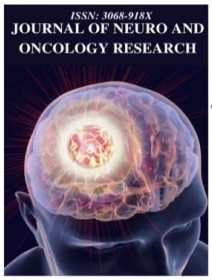

ISSN: 3068-918X
Journal of Neuro and Oncology Research

ATHENAEUM SCIENTIFIC PUBLISHERS

Research Article

Clinical and Demographic Outcomes of Brain Metastases Receiving Whole Brain Radiation: A Retrospective Study from a Tertiary Care Institute in Eastern India

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Citation: Sahoo B, et al. Clinical and Demographic Outcomes of Brain Metastases Receiving Whole Brain Radiation: A Retrospective Study from a Tertiary Care Institute in Eastern India. J Neuro Onco Res. 2025;5(3):1-10.

https://doi.org/10.46889/JNOR.2025.5302

Received Date: 01-09-2025

Accepted Date: 29-09-2025

Published Date: 06-10-2025

Abstract

Background: Brain Metastasis (BM) is associated with poor prognosis. It affects the Quality of Life (QOL) and causes significant morbidity. BMs are the most common intracranial neoplasm, with a total number that outnumber primary neoplasms by a ratio of 10:1. In the present study, we aim to analyze the clinicodemographic profile and treatment outcomes of brain metastasis. Also, try to identify factors associated with survival in patients with brain metastasis.

Methods: A retrospective, single-institutional study of 151 patients with brain metastases was conducted from January 2018 to May 2019. Medical records were reviewed to collect demographic and clinical information. The aim was to analyze the demographic and clinical profiles of patients with brain metastasis. Additionally, it analyzes patient factors, tumor characteristics and treatment plans that may impact overall survival in patients with brain metastases.

Results: The median age for diagnosis of brain metastasis was 50 years. 82 patients were male. The common primary metastasizing to the brain was lung carcinoma (61%), followed by breast carcinoma (16%). 58% had adenocarcinoma histology and 14% of patients had infiltrating ductal carcinoma. (54%) showed multiple metastases, which is more common than a single metastasis (39%). 7% of patients showed two sites of metastases. 60% of patients have Supratentorial lesions. 29% of patients showed both supra and infratentorial lesions. Among them, the frontal lobe was the most commonly involved site. Out of 151 patients, 90 patients showed frontal lobe metastasis. Parietal and cerebellar metastasis is the next common site for metastasis 60% of patients are diagnosed upfront for brain metastasis. 3% of patients developed brain metastasis after five years of primary diagnosis. The most commonly used dose prescription for Whole Brain Radiation (WBRT) is 30Gy/10 fractions or 20Gy/5 fractions. 54% patients treated with 30Gy/10fx dose prescription. Median survival for patients with brain metastasis was eight months (ranging from 1 month to 32 months). Younger age (40-50 years), breast primary with a single metastasis and developed brain metastasis after 1-2 years of primary diagnosis were associated with better survival.

Conclusion: The study highlights that in patients with brain metastasis, the overall prognosis remains poor; however, younger patients (40-50 years) and those with a single brain lesion demonstrate relatively better survival outcomes. Other factors, such as gender, WBRT dose and site of lesion, did not significantly affect survival.

Keywords: Brain Metastasis; Carcinoma Lung; Clinicodemographic Profile; Median Survival; Multiple Lesions

Abbreviations

BM: Brain Metastasis; WBRT: Whole Brain Radiotherapy; CE-MRI: Contrast Enhanced Magnetic Resonance Imaging

Introduction

Brain Metastasis (BM) is the most common intracranial neoplasm in adults and occurs in 10-30% of adults with disseminated tumors [1,2]. Brain metastasis is usually diagnosed between the 5th and 7th decades of life [3]. An estimated 20% of all cancer patients develop brain metastasis. Most brain metastases originate from the Lungs, Breast, Colorectal carcinoma and Melanoma [4]. Hematological neoplasm constitutes only 10% of all brain metastases and primarily affects the leptomeninges [5,6]. Adenocarcinoma and small cell carcinoma of the lungs are the most common histologies associated with brain metastasis. 80% of cases of BMs are located in the cerebral hemisphere, followed by 15% in the cerebellum and 5% in the brainstem [7]. The frontal lobe has been reported to be the most frequent site of metastasis within the brain [8]. However, primary cancer type and specific biological features strongly influence the site preferences of central nervous system spread.

