

Assessment of Brain Metastasis at Diagnosis in Non–Small-Cell Lung Cancer: A Prospective Observational Study From North India

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PURPOSE The incidence of symptomatic brain metastasis at diagnosis in non–small-cell lung cancer (NSCLC) is 5%-10%, and up to 40% develop during the disease course. There is a paucity of data supporting the role of brain imaging at diagnosis in asymptomatic cases particularly from resource-constraint settings. Here, we present our experience of mandatory baseline brain imaging with contrast-enhanced computed tomography (CECT) scans of all patients with NSCLC.

MATERIALS AND METHODS This was a prospective observation study of patients with NSCLC with mandatory baseline brain CECT and a CNS examination. All histology proven patients with NSCLC diagnosed between January 2018 and October 2019 were included irrespective of stage.

RESULTS A total of 496 patients were enrolled. The median age was 57 years (range, 23-84) with majority being males (75%) and smokers (66%). The prevalence of epidermal growth factor receptor mutations and anaplastic lymphoma kinase fusions was 33.4% and 12%, respectively. Brain imaging leads to upstaging in 7% cases. The prevalence of brain metastases was 21% (n = 104), with half being asymptomatic (51%). Factors associated with higher proportion of brain metastasis were young age (≤ 40 years), adenocarcinoma histology, poor Eastern Cooperative Oncology Group performance status (3 and 4), and high neutrophil-lymphocyte ratio (NLR) (> 2.5). After a median follow-up of 10.8 months (95% CI, 7.33 to 12.73), the median overall survival was 7.46 versus 12.76 months (hazard ratio 0.67; 95% CI, 0.46 to 0.96; $P = .03$) in patients with and without brain metastases, respectively. On multivariate analyses, high NLR and molecular graded prognostic assessment affected the overall survival significantly.

CONCLUSION In our study, 21% of patients had brain metastasis at diagnosis detected with a mandatory baseline brain imaging with CECT. NLR and molecular graded prognostic assessment are significant predictors of survival in patients with brain metastasis.

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INTRODUCTION

Lung cancer has been one of the most common cancers in the world for the last several decades. As per GLOBOCAN 2018, it is the most commonly diagnosed cancer (11.6%, 2.1 million new cases) and the leading cause of cancer death (18.4%, 1.8 million deaths).¹ Non–small-cell lung cancer (NSCLC) constitutes about 85% of all lung cancers. About 60%-70% of patients with NSCLC have either stage III B or stage IV disease at presentation.² The prevalence of brain metastasis at presentation is 15%-20%,^{3,4} and up to 40% eventually develop during its disease course.⁵ In about 25% of cases, brain is the first site of disease recurrence.⁶ The established risk factors for developing brain metastases are adenocarcinoma histology, positive driver mutation status, advanced nodal status, advanced tumor stage, and younger

age.^{6,7} Brain metastases are associated with significant morbidity, mortality, and impaired quality of life. The available therapeutic approaches include whole brain radiotherapy (WBRT), surgery, stereotactic radiosurgery (SRS), chemotherapy/tyrosine kinase inhibitors (TKIs), and symptomatic or supportive treatment.^{5,8}

The advancement in the diagnosis and better systemic control of extracranial disease have resulted in increased incidence of brain metastases in recent times.⁹ The baseline use of brain imaging in asymptomatic patients is a topic of conflict.¹⁰ A significant fraction of asymptomatic brain metastasis may be missed by neurologic examination alone in patients with lung cancer.⁴ Although NCCN recommends brain imaging, a contrast magnetic resonance imaging (MRI) is preferred, from stage II onward. However, recommendations for baseline brain imaging particularly in patients with advanced NSCLC

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CONTEXT

Key Objective

In this study, we evaluated the role of mandatory brain imaging using contrast-enhanced computed tomography (CECT) in patients with non-small cell lung cancer.

Knowledge Generated

With mandatory CECT brain at baseline, we could detect brain metastasis in 21% of patients, and half of them were asymptomatic. It resulted in over staging in 7% of patients. Neutrophil-lymphocyte ratio and molecular GPA (graded prognostic assessment) could significantly predict survival in patients with brain metastasis.

