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One-Year Overall Survival of Patients with Brain Metastasis After Receiving Palliative Radiotherapy

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Abstract

Background: Brain metastases represent a significant oncological challenge, adversely impacting survival and quality of life. This study aims to assess the one-year overall survival of patients with brain metastases following palliative radiotherapy, focusing on the influence of demographic and clinical factors.

Methods: This prospective observational study enrolled 100 patients with brain metastases treated at Oncology Centers in Erbil, Iraq, from November 2022 to November 2023. Survival outcomes were analyzed in relation to primary cancer type, age, gender, number of brain metastases, and response to radiotherapy. Statistical analyses were conducted using SPSS version 28, with significance set at $p \leq 0.05$.

Results: The cohort had a mean age of 55.7 years, with a predominance of female (61%) patients. Breast cancer (42%) and NSCLC (33%) were the most common primary cancers. One-year survival was 36%, with younger age and surgical intervention for metastases significantly associated with improved survival. The response to radiotherapy also correlated with better outcomes. No significant association was found between survival and tumor grade, stage at diagnosis, presence of extracranial metastases, or performance status.

Conclusions: The study highlights the significant impact of patient age, surgical treatment of metastases, and response to radiotherapy on the survival of patients with brain metastases. These findings underscore the necessity for early detection and tailored treatment strategies. The limitations of this study, including its sample size and observational design, suggest a need for further research in diverse populations and across multiple centers.

Introduction

The phenomenon of brain metastases constitutes a critical oncological challenge, affecting approximately 30% of patients diagnosed with solid tumors. ⁽¹⁾ These metastatic entities originate from the dissemination of malignant cells from a primary site, subsequently colonizing cerebral tissues. Primarily, cancers such as lung, breast, melanoma, renal cell carcinoma, and colorectal are known to metastasize to the brain. ⁽²⁾ The prognosis for patients with brain metastases is markedly variable, with survival rates spanning from 2 to 25 months. ⁽³⁾ This variation is influenced by several determinants, including the histological nature of the primary cancer, disease burden, patient demographics, and overall health status.

Historical treatment modalities for brain metastases have included surgical excision, whole-brain radiation therapy (WBRT), and systemic chemotherapy, predominantly aimed at palliation—enhancing neurological function, preserving quality of life, and extending survival. ⁽⁴⁾ WBRT, in particular, has been a mainstay of palliative care, offering symptomatic relief and a modest increase in median survival of 3 to 6 months. ⁽⁵⁾

Recent advancements have positioned Stereotactic Radiosurgery (SRS) as an effective alternative to WBRT, providing comparable survival outcomes while preserving neurocognitive functions and enhancing quality of life. ^(6,7) Prognostic evaluation and survival prediction are crucial for therapeutic decision-making and patient counseling. The Radiation Therapy Oncology Group (RTOG) has developed prognostic tools such as the Recursive Partitioning Analysis (RPA), Score Index for Radiosurgery (SIR), and Basic Score for Brain Metastases (BSBM), enabling the categorization of patients into prognostic groups to refine survival predictions. ^(3,8,9)

Studies examining the efficacy of palliative radiotherapy report one-year overall survival rates ranging from 8% to 42%. ⁽¹⁰⁻¹⁴⁾ Adverse prognostic factors, including advanced age, poor functional status, multiple brain lesions, active extracranial disease, and certain primary cancers (e.g., lung cancer, melanoma), have been identified as indicators of reduced survival. In contrast, positive prognostic indicators such as optimal performance status and primary tumors with better prognostic outlooks (e.g., solitary brain metastasis, breast cancer, renal cell carcinoma) are associated with improved survival rates. ⁽¹⁵⁾

The management landscape for brain metastases is evolving with the advent of targeted therapies and immunotherapy, offering a broader range of treatment options. Recent studies indicate improved survival for specific patient subsets, such as those with BRAF-mutated melanoma treated with BRAF inhibitors, underscoring the potential of integrating radiotherapy with systemic treatments. This evolving paradigm emphasizes the need for continuous research into novel therapeutic combinations to enhance efficacy and survival for patients with brain metastases.