In recent years, brain metastasis has increased due to improved diagnosis by advanced imaging techniques, prolonged survival due to advanced anti-cancer treatment and the brain being a pharmacological sanctuary site due to the blood-brain barrier [9-11].

The clinical presentation of brain metastasis is similar to other intracranial neoplasms, like headache (30-60%), cognitive impairment (30%), seizure, focal neurological deficit, ataxia, nausea and vomiting [12,13]. At diagnosis, 60-70% of patients can be asymptomatic [14]. Contrast-Enhanced Magnetic Resonance Imaging (CE-MRI) is the cornerstone for diagnosing brain metastasis. The radiological features of cerebral metastasis are multiple and typically present at the grey-white matter junction or in arterial watershed areas.

Brain metastasis itself added an adverse factor in the primary disease due to its impact on Survival and Quality of Life. The prognosis of the patients with BMs has been inferior, with a median overall Survival of 1-2 months if any treatment for brain metastasis [15]. Considering the above, this study was designed to retrospectively analyze the demographic and clinical profiles of patients with brain metastasis and evaluate their survival. This study also analyzed the correlation between various clinicodemographic factors and survival.

Methods

A total of 151 patients were retrospectively analyzed who were treated with radiation therapy for brain metastasis between January 2018 and May 2019. Patients with a histologically proven primary site with brain metastasis were included and all data about these patients were entered in a standardized case record form.

Study Variables: The parameters documented included age, gender, primary site, stage, histology of the primary tumor, site of metastasis, number of brain metastases, any other site of metastasis (excluding the brain) and survival in months.

Statistics

Data were entered into a Microsoft Excel spreadsheet for statistical analysis and then analyzed by SPSS 29.0. Data were summarized as means, medians and standard deviations for numerical variables and counts and percentages for categorical variables. Kaplan-Meier curves were plotted to evaluate survival and the log-rank test was used for univariate analysis. P-value ≤ 0.05 was considered for statistical significance.

Results

In the study, out of 151 patients, 47 patients (31%) were between 40 and 50 years of age and 45 patients (29%) were between 50 and 60 years of age. So, the maximum number of patients (60%) are between the 40-60 age group. The age range was from 20 to 75 years. There were no significant differences in the distribution of brain metastases by gender. Male patients (n=82) are slightly more 54% than female patients (n=69). Lung cancer was the most common primary (61%) for metastasis to the brain, followed by Ca Breast (16%) (Fig. 1).

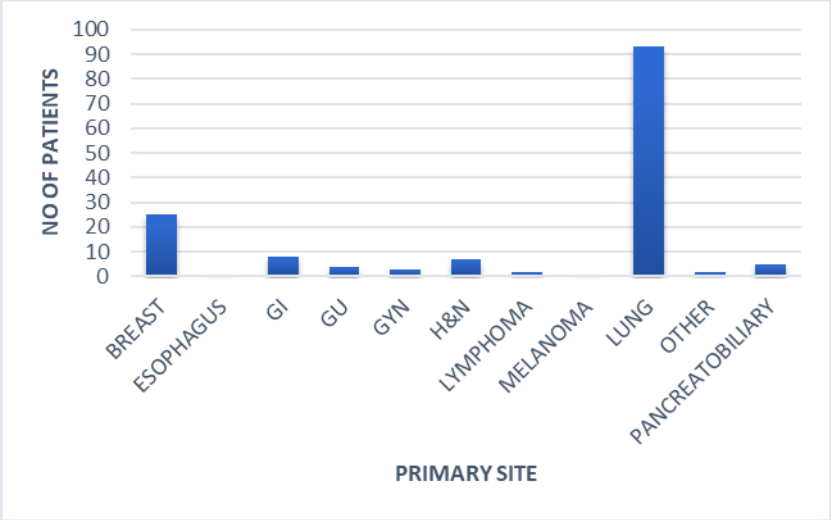

Figure 1: Bar diagram depicting the primary site giving rise to brain metastasis.