Relevance

Our study is particularly relevant in resource constraint settings and support that CECT based brain imaging can help in diagnosis and appropriate stratification of patients with brain metastasis.

who are asymptomatic for brain metastases are weak and controversial.^{11–13} There is a paucity of data regarding the exact frequency, risk factors, and clinicopathologic and molecular correlation of asymptomatic and symptomatic brain metastasis at presentation. Performing MRI for all the patients may not be feasible in resource-constraint settings like ours. Although contrast-enhanced computed tomography (CECT) is considered optional imaging modality for this purpose, data on its use as a screening modality to detect brain metastasis are sparse. In this prospective observational study, we aimed to assess the frequency of brain metastases detected by mandatory CECT in patients with NSCLC at the time of diagnosis and their associated clinicopathologic and molecular variables, and effect on survival outcome.

MATERIALS AND METHODS

It was a single-center prospective observational study conducted between January 2018 and July 2019, and

patients were followed for a minimum of 6 months at an interval of 2 months. We included treatment-naïve patients of age 18-75 years with a histopathologic diagnosis of NSCLC. Patients who have been treated outside before referral to our center or with renal failure defined as creatinine clearance < 30 mL/min were excluded. All patients underwent complete physical examination and comprehensive neurologic assessment. At baseline, a CECT head was performed to evaluate brain metastases and leptomeningeal involvement along with the extracranial staging evaluation. In view of financial constraints and logistics at our center, computed tomography (CT) was included as an imaging modality rather than MRI. Patients who had MRI or a positron emission tomography (PET), which included a contrast CT of brain already done before referral, were included in the study, and CECT was not repeated. All the images were reviewed by our radiology team. All patients were staged according to AJCC (8th ed). Extracranial staging was done either by PETCT or CECT. Epidermal growth factor receptor (EGFR) testing was done by polymerase chain reaction, or anaplastic lymphoma kinase (ALK) testing was done by IHC D5F3 on Ventana staining platform (Immunohistochemistry). Molecular graded prognostic assessment (molGPA) (20) was done, which is a composite score of variables such as age, number of brain metastases, extracranial metastases, Karnofsky performance scale, *EGFR*, or *ALK* gene status, and the score ranges from 0 to 4. Neutrophil lymphocyte ratio (NLR) was calculated by manual peripheral blood smear examination, and the cutoff level for high NLR was taken as ≥ 2.5 (16). The clinicopathologic, treatment, and molecular status details were collected. Patients were followed from the date of enrollment until last date of follow-up or death, whichever was earlier and those who stopped attending clinic were contacted on telephone. The data were censored on December 31, 2019. Overall survival was calculated from date of enrollment until the date of death or last contact when patient was known to be alive. Study protocol was approved by Institute Ethics Committee.

Study protocol was approved by Institute Ethics Committee with effect from January 31, 2018, Ref No. IECPG-570/20.12.12.2017,RT—42/31.1.2018, and all subjects have

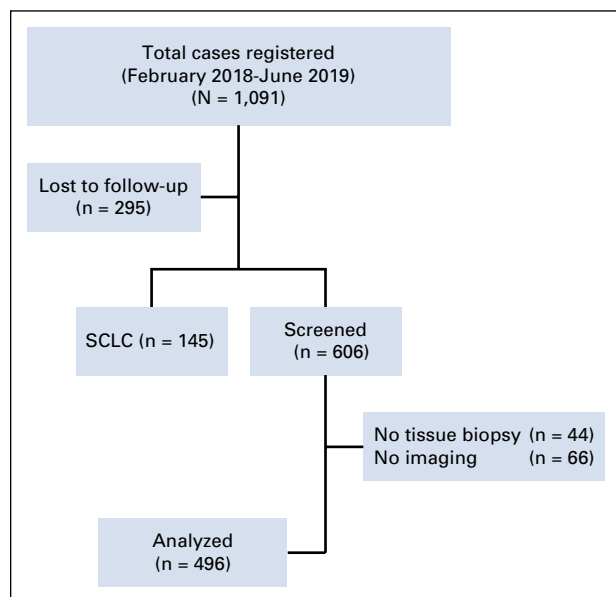


FIG 1. Flowchart depicting screening and final inclusion of the study patients. SCLC, small-cell lung cancer.

