

ORIGINAL ARTICLE

SURVIVAL OF PATIENTS WITH BRAIN METASTASES AFTER PALLIATIVE WHOLE-BRAIN RADIOTHERAPY – AN EXPERIENCE FROM A SINGLE INSTITUTE

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Background: Brain metastases are a common complication of cancer and approximately 20% of cancer patients develop them over time. Presently palliative whole-brain radiotherapy is used as a palliative treatment for brain metastases because of its cost-effectiveness and easy availability, especially in patients with multiple metastases who are not candidates for surgery or Stereotactic radiosurgery. This study aims to determine the survival in patients who have received palliative whole-brain radiotherapy for brain metastases and to evaluate some of the prognostic factors determining survival in patients with brain metastases. **Methods:** It was a cross-sectional study conducted in Shaukat Khanum Memorial Cancer Hospital and Research Centre and all the patients with brain metastases who had completed palliative whole-brain radiotherapy between July 2015 and July 2020 were included. Data was retrospectively collected and analyzed using SPSS 21.0. Overall survival was calculated using the Kaplan-Meier method, taking into consideration the period from the date of diagnosis of brain metastases until death or to the date of last follow-up, whichever was applicable. *p*-value of <0.05 was regarded as statistically significant. **Results:** Almost half (45%) of the brain metastases were secondary to breast cancer followed by lung and genitourinary cancers at 16.3% and 15.5% respectively. The median overall survival was lowest in breast carcinoma patients at 5 months followed by lung carcinoma at 7 months. The median overall survival was 5 months in patients having extracranial disease as compared to 12 months in those having no extracranial disease or those in whom the disease status was unknown. **Conclusions:** Our study revealed that the most common tumour to metastasize to the brain was breast cancer. The younger age group had a poorer prognosis because most of them had breast cancer with triple-negative disease. Controlled extracranial disease significantly prolonged overall survival in patients with brain metastases.

Keywords: Brain Neoplasm; Radiotherapy; Survival; Quality of Life

Citation: Misbah D, Qamar MFU, Khaleeq N, Zaidi A, Shah SZA, Sajjad K. Survival of patients with brain metastases after palliative whole-brain radiotherapy – an experience from a single institute. J Ayub Med Coll Abbottabad 2023;35(4):599–602.

DOI: 10.55519/JAMC-04-12111

INTRODUCTION

Brain metastases are a common complication of cancer and approximately 20% of the cancer patients develop them over time. They can significantly affect quality of life due to their debilitating signs and symptoms.^{1,2} Lung cancer is found to be the most frequent primary tumour metastasizing to the brain accounting for almost 20% of Brain metastases, followed by breast cancer, melanoma, and renal and colorectal cancer.³ It has a wide array of presentations like headache, focal neurological deficits, seizures and impaired cognition depending on the site and extent of metastases.⁴

Management of Brain metastases is multidisciplinary including medical, radiation and surgical interventions. Medical management includes

steroids, which are commonly used to control cerebral oedema due to brain metastases and provide marked symptomatic relief.⁵ The treatment strategy is patient-specific depending on the age⁶, extent and status of the primary tumour, performance status and number of metastases. Karnofsky Performance Scale (KPS) score <70 carries a poor prognosis and these patients are generally recommended for best supportive care, whereas KPS >70 have options of either surgical resection for large-sized solitary metastasis >3cm followed by Radiotherapy (RT); Stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) for multiple metastasis ≤10, and palliative whole-brain radiotherapy (WBRT) for multiple metastasis > 10.^{7,8} These, however, do not strictly apply and still warrant further clinical trials regarding benefits over each other.⁷ Presently WBRT is

used as a palliative treatment for Brain metastases because of its cost-effectiveness and easy availability especially in patients with multiple brain metastases who are not candidates for surgery or SRS.⁹ The optimal dose and fractions remain questionable, though a study indicated that there was no considerable difference between the six-monthly survival of those treated with 30 Gray in 10 fractions compared to 20Gray in 5 fractions.¹⁰ Some recent studies have indicated that the median overall survival increased significantly after WBRT and was between 4 and 6 months. Also, the overall 1-year survival in those receiving radiotherapy against controls was 42.4% vs 35.3%.^{11,12} The main aim of WBRT is to control symptoms and improve quality of life.¹²

Palliative WBRT is a commonly used treatment for patients with brain metastases at SKMC and RC because of its cost effectiveness and easy availability. Also, most of the patients presenting with brain metastases have either got significant extra cranial disease or have poor performance status from the disease so would not be suitable to have stereotactic radiotherapy or neurosurgery.