When analyzing different histologies of the primary site, 58% of the patients have adenocarcinoma histology, followed by 14% of patients with infiltrating duct carcinoma. Few cases have squamous and Adenocarcinoma (Fig 2).

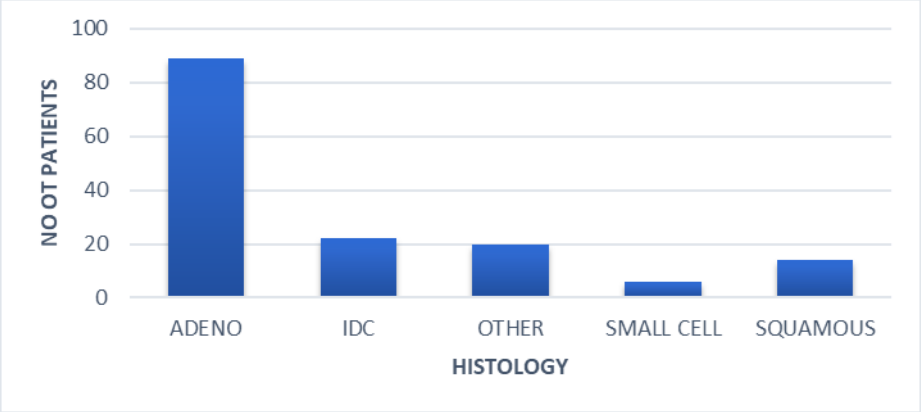

Figure 2: Bar diagram showing histology of primary.

Of 151 patients, 54% (n = 82) showed multiple metastases and 39% (n = 58) had a single metastasis. 7% of patients (n = 11) have only two metastases (Fig. 3).

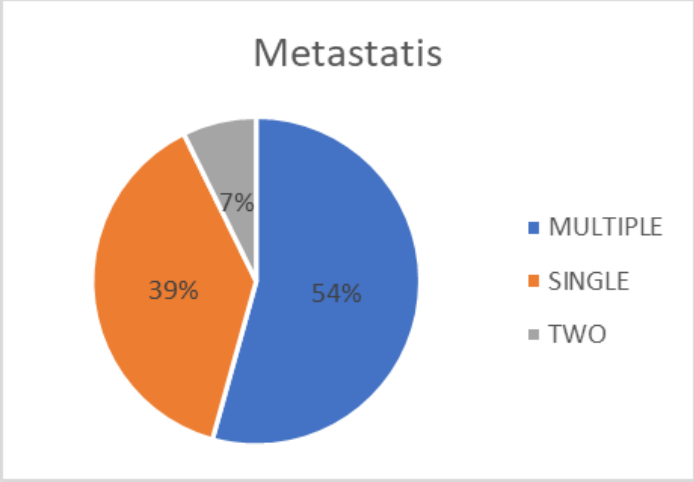

Figure 3: Pie diagram showing the distribution of patients according to the number of brain metastases.

Most metastases (60%) were located in the supratentorial region, while 11% were located in the infratentorial region. 29% of patients showed lesions in both supra-tentorial and infratentorial locations (Fig. 4).