TABLE 1. Baseline Characteristics of Patients (N = 496)

Baseline Characteristic	No. (%)
Age (median)	57 years (range, 23-84 years)
Sex	
Male	374 (75)
Female	122 (25)
Smokers	326 (66)
ECOG PS	
0	12 (2)
1	193 (39)
2	203 (40)
3	64 (13)
4	24 (5)
Histology	
Adenocarcinoma	315 (64)
Squamous cell carcinoma	134 (27)
NSCLC NOS	47 (9)
<i>EGFR</i> mutation status (n = 293)	
Positive	98 (33.4)
Negative	185 (66.6)
<i>EGFR</i> mutation type (n = 105)	
Exon 18	2 (2)
Exon 19	61 (62)
Exon 20	4 (4)
Exon 21	30 (30)
<i>ALK</i> rearrangement status (n = 265)	
Positive	33 (12)
Negative	232 (88)
Extracranial stage (AJCC, 8th ed)	
I	2 (0.4)
IIA	8 (1.6)
IIB	10 (2)
IIIA	37 (7)
IIIB	66 (13)
IIIC	41 (8)
IV	332 (64)
Overall stage (AJCC, 8th ed)	
I	2 (0.4)
IIA	7 (1.4)
IIB	7 (1.4)
IIIA	29 (5.8)
IIIB	52 (10.5)
IIIC	31 (6.2)
IV	368 (74)

(Continued in next column)

TABLE 1. Baseline Characteristics of Patients (N = 496) (Continued)

Baseline Characteristic	No. (%)
Brain metastases	
Present	104 (21)
Absent	392 (79)
Upstaging to stage 4	36 (7)
IIA-III A	12
IIIB	14
IIIC	10
Brain imaging modality	
CECT	412 (83)
MRI	84 (17)

Abbreviations: AJCC, American Joint Cancer Committee; ALK, anaplastic lymphoma kinase; CECT, contrast enhanced computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; MRI, magnetic resonance imaging; NSCLC NOS, non-small-cell lung cancer not otherwise specified.

given their written informed consent before their inclusion. The research was conducted in accordance with the World Medical Association Declaration of Helsinki. Consent has been taken by the patients for the publication.

Statistical Analysis

The descriptive statistics were used to assess the baseline parameters. Overall survival was calculated by Kaplan-Meier method. Chi-square test was used to assess the correlation of variables with brain metastases. Logistics univariate and multivariate analyses were done by Cox proportion hazard model for evaluating factors affecting the survival. STATA version 13 (Stata Statistical Software: Release 13; StataCorp LP, College Station, TX) was used for all the statistical analysis.

RESULTS

A total of 1,091 patients were registered at our lung cancer clinic during January 2018 to October 2019. Small-cell lung cancer was diagnosed in 145 patients, and 295 were lost to follow-up before complete evaluation. Eventually, 606 patients were screened of which 44 patients were excluded because of lack of a confirmed tissue diagnosis, and brain imaging could not be performed in 66 patients because of various reasons (20 had lost to follow-up, 24 did not undergo imaging despite advising, and 22 did not give consent). Finally, 496 patients were eligible for analysis as depicted in [Figure 1](#).

The median age was 57 years (range, 23-84) with the male predominance (75%, n = 374). Smokers constituted 66% (n = 326). Most patients (79%, n = 396) had good Eastern

Cooperative Oncology Group performance status (ECOG PS) 1-2. The most common histopathology was adenocarcinoma (64%, $n = 315$) followed by squamous (27%, $n = 134$). EGFR mutation status was done in 81% ($n = 283$) of adenocarcinoma including NSCLC not otherwise specified, and a mutation was detected in 98 (33.4%) cases. The most common mutations were exon 19 deletion (62%, $n = 61$) and L858R (exon 21) (30%, $n = 30$). The ALK gene rearrangement status was available in 73% ($n = 265$) of adenocarcinoma and NSCLC not otherwise specified, with a positivity rate of 12% ($n = 33$). Molecular testing was not available in all the patients because of various reasons like tissue inadequacy and other logistics. Staging workup was done predominantly by CECT, and only 8.3% ($n = 45$) had staging by PETCT. On extracranial staging, patients with stage I were II (0.4%), stages IIA and IIB in 8 (1.6%) and 10 cases (2%) respectively, stages IIIA, IIIB, and IIIC in 37 (7%), 66 (13%), and 41 cases (8%), respectively, and stage IV disease in 332 cases (64%). Brain imaging leads to upstaging in 7% ($n = 36$) of cases, mostly from stage III (6%, $n = 32$) followed by stage II (1%, $n = 4$). Of patients who were upstaged, about 16 were asymptomatic for brain metastases. Baseline characteristics are described in [Table 1](#). The imaging modality used for brain imaging was CECT (83%, $n = 412$) and MRI (17%, $n = 84$) as depicted in [Table 1](#).