The prognostic landscape and survival outcomes for brain metastases have notably advanced in the targeted therapy and immunotherapy era. Recent evidence suggests a one-year overall survival rate of 58% in patients with BRAF-mutated melanoma undergoing BRAF-targeted therapy ⁽⁹⁾ illustrating the benefits of combining radiotherapy with systemic treatments. Ongoing clinical trials are exploring innovative combinations of WBRT and immunotherapy. Effective management of brain metastases necessitates a multidisciplinary approach, tailored to the individual patient's condition and the spectrum of available treatments. This study, conducted within the unique context of the Kurdistan region of Iraq, seeks to elucidate the one-year overall survival rates of patients with brain metastases following palliative radiotherapy, aiming to contribute valuable insights to the clinical management and therapeutic strategies in this challenging field. ⁽¹⁶⁾

Patients and Methods

Study Design and Setting

This prospective observational study was conducted at the Oncology Centers of Awat and Rizgary Hospitals in Erbil, Iraq. The primary objective was to evaluate the one-year overall survival of 100 patients with brain metastases following palliative radiotherapy. The study period extended from November 2022 to November 2023, focusing on a cohort subjected to various radiotherapeutic modalities.

Data Collection

Patients were recruited from the Department of Radiation Oncology. The cohort was stratified based on one-year overall survival, incorporating variables such as the type of primary cancer, age, gender, number of brain metastases, and performance status, as determined by the Karnofsky Performance Scale. Radiotherapy techniques evaluated included Two-Dimensional Radiotherapy (2DRT), Three-Dimensional Conformal Radiotherapy (3DRT), and Stereotactic Radiosurgery (SRS), administered in one, five, or ten fractions. Data were collected on 100 individuals diagnosed with adenocarcinoma, squamous cell carcinoma (SCC), or other histological types of cancer, alongside their brain metastasis performance status.

Data Management and Statistical Analysis

Data collection was facilitated by a custom-designed questionnaire, with data entry conducted using Microsoft Excel (2016). The Statistical Package for the Social Sciences (SPSS) software, version 28, was utilized for data analysis. Comparative analysis of patient variables was performed, with statistical significance established at a p-value of ≤ 0.05 . Results were presented through rates, ratios, frequencies, and percentages, and illustrated with tables and figures. T-tests and Chi-square tests were applied for analytical assessments.

Exclusion and Inclusion Criteria

Patients without brain metastases, those younger than 18 or older than 90 years, and individuals with a Karnofsky performance status below 40% were excluded. The study included patients aged 18 to 90 years, diagnosed with brain metastases originating from a primary cancer, and having a Karnofsky performance status ranging from 40 to 100%.

Ethical Considerations

Ethical approval was granted by the Ethics and Scientific committees of the Radiology Department under the Kurdistan Higher Council of Medical Specialties. The study was conducted in strict adherence to ethical standards, ensuring the confidentiality and anonymity of all patient data. Conflicts of interest were comprehensively addressed. Consent procedures were meticulously followed, ensuring all participants were adequately informed about the study's aims, methodologies, potential risks, and benefits.

Results

Our study enrolled a total of 100 participants, with the age range spanning from 18 to 82 years. The mean age of the cohort was 55.7 years. A majority (61%) of the participants were female, and less than half (48%) resided in Erbil, with a minimal representation (1%) from Duhok. Notably, 91% of the participants were married, and a significant portion (61%) were housewives. Regarding lifestyle factors, 21% were current smokers, 23% were former smokers, and a minor fraction (3%) reported alcohol consumption.

Demographic and Clinical Characteristics

The primary cancers most represented in our cohort were breast cancer (42%), followed by non-small cell lung cancer (NSCLC) (33%), with a rare incidence of cancer of unknown primary (CUP) at 1%. Pathological findings revealed adenocarcinoma in 21% of cases and squamous cell carcinoma (SCC) in 20%. The majority of patients (54%) were diagnosed with Grade III tumors, while Stage IV disease at diagnosis was identified in 37% of the participants. Magnetic Resonance Imaging (MRI) was the predominant modality for diagnosing brain metastases, utilized in 81% of cases. A notable portion of patients (41%) presented with 4 to 10 brain metastases at the time of diagnosis.