This study aims to determine the survival in patients who have received palliative whole brain radiotherapy (WBRT) for brain metastases at Shaukat Khanum Memorial Cancer Hospital and Research Centre and to evaluate some of the prognostic factors (age, primary site of cancer and status of extra cranial disease) determining the survival in patients with brain metastases.

MATERIAL AND METHODS

It was a cross-sectional study conducted in Shaukat Khanum Memorial Cancer Hospital and Research Centre and all the patients with brain metastases who had completed palliative whole brain radiotherapy between July 2015 and July 2020 were included. Those having primary brain tumours were subsequently excluded. Data was collected from hospital information system (HIS) and ARIA (radiotherapy planning software) and included details regarding the age, gender, primary site of cancer, date of diagnosis of brain metastases on imaging (Computed Tomography (CT) scan/Magnetic Resonance Imaging (MRI) brain or both if appropriate), status of extra cranial disease on the recent staging CT, dose of palliative WBRT [30 Gray in 10 fractions or 20 Gray in 5 fractions], date of completion of radiotherapy, date of last follow up and if the patient was still alive.

Since it was a retrospective study based purely on hospital records, therefore an informed consent was not required for this study. Moreover, data was fully anonymized to avoid the breach of patients' confidentiality. The study was approved by the IRB (Institutional Review Board) of Shaukat Khanum Memorial Cancer Hospital and Research Centre.

Overall survival was determined from the date of completion of palliative WBRT to the date of last follow up or death of the patient, which ever was applicable. Data was compiled and analyzed using IBM SPSS version 21. Survival analysis was done using Kaplan–Meier survival curve. *p*-value of ≤0.05 was regarded as statistically significant.

RESULTS

The total sample size was 250 patients. Almost half (45%) of the brain metastases were secondary to breast cancer followed by lung and genitourinary cancers at 16.3% and 15.5% respectively. Gastrointestinal tumours comprised only 11.6% of the brain metastases.

The median overall survival was lowest in breast carcinoma patients at 5 months followed by lung carcinoma at 7 months. The median overall survival was significantly higher for gastrointestinal (GI) cancers at 19 months. For genitourinary (GU) tumours and other types of tumours, it was 11 months and 12 months respectively.

The median overall survival in the age group above 50 was 8 months, whereas in those below 50 it was 6 months. The median overall survival was 5 months in patients having extracranial disease as compared to 12 months in those having no extracranial disease or those in whom the disease status was unknown.

Table-1: Most common primary cancer sites causing brain metastases

Primary Site	Number	Percentage
Breast	112	45
Gastrointestinal (GI)	29	11.6
Lung	41	16.3
Genitourinary (GU)	39	15.5
Head and Neck (HN)	13	5.2
Others	16	6.4
Total	250	100

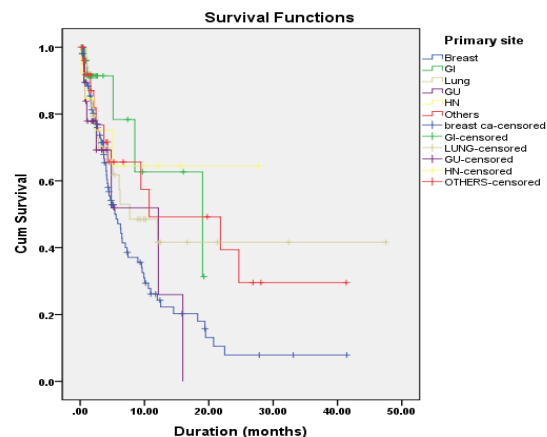


Figure-1: Kaplan Meier survival curves depicting survival with brain metastases based on different primary sites

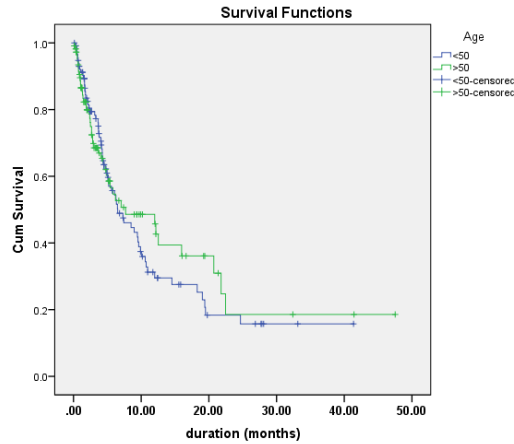


Figure-2: Kaplan Meir survival curves depicting survival with brain metastases based on age