Brain metastases were detected in 104 cases (21%), and half of them (51%, $n = 53$) were asymptomatic. CECT was the modality in 51 (49%) patients, and MRI in 53 patients (51%). The CNS lesions were solitary in 41% ($n = 43$), 2-4 in number in 19% ($n = 20$), and > 4 in 38% ($n = 40$) and leptomeningeal disease in 1% ($n = 1$). Nearly half (52%, $n = 54$) of the lesions were supratentorial. Imaging characteristics were perilesional edema, enhancement, midline shift, and hemorrhage in 82% ($n = 86$), 68% ($n = 71$), 18% ($n = 19$), and 2% ($n = 2$) of cases, respectively. Few representative CECT images are shown in [Figures 2A](#) and [2B](#). Among the various strategies used, the CNS-directed and systemic therapy was used in 45% ($n = 45$), only systemic therapy in 32% ($n = 33$), and 27% ($n = 28$) did not

receive any therapy. WBRT was given in 41% ($n = 43$) of patients, of which 53% ($n = 23$) received before starting systemic therapy. Among patients with brain metastases, 12 of 26 EGFR-positive (46%), 8 of 13 ALK-positive (61%), and 22 of 66 mutation-negative or unknown (33%) received WBRT. Four patients (one ALK-positive and three mutation-negative) underwent surgical resection of brain metastasis.

The factors predictive for brain metastases were younger age (≤ 40 years) ($P = .008$), adenocarcinoma histology ($P = .001$), ECOG PS 3-4 ($P = .002$), and high neutrophil lymphocyte ratio ($NLR > 2.5$) ($P = .03$) as depicted in [Table 2](#). Although EGFR- and ALK-mutated patients had numerically higher frequency of brain metastasis as compared with wild type, the differences were not statistically significant.

Patients who had not received any treatment were excluded from survival analysis. After a median follow-up of 10.8 months (95% CI, 7.33 to 12.73), the median overall survival was 7.46 versus 12.76 months (hazard ratio [HR] 0.67; 95% CI, 0.46 to 0.96; $P = .03$) in patients with and without brain metastases, respectively ([Fig 3](#)). Univariate analyses using Cox proportional hazards model for factors predicting survival in patient with brain metastases revealed that ECOG PS 3-4 (HR 2.31; 95% CI, 1.16 to 4.63; $P = .017$), $NLR (> 2.5)$ (HR 5.56; 95% CI, 1.66 to 18.54; $P = .005$), and molGPA (HR 0.2; 95% CI, 0.07 to 0.51; $P = .001$) significantly affected the overall survival, as depicted in [Table 3](#). On multivariate analyses, high NLR (HR 5.16; 95% CI, 1.43 to 18.63; $P = .03$) and molGPA (HR 0.53; 95% CI, 0.32 to 0.88; $P = .012$) remained significant as depicted in [Table 3](#). There was no difference in survival of patients presenting with or without CNS symptoms. [Figures 3](#) and [4](#) show the overall survival difference according to NLR and molGPA.

DISCUSSION

The incidence of brain metastasis at the time of diagnosis detected predominantly with CECT in our study was 21%, with half of the cases being asymptomatic. Similar to our study, Kim et al³ in a prospective cohort of 183 patients with

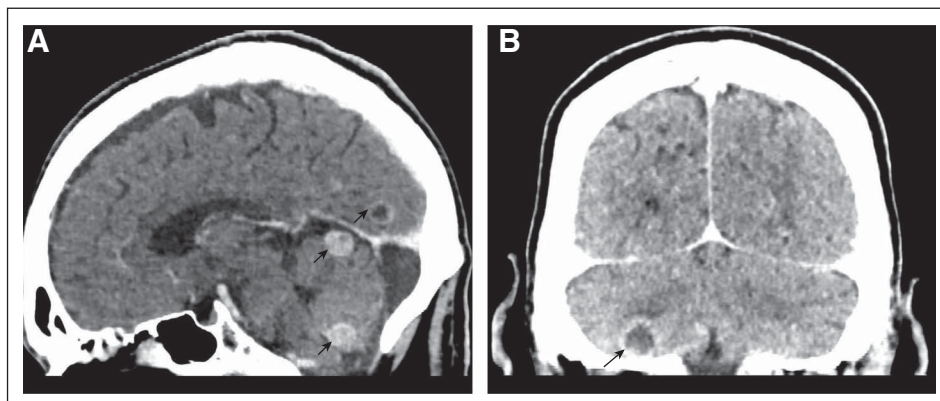


FIG 2. Contrast enhanced computed tomography brain imaging showing (A) a well-defined round enhancing lesions in cerebellum and ring enhancing lesion in occipital lobe and (B) a well-defined ring enhancing lesion in the right inferior cerebellar region (indicated by arrows).