Treatment and Outcome

A majority of patients (87%) received treatment for their primary cancer, and 12% underwent brain surgery for metastasis. Prior to the current study, 10% had received Two-Dimensional Radiotherapy (2DRT) for brain metastases. The treatment modalities during the study predominantly included Three-Dimensional Conformal Radiotherapy (3DRT) (62%) and Stereotactic Radiosurgery (SRS) (13%). The treatment was typically administered in 5 fractions (86% of cases). Corticosteroids were prescribed to 84% of the patients as part of their management strategy.

Neurological and Clinical Outcomes

Increased intracranial pressure was observed in 65% of cases, and seizures were reported in 26%. The overall survival data indicated that 60% of patients remained alive at the study's conclusion, with 33% exhibiting a good response to radiotherapy, whereas 54% showed no response. Survival rates decreased over time, with only 36% of patients surviving one year after follow-up.

Statistical Associations

Analysis of factors associated with one-year survival revealed no statistically significant association with tumor grade, stage at diagnosis, the presence of extracranial disease, or performance status at the time of brain metastasis ($p > 0.05$). However, age showed a significant correlation with outcomes; deceased patients had a higher mean age (58.72 years) compared to survivors (50.32 years), with a p-value of 0.001. Additionally, undergoing brain surgery for metastasis significantly impacted survival, with 66.7% of survivors having undergone surgery compared to 33.3% of deceased patients ($p = 0.026$). The response to radiotherapy also showed a significant association with outcomes, where a good or somewhat response correlated with higher survival rates ($p < 0.05$).

Figures and Tables

Table 1: Background variables of participants.

Variables	Categories	Frequency and percent
Sex	male	39
	female	61
Address	Erbil	48
	Mosul	25
	Kirkuk	6
	Sulaymaniyah	20
	Duhok	1
Marital status	single	9
	married	91
Occupation	housewife	61
	retired	32
	Peshmerga	7
Smoking	no	56
	yes	21
	ex-smoker	23
Alcohol	no	97
	yes	3
Total		100

Table 2: Primary cancer, pathology, stage, and modality of diagnosis.

Variables	Categories	Frequency and percent
Primary cancer	breast	42
	SCLC	6
	NSCLC	33
	Melanoma	4
	Rectal	2
	Head and neck	1
	CUP	1
	Others	11
Pathology	Adenocarcinoma	21
	SCC	20
	Others	59
Grade	I	3
	II	24
	III	54
	IV	19
Stage at diagnosis	II	32
	III	31
	IV	37
Modality of diagnosis	MRI	83
	CT scan	15
	PET scan	2
Number of brain metastasis	1	14
	2-3	38
	4-10	41
	>10	7
Total		100

Table 3: Performance state and Glasgow Coma Scale.

Variables	Categories	Frequency and percent
Extra cranial site	No	40
	Yes	60
Performance state prior of brain metastasis	50%	6
	60%	18
	70%	40
	>80%	36
Performance state at time of brain metastasis	40%	3
	50%	37
	60%	28
	70%	20
	>80%	12
Glasgow coma scale	13-15	92
	9-12	8
Total		

Table 4: Neurological signs, treatments, and outcomes.

Variables	Categories	Frequency and percent
Neurological signs and symptoms	No	2
	Increased intracranial pressure	65
	Weakness	7
	Seizure	26
Treatment for primary cancer	Yes	87
	No	13
Brain surgery for metastasis	Yes	12
	No	88
Previous radiotherapy for brain metastasis	Yes	10
	No	90
Type of previous radiotherapy	No	90
	2DRT	10
Type of current radiotherapy	2DRT	25
	3DRT	62
	SRS	13
Radiotherapy fractions	1 Fraction	3
	5 Fractions	86
	10 Fractions	11
Drug history	None	6
	Corticosteroids	84
	Anticonvulsants	3
	Both	7
Comorbidities	None	45
	Hypertension	22
	Ischemic heart diseases	9
	Diabetes mellitus	24
Outcome	Alive	36
	Dead	64
Response to radiotherapy	good	33
	somewhat	13
	no response	54
Total		100

Figure 1: Survival rate of brain metastasis cases every three months until one year.