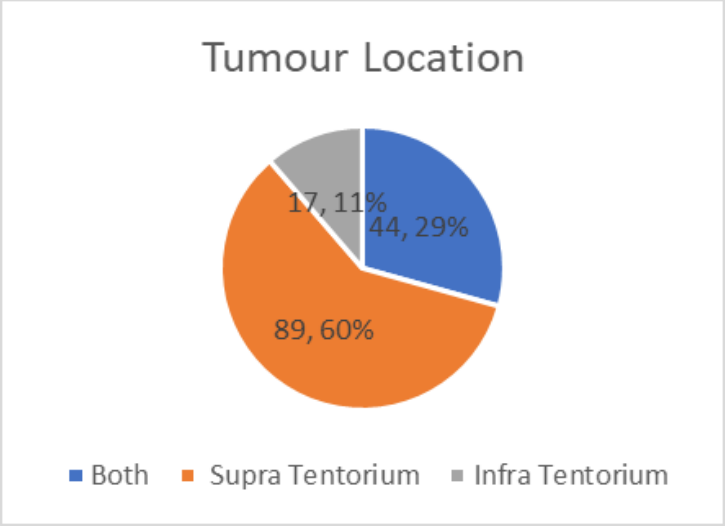

Figure 4: Pie diagram showing different locations of brain metastasis (supratentorial, infratentorial or both).

Among them, the frontal lobe is the most common site of brain metastasis. Of 151 patients, 90 (59%) had frontal lobe metastasis. 58 patients (38%) had parietal and cerebellar metastasis. Two patients also showed meningeal metastasis and both had primary hematological malignancy. 82 Patients (54%) showed bilateral involvement. Of the remaining patients, 27% had left-sided brain involvement and 19% had right-sided involvement, with no statistically significant result (Fig. 5).

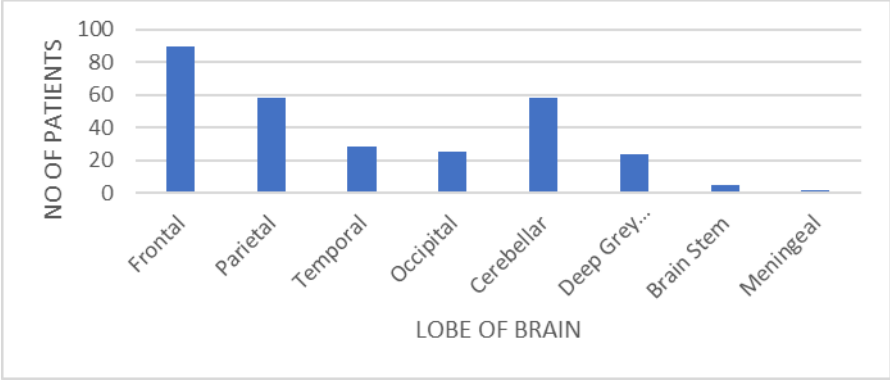

Figure 5: Bar diagram depicting distributions of patients according to different lobes of brain involvement.

In this study, out of 151 patients, 105 patients (70%) had uncontrolled primary tumors and 46 patients (30%) had controlled primary tumors during the diagnosis of brain metastasis.

Headache is the most common presenting symptom, followed by vomiting and Focal Neurological Disease (FND). 78 patients presented with headaches and 44 patients with vomiting. 35 patients don't have any symptoms. They were all diagnosed through an evaluation, which included a CE-MRI scan of the brain. 26 patients presented with other symptoms like head reeling, dizziness, vision problems and scalp pain.

In this study, 35% of patients exhibited only brain metastasis, while 65% had metastasis at another site in addition to the brain. Out of these, 65% of patients have bone metastasis as the most common site (28%), followed by lung and liver metastasis. 16% of patients showed another site of metastasis, like the adrenal gland, kidney, skin nodules or retroperitoneal lymph node.

Most patients with brain metastasis (60%) are diagnosed upfront during primary evaluation. Only five patients (3%) developed

brain metastasis five years after diagnosis of the primary. 20 patients (13%) developed brain metastasis within 1-2 years of diagnosing the primary disease. The most common dose prescriptions for Whole Brain Radiation Therapy (WBRT) are 30Gy/10 fractions and 20Gy/5 fractions. In our study, 54% of patients received 30Gy in 10 fractions and 43% received 20Gy in 5 fractions. Only 3% of patients were treated with other dose prescriptions, such as 25Gy/10 fractions, 30Gy/15 fractions and 25Gy/5 fractions, depending on the patient's performance status. All the clinicodemographic parameters are summarized in Table 1.