TABLE 2. Predictors of Brain Metastases

Clinical Factor	Brain Metastases, No. (%)		P
	Present, n = 104 (21%)	Absent, n = 392 (79%)	
Age, years			.008
< 40	18 (36)	31 (64)	
41-60	54 (21)	202 (79)	
> 61	31 (15)	158 (85)	
Sex			.9
Male	78 (21)	296 (79)	
Female	26 (21)	96 (79)	
Smoking history			.3
Smokers	64 (20)	262 (80)	
Nonsmokers	40 (24)	130 (76)	
ECOG PS			.002
0-2	75 (19)	333 (81)	
3-4	29 (33)	59 (67)	
NSCLC type			.001
Squamous	5 (4)	129 (96)	
Adenocarcinoma	89 (28)	226 (72)	
NSCLC NOS	10 (21)	37 (79)	
Extracranial stage (AJCC, 8th ed)			.78
I-III A	12 (21)	45 (79)	
IIIB-IIIC	25 (23)	82 (77)	
IV	67 (20)	265 (80)	
EGFR status			.39
Positive	26 (26)	72 (74)	
Negative	58 (31)	127 (69)	
ALK status			.23
Positive	13 (39)	20 (61)	
Negative	68 (29)	164 (71)	
NLR			.03
≤ 2.5	23 (14.8)	134 (85.2)	
> 2.5	62 (22.7)	210 (77.3)	

NOTE. Bold type indicates statistical significance.

Abbreviations: AJCC, American Joint Cancer Committee; ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NLR, neutrophil lymphocyte ratio; NSCLC NOS, non-small-cell lung cancer not otherwise specified.

lung cancer using limited MRI brain reported brain metastases in 20.8% cases of which 81% were asymptomatic. In a retrospective analysis, Jena et al¹⁴ have reported a higher rate of brain metastasis (35%) using MRI and 46% of these patients were asymptomatic. Mandatory brain imaging at the time of diagnosis in NSCLC tends to pick up more asymptomatic metastasis, and the frequency varies as per the sensitivity of the modality used. The screening modality used in our study was CECT with the limited use of MRI, which might have affected the sensitivity in detection of brain metastases. Schoenmaekers et al¹¹ have previously reported additional

detection of brain metastasis in 4.7% of cases by MRI where CECT was negative. This would probably imply that CT scan is a good option as an initial screening modality as part of baseline staging where MRI could not be done in view of logistics and MRI can be preferred in highly suspicious CT-negative patients. It would have practical implications in resource-limited settings where MRI is not routinely available or affordable. European Society for Medical Oncology clinical practice guidelines do recognize CECT as an optional strategy for detection of brain metastasis in advanced disease but prefer MRI for patients undergoing curative intent treatment.^{12,13}

TABLE 3. Univariate and Multivariate Analysis of Outcome in Brain Metastasis Using Cox Proportional Hazards Model

Variable	n = 76	Median OS (months)	Univariate Analysis			Multivariate Analysis		
			HR	95% CI	P	HR	95% CI	P
Age, years								
< 40	17	6.7 (4.8-NR)	1					
41-60	37	7.5 (4.9-NR)	0.86	0.39 to 1.85	.7			
> 61	22	16.1 (2.7-NR)	0.73	0.34 to 2.10	.73			
Sex								
Male	58	6.1 (4.9-8.9)	1					
Female	18	NR (6.1-NR)	0.48	0.21 to 1.11	.09			
ECOG PS								
0-2	57	12.3 (6.13-NR)	1					
3-4	19	4.86 (1.6-11)	2.31	1.16 to 4.63	.017			
Smoking history								
Nonsmoker	34	12.36 (6.1-NR)	1					
Smoker	42	6.1 (4.4-8.9)	1.8	0.94 to 3.59	.07			
EGFR								
Negative	42	6.1 (4.9-16.1)	1					
Positive	23	13.4 (6.1-NR)	0.66	0.31 to 1.39	.27			
ALK								
Negative	55	7.5 (4.96-13.4)	1					
Positive	11	NR (5.06-NR)	0.28	0.06 to 1.18	.08			
CNS symptoms								
Absent	43	7.53 (5.03-16.16)						
Present	33	7.46 (4.96-NR)	0.98	0.51 to 1.87	.95			
NLR								
≤ 2.5	18	NR (8.9-NR)	1					
> 2.5	48	6.36 (4.8-13.4)	5.56	1.66 to 18.54	.005	5.16	1.43 to 18.63	.012
molGPA ^a								
0	14	4.96 (1.63-6.36)	1					
1	19	7.46 (3-NR)	0.48	0.20 to 1.1	.09			
2	28	16.16 (6.16-NR)	0.20	0.07 to 0.51	.001	0.53	0.32 to 0.88	.015
3	5	6.1 (1.6-NR)	0.71	0.21 to 2.36	.5			
WBRT								
Not received	34	8.9 (2.7-NR)	1		.37			
Received	42	7.46 (5.0-NR)	0.74	0.39 to 1.45				