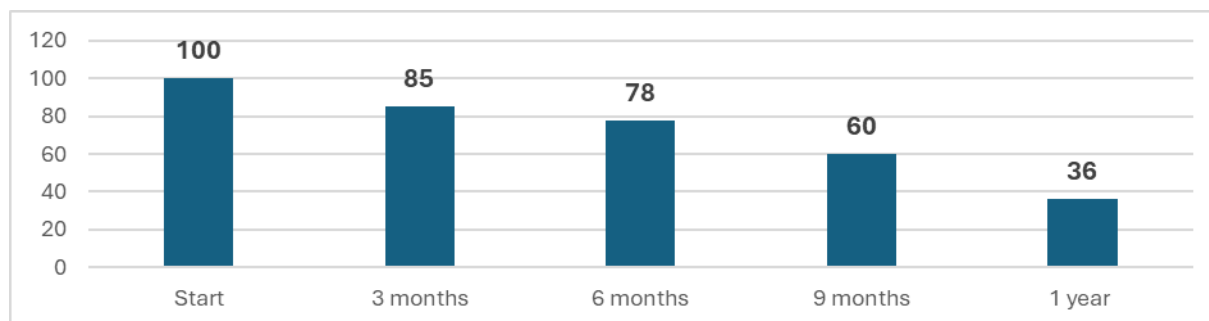


Table 5: Factors associated with better one-year survival rates.

Variable	Categories	Outcome		p-value
		Alive	Dead	
Grade	I	1 (33.3%)	2 (66.7%)	0.253
	II	12 (50%)	12 (50%)	
	III	19 (35.2%)	35 (64.8%)	
	IV	4 (21.1%)	15 (78.9%)	
Stage at diagnosis	II	14 (43.8%)	18 (56.3%)	0.494
	III	11 (35.5%)	20 (64.5%)	
	IV	11 (29.7%)	26 (70.3%)	
Extra cranial site	No	16 (40%)	24 (60%)	0.529
	Yes	20 (33.3%)	40 (66.7%)	
Performance state at time of brain metastasis	40%	1 (33.3%)	2 (66.7%)	0.215
	50%	9 (24.3%)	28 (75.7%)	
	60%	10 (35.7%)	18 (64.3%)	
	70%	9 (45%)	11 (55%)	
	>80%	7 (58.3%)	5 (41.7%)	
Age in years	Mean ± S.D	50.32 ± 12.48	58.72 ± 12.91	0.001
Brain surgery for metastasis	Yes	8 (66.7%)	4 (33.3%)	0.026
	No	28 (31.8%)	60 (68.2%)	
Response to radiotherapy	Good	20 (60.6%)	13 (39.4%)	0.001
	Somewhat	8 (61.5%)	5 (38.5%)	
	No response	8 (14.8%)	46 (85.2%)	
Total		60 (60%)	40 (40%)	

Discussion

Our analysis of 100 patients with brain metastases revealed a mean age of 55.7 with a predominance of female patients, most of whom were married and identified as housewives. Sperduto et al. presented the Graded Prognostic Assessment (GPA) tool, which identified prognostic factors including patient age, performance status, and brain metastases to predict survival outcomes. The findings in this study align with those of other studies, which found that age and surgical intervention were significantly associated with better survival outcomes, supporting the GPA's identification of age as a key prognostic factor. However, our study did not find a significant association between survival and other GPA factors such as tumor grade, diagnosis stage, or extracranial metastases. This discrepancy could be due to sample size or demographic differences. ⁽¹⁷⁾