SL No	Variables	Group	No of Patients (Percentage)
1	Age Group in Years	<20	0 (0%)
		20-30	4 (2.64%)
		30-40	18 (11.9%)
		40-50	47 (31.12%)
		50-60	45 (29.8%)
		60-70	29 (19.2%)
		>70	8 (5.29%)
2	Gender	Male	82 (54.3%)
		Female	69 (45.69%)
3	Primary	Lung	93 (61.5%)
		Breast	25 (16.5%)
		Esophagus	1 (0.66%)
		Gastrointestinal	8 (5.29%)
		Genito-Urinary	4 (2.64%)
		Gynaecological	3 (1.98%)
		Head And Neck	7 (4.63%)
		Lymphoma	2 (1.32%)
		Melanoma	1 (0.66%)
		Pancreato-Biliary	5 (3.31%)
		Other	2 (1.32%)
4	Histology	Adenocarcinoma	89 (58.9%)
		Idc	22 (14.5%)
		Small Cell Carcinoma	6 (3.97%)
		Squamous Cell Carcinoma	14 (9.27%)
		Other	20 (13.2%)
5	No. of Mets	Single	58 (38.4%)
		Two	11 (7.28%)
		Multiple	82 (54.3%)
6	Tentorial Site	Supratentorial	89 (58.9%)
		Infratentorial	17 (11.2%)
		Both	44 (29.1%)
7	Lobe of Brain	Frontal	90 (59.6%)
		Parietal	58 (38.4%)
		Temporal	28 (18.5%)
		Occipital	25 (16.5%)
		Cerebellar	58 (38.4%)
		Deep Gray Matter	24 (15.8%)
		Brainstem	5 (3.31)
		Meningeal	2 (1.32%)
8	Site of Involvement	Right	28 (18.5%)

		Left	41 (27.1%)
		Bilateral	82 (54.3%)
9	Primary Disease Status	Controlled	46 (30.4%)
		Uncontrolled	105 (69.5%)
10	Symptoms	Headache	78 (51.6%)
		Vomiting	44 (29.1%)
		Seizure	8 (5.29%)
		Fnd	33 (21.8%)
		Ataxia	10 (6.62%)
		Other	26 (17.2%)
		No Symptoms	35 (23.1%)
11	Other Sites of Metastasis	No	67 (44.3%)
		Lung	22 (14.5%)
		Liver	19 (12.5%)
		Bone	55 (36.4%)
		Other	30 (19.8%)
12	Duration for Bm Diagnosis	Upfronts	91 (60.2%)
		0-1	18 (11.9%)
		1-2	20 (13.2%)
		2-3	10 (6.62%)
		3-4	3 (1.98%)
		4-5	4 (2.64%)
		>5	5 (3.31%)
13	Dose Prescription	20gy	65 (43.0%)
		30gy	81 (53.6%)
		Other	5 (3.31%)

Table 1: Clinicodemographic parameters.

In this study, the median survival rate of patients with brain metastasis was eight months [from 1 to 32 months]. The mean survival was 9.07 ± 5.487 months (Table 2).

SL No	Parameter	Value
1.	Mean (In Months)	9.07
2.	Standard Error of Mean	0.446
3.	Median (In Months)	8
4.	Mode (In Months)	7
5.	Standard Deviation	5.487
6.	Variance	30.102
7.	Minimum	1 Month
8.	Maximum	32 Months

Table 2: Survival factors.

Univariate Analysis (Table 3).