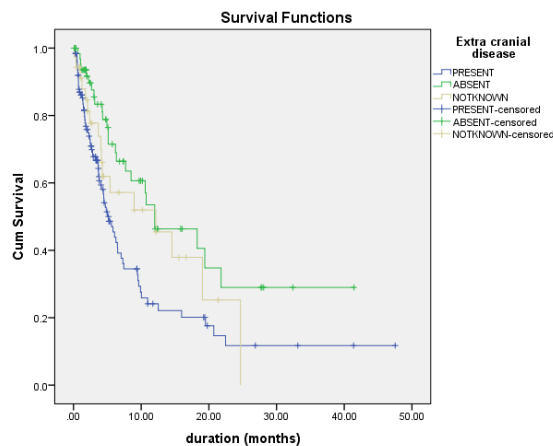


Figure-3: Kaplan Meir survival curves of patients with brain metastases stratified by status of extra-cranial disease

DISCUSSION

This was a retrospective study conducted to determine prognostic factors and median survival in patients after treatment with WBRT. Absence of extracranial disease was significantly associated with improved survival outcome in patients treated with WBRT for brain metastases. Most common primary site was breast cancer and median survival was higher for patients with gastrointestinal primary.

Past studies have significantly associated improved survival outcomes in lower age groups.^{13,14} However, in this study median survival for age group below 50 years was 6 months whereas, in age group above 50 it was 8 months. These findings can be explained by the fact that most of the patients in our study had breast cancer diagnosed at a young age and

had triple negative disease, which carries a poorer prognosis. Nevertheless, it warrants further primary site-specific studies in our population with additional prognostic factors taken into account.

A significant prognostic factor in this study was the status of extracranial disease. In patients with controlled extracranial disease the median survival was 12 months whereas, in those having uncontrolled extracranial disease the median survival was significantly shortened to 5 months. This has been demonstrated in past studies. Datsenko PV *et al* found a significant decrease in > 6-month mortality in patients treated with WBRT for brain metastasis.¹⁵ Similarly, survival benefit was illustrated in those with controlled primary in studies done by Gallego P *et al* and Saito EY *et al*.^{13,16}

In this study, the median overall survival for breast cancer patients after WBRT was 5 months which is significantly poorer as compared to other sites. Our findings are comparable to a study done by Okada *et al*, in which the median survival was 4.4 months.¹⁷ This could be attributed to the fact that majority of our breast cancer population who develop brain metastases have a triple negative disease which generally carries a poor prognosis despite systemic chemotherapy and WBRT.¹⁸ On the other hand, human epidermal growth factor receptor 2 (HER-2) molecular subtype carries a better prognosis with administration of immunotherapies such as trastuzumab; however, unfortunately in developing countries such as ours, affordability is a major hurdle and hence, the poor overall median survival in our breast cancer patients with brain metastases.^{18,19}

Median overall survival was found to be 7 months in brain metastases patients with lung cancer. In a study done by Bernhardt D *et al*, in patients with small cell lung carcinoma the median survival after WBRT was 6 months which is consistent with our findings.²⁰

In this study, 45% of the brain metastases had breast primary followed by lung (16.3%). This is in contrast to most of the studies done in the past in which the lung is the most common primary for brain metastases.^{21,22} However, a study conducted by Saito EY *et al* had similar findings as ours with 33% breast and 29% lung, respectively.¹³ Nevertheless, in both our study and the study by Saito EY *et al*, the majority of the patients were female which could be regarded as the confounding factor.

CONCLUSION

Our study revealed that the most common tumour to metastasize to the brain was breast cancer. The younger age group carried a poorer prognosis because the majority of them had breast cancer with triple-negative disease. Controlled extracranial disease

significantly prolonged overall survival in patients with brain metastases.

AUTHORS' CONTRIBUTION

DM: Literature search, Write-up. MF: Study design, data analysis, write-up, proof reading. NK: Data analysis, data interpretation. AZ: Literature search, data collection. SZAS: Literature search, data collection. KS: Study design, proof reading.

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Submitted: May 29, 2023

Revised: August 25, 2023

Accepted: September 25, 2023

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