NOTE. Bold type indicates statistical significance.

Abbreviations: ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; molGPA, molecular graded prognostic assessment; NLR, neutrophil lymphocyte ratio; NR, not reached; OS, overall survival; WBRT, whole brain radiotherapy.

^aMolecular GPA categories divided according to MolGPA scores as follows: (category) 0 = (score) 0-1, 1 = 1.5-2, 2 = 2.5-3, and 3 = 3.5-4.

Asymptomatic detection eventually results in upstaging of disease, which happened in 7% of patients in our study. Almost similar rates of upstaging have been reported by others.^{3,4} Early detection of brain metastases may result in timely initiation of locoregional therapies, which may affect the survival.

The majority of brain lesions in our study were solitary (41%), which was expected by routine imaging. The probability of offering local ablative-like SRS or surgery is higher in solitary brain lesion, which eventually may result in better survival outcome.¹⁵ However, in our cohort, none of these patients could undergo SRS or surgery because of various logistic reasons.

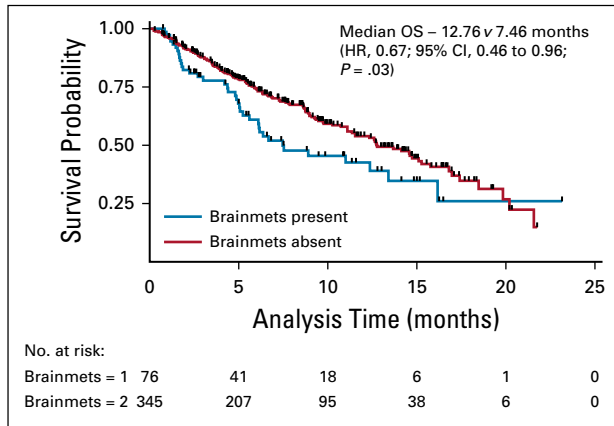


FIG 3. OS with and without brain metastases. HR, hazard ratio; OS, overall survival.

The predictive factors for brain metastases in our study were younger age (< 40 years), adenocarcinoma histology, poor ECOG PS, and high NLR (≥ 2.5). The adenocarcinoma histology is an established risk factor for brain metastases.⁷ It has been previously reported that the younger age group have an increased propensity for brain metastases similar to our study⁷ and timely management in this cohort might improve survival. In our study, poor ECOG PS has been associated with increased risk for brain metastases, which might indicate a more extensive stage or could be vice versa as the patients with brain metastases have a poor general condition overall. NLR is marker of systemic inflammatory response. Meta-analyses have shown adverse effect on overall survival in various solid malignancies with high NLR.¹⁶ It could also reflect higher disease burden or aggressive disease biology.¹⁷ In our study, it was found to be associated with brain metastases as reported earlier in another study.¹⁸ Higher nodal burden has also been reported to have a higher incidence of brain metastases in early and locally advanced disease. However, we could not

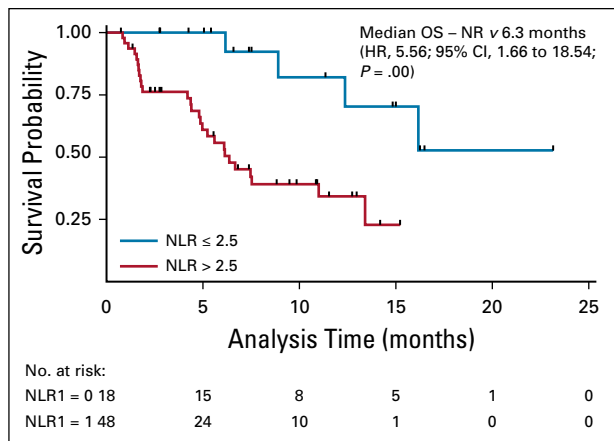


FIG 4. OS in brain metastasis stratified by NLR. HR, hazard ratio; NLR, neutrophil-lymphocyte ratio; NR, not reached; OS, overall survival.