The study by Rodrigues et al. utilized Recursive Partitioning Analysis (RPA) to predict outcomes for patients treated with Stereotactic Radiosurgery (SRS), emphasizing the importance of patient selection criteria in predicting lesion control and survival. The data in this investigation similarly highlighted the importance of response to radiotherapy in predicting survival outcomes, with a significant correlation between positive radiotherapy response and better survival. Both studies underscore the efficacy of tailored radiotherapeutic approaches. Geographic distribution showed a concentration in Erbil, with limited representation from Duhok. Lifestyle factors varied across the cohort, including smoking habits and alcohol consumption, reflecting a diverse patient demographic. ⁽¹⁸⁾

Consistent with extant literature, breast cancer and non-small cell lung cancer (NSCLC) emerged as the most frequent primary cancers metastasizing to the brain within our study population. This aligns with previous research underscoring lung and breast cancers as predominant sources of brain metastases, highlighting the pervasive nature of these malignancies and their propensity for cerebral dissemination. ⁽¹⁷⁾ The prevalence of adenocarcinoma and squamous cell carcinoma (SCC) pathologies further underscores the significant representation of lung cancer within our cohort. Notably, a substantial fraction of participants presented with Grade III tumors, which, coupled with the advanced stages at diagnosis for many, underscores the aggressive clinical trajectory often characteristic of brain metastases. ⁽¹⁹⁾

Diagnostic practices within the cohort favored Magnetic Resonance Imaging (MRI), reinforcing its role as the gold standard for identifying and characterizing brain metastases. This preference

reflects the critical need for precise and detailed imaging in diagnosing cerebral metastatic disease. ⁽²⁰⁾

Survival trends observed over the study's duration revealed a gradual decline, with one-year survival rates standing at 36%. This figure, while aligning with the generally poor prognosis associated with brain metastases, notably surpasses some earlier reported rates. This disparity may be attributable to advancements in treatment modalities, diagnostic precision, or potentially, demographic, and clinical characteristics unique to our study population.

Age emerged as a significant determinant of survival, with younger patients exhibiting more favorable outcomes. This observation is congruent with existing studies that have identified age as a pivotal prognostic factor, suggesting that younger patients may harbor a more robust capacity for recovery and tolerability towards aggressive treatments. ⁽²¹⁾

Another critical finding was the positive correlation between surgical intervention for metastases and improved survival rates, advocating for the consideration of surgical options in appropriate cases. ⁽²²⁾ Additionally, responses to radiotherapy markedly influenced survival outcomes, underscoring the efficacy of radiotherapeutic interventions in managing brain metastases and enhancing patient longevity. ⁽²³⁾

The lack of significant associations between survival and variables such as tumor grade, stage at diagnosis, presence of extracranial metastases, and performance status may reflect the limitations posed by our study's sample size or the influence of unaddressed confounding factors. These findings highlight the complexity of prognosticating outcomes in brain metastases and underscore the necessity for comprehensive, multidimensional approaches in patient evaluation and management.

Conclusions

This study contributes valuable insights into the demographic and clinical landscapes of patients with brain metastases, emphasizing the predominance of breast and NSCLC as primary sources of metastatic brain tumors. Our findings underscore the importance of early detection, particularly given the advanced stages at which many patients are diagnosed. The pivotal role of MRI in diagnosis, the impact of patient age and surgical interventions on survival, and the beneficial effects of radiotherapy response on patient outcomes are underscored. While some expected prognostic factors did not show significant associations with survival, this highlights the need for further research, larger sample sizes, and consideration of additional variables. Ultimately, our study reaffirms the critical need for tailored, multidisciplinary treatment strategies and underscores the ongoing challenges in improving prognoses for patients with brain metastases.

Limitations

Our study's insights are tempered by several limitations, including its modest sample size and single-center design, which may affect the generalizability of the findings. The observational nature of the study limits our ability to establish causality, and the lack of consideration for potentially confounding variables, as well as emerging cancer treatments, could influence the observed outcomes. Additionally, the focus on survival rates without assessing quality of life or neurocognitive effects represents a gap in our analysis. Future research should aim to address these limitations by incorporating larger, multi-center cohorts and a broader range of outcomes.

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