contributions

Each author has equally collaborated in designing the research, conducting thorough analysis, drafting the manuscript, and refining its content. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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