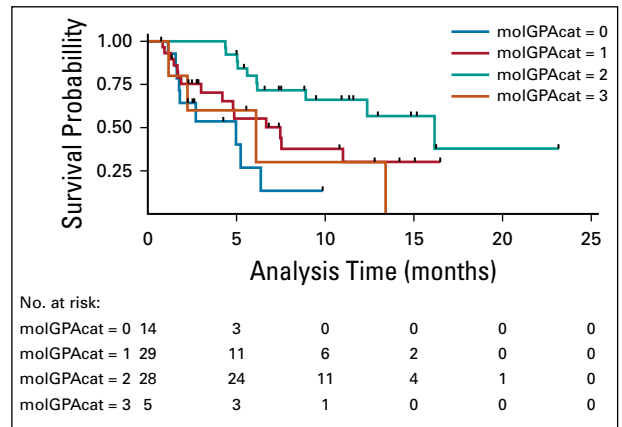


FIG 5. OS in brain metastases stratified by molGPA. molGPA categories divided according to molGPA scores as follows: (category) 0 = (score) 0-1, 1 = 1.5-2, 2 = 2.5-3, and 3 = 3.5-4. molGPA, molecular graded prognostic assessment; OS, overall survival.

demonstrate this association possibly because of smaller numbers of early and locally advanced cases in our cohort.

The frequency of brain metastases in ALK-positive patients was higher (39%) as compared with ALK-negative patients (29%); however, it was not significant statistically. We did not observe any difference in frequency of brain metastases in EGFR-mutated patients, perhaps owing to smaller numbers. This is in contrary to the studies, which have demonstrated higher incidence of brain metastases in EGFR- and ALK-mutated patients.^{19,20} Another study, which included majority patients from India, reported approximately two-fold higher incidence of brain metastasis in patients harboring EGFR mutations.²¹

The survival of patients with brain metastasis remains dismal. The median overall survival of 7.46 and 12.76 months in patients with and without brain metastases in our study is lower compared with that in other studies.^{3,21} It could be possibly due to the fact that it was not an interventional study and the treatment arms were not supervised. Even WBRT could be received by only 41% of the patients with brain metastasis, and the use of CNS effective newer TKIs was very limited.

The stratification of the patients with brain metastases using validated molGPA score can help the clinician for the prognosis and for therapeutic decisions. We have used this score in our Indian population, which helps in better categorization and intensification of treatment from the very beginning. Sperduto et al²² stratified patients with brain metastases using molGPA score, but the median survival was remarkable (nearly 4 years) in those with adenocarcinoma histology and a molGPA score of 3.5-4 compared with ours, which might be due to the lower use of targeted therapy, and only half received combined systemic and CNS-directed therapy because of the logistics and patient preferences. The patients who had an NLR of ≤ 2.5 had significantly better median survival in our study (Fig 5). A

similar study had shown a better overall survival in low NLR cohort.²³

The strengths of our study are being the largest prospective study from resource-limited setting and demonstrating feasibility of CECT-based screening for brain metastasis. The limitations include the limited use of MRI in CECT-negative patients. As it was an observational study, treatment interventions like SRS and WBRT were not controlled based on the symptoms or number of brain metastases.

WBRT could be delivered only in 41% of patients because of logistics, which might have an impact on survival. It was a single-center study. There was limited use of CNS-effective TKIs because of high cost.

In conclusion, mandatory baseline brain imaging with CECT leads to detection of brain metastases in up to 21%, with half being asymptomatic. The disease is upstaged in 7% after brain imaging. molGPA helps in appropriate risk stratification for a better patient care and management.

AFFILIATIONS

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PRIOR PRESENTATION

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DATA SHARING STATEMENT

The authors declare that the data are available in Microsoft Office Sheets format and can be verified by the authors when needed. Patient personal details have been deidentified.

AUTHOR CONTRIBUTIONS

Conception and design: Prabhat