SL No	Parameter	Group	Survival In Months	Chi-Square	P Value
1.	Age	20-30	8		
		30-40	8		
		40-50	9	142	0.041

		50-60 60-70 >70	8 7 7		
2.	Gender	Male Female	8 8	22.23	0.506
3.	Primary	Breast Lung Other	9 8 8	242.479	0.273
4.	Histology	Adenocarcinoma Idc Other	8 8.5 8	100.41	0.832
5.	Number of Mets	Single Two Multiple	8.5 8 8	122.61	0.001
6.	Tentorial	Supratentorial Infratentorial Both	8 8 8.5	83.89	0.715
7.	Primary Disease Status	Controlled Uncontrolled	8 8	50.238	0.309
8.	Duration Of Brain Mets Diagnosis (In Years)	Upfront 0-2 2-5 >5	8 9 8 8	114.37	0.93
9.	Dose In Gray	20 30 OTHER	8 8 9	25.95	0.303

Table 3: Survival according to analyzed parameters.

Survival With Age

The median survival for a patient with brain metastasis is nine months for the age group of 40-50 years and for the age group of > 60 years, it is only seven months. This result is statistically significant ($p < 0.041$) (Fig. 6).

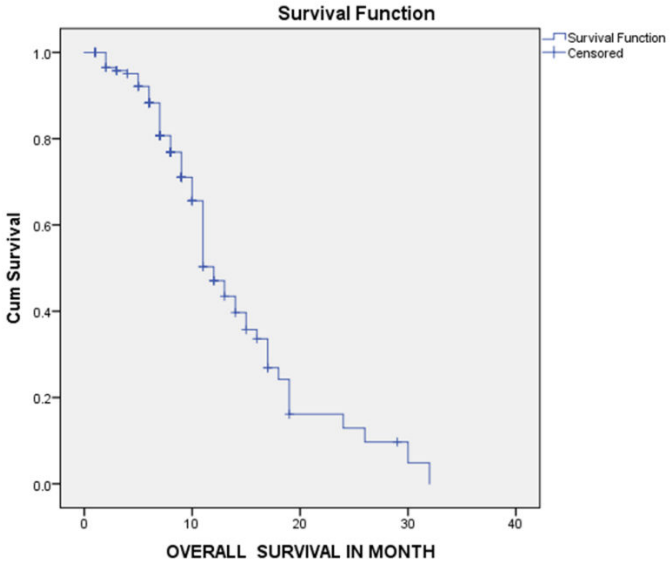

Figure 6: Showing the Kaplan Meier Survival Curve.

Survival With Gender
The median survival was eight months for both male and female genders without a statistically significant result (p=0.506).

Survival With Primary Cancer Site
Median survival after diagnosis of brain metastasis is nine months in patients with breast cancer (n=25) and eight months for lung cancer primary (n=93) and other malignancies (n=33). However, this result was not statistically significant (p = 0.273).

Survival With Histology of Primary
The median survival for patients with infiltrating ductal carcinoma was 8.5 months and for all other histologies, eight months, without any statistically significant result (p=0.832).

Survival With the Number of Brain Metastasis
The median survival times were eight months for patients with multiple lesions and 8.5 months for those with a single lesion. This difference is the statistical significance (p=0.001).

Survival With Lesion Site
The median survival was eight months for both supratentorial and infratentorial lesions, with a survival rate of 8.5 months for both groups. However, this result was not statistically significant (p = 0.715).

Survival With Primary Tumour Status
The median survival was eight months for both patients with controlled and uncontrolled primary disease (p = 0.309).

Survival With Duration of Metastasis
The survival was only eight months for patients with an upfront diagnosis of brain metastasis. The patients were diagnosed within 0-2 years; the survival rate was nine months. Again, the survival was only eight months for patients diagnosed with brain metastasis after two years (p=0.93).

Survival With Treatment
The survival rate was eight months for patients treated with either dose prescriptions of 30Gy/10 fractions or 20Gy/5 fractions (p = 0.303).

Discussion
Brain metastasis is the most common intracranial neoplasm in adults. It occurs in 10-30% of adults with disseminated tumors (1). 1,00,000-1,70,000 new brain metastasis cases are diagnosed annually in the United States [12]. A study by Victor showed that about 60% of patients with brain metastasis are aged between 50 and 70 years [16]. Similarly, in our study, the median age was 50 years (ranging from 20 to 75 years), with 60% of patients falling within the 40- to 60-year age range. In this study, the age of diagnosis significantly affects survival, with better outcomes in the 40-50 years age group (p < 0.041).

Brain metastasis is most commonly associated with lung primary (40-50%), followed by Breast and melanoma [4]. In our study, lung carcinoma constituted 61%, followed by breast cancer at 16%. Out of all lung primaries, 58% were adenocarcinoma histology, followed by 3% small cell carcinoma. 14% of patients showed infiltrating duct carcinoma histology. Brain metastasis is primarily diagnosed synchronously in 60% of cases and less commonly metachronous in 40%. The study by Nussbausm and Delattre, et al., showed that approximately 80% of Brain metastatic lesions are in the cerebrum, 15% in the cerebellum and 5% in the brainstem [17]. In our study, 60% of the cases showed a supratentorial location. According to the location in different lobes, the frontal lobe is the most common site of BMs (n = 90), followed by the parietal lobe (n = 58). Only 0.5% of patients showed meningeal metastasis, which is more common in hematological malignancies.

The most common symptoms of BMs included headache, vomiting, seizure, focal neurological deficit and ataxia. Victor, et al., study showed headache (42%) and seizure (21%) are the two most common presenting symptoms [16]. In the present study, 78 patients presented with headaches, followed by 44 patients with vomiting and 35 patients were asymptomatic. A study by Victor

opined that brain secondaries are most common in patients with uncontrolled primary tumors [16]. 70% of our patients had an uncontrolled primary, which indicates that brain metastasis mainly develops in patients with an uncontrolled primary.

The decision regarding treatment for brain metastasis depends on the patient's performance status, the number of brain metastases, the status of the primary disease and the presence of metastases in other organs. Management strategies for brain metastasis include surgery, Whole-Brain Radiotherapy (WBRT), Stereotactic Radiosurgery (SRS) and Stereotactic Radiotherapy (SRT) [18]. Doses for WBRT are typically 30Gy in 10 fractions or 20Gy in 5 fractions. This two-fractionation schedule does not differ in terms of symptom control or overall survival.[19] In this study, 54% of patients were treated with WBRT at 30Gy/10 fractions and 43% with 20Gy/5 fractions. Only 3% of patients received prescriptions for any other dose. Similar to the Borgelt, et al., study, our study showed a comparable overall survival of 8 months for patients treated with either dose prescription. Popper, et al., showed that lung cancer has a greater propensity to spread to the bone, adrenal glands and brain [20]. 65% of patients exhibited metastasis to sites other than the brain. Out of this, the bone is the most common site of metastasis (28%). Other common sites of metastasis are the liver and adrenal glands.

Out of 151 patients, 43 patients survived up to 6 months. In our study, the Median Survival was eight months (range, 1 to 32 months). Our analysis yielded similar survival rates to those reported by Ekici, et al., with a median survival of 6.7 months [21]. They also identified a patient with a single brain metastasis from a controlled primary tumor who had better survival. The younger age group (40-50 years old) with single brain lesions had better survival, with a statistically significant result ($p < 0.05$) in our study. Rostagi, et al., identified that female gender, performance status, breast primary, metachronous brain metastasis, solitary outcome and controlled primary were associated with better survival in brain metastasis [22].

Limitations

It employs a retrospective and non-randomized design. So, a larger sample size and disease-specific graded factors for each disease site could reveal more factors affecting survival. SRS or SBRT treatment may improve survival in patients with limited lesions and a controlled primary tumor.

Conclusion

This study highlights that brain metastasis is most common in elderly males with lung adenocarcinoma, with the frontal lobe being the predominant site. Most lesions were multiple and the most common WBRT prescription was 30Gy in 10 fractions. While the overall prognosis remains poor, younger patients (40-50 years) and those with a single brain lesion demonstrated relatively better survival outcomes. Other factors, such as gender, WBRT dose and site of lesion, did not significantly affect survival. These findings should be consolidated with a larger prospective study.

Conflict of Interests

The authors have no conflict of interest to declare related to this article.

Funding

No source of funding for this study.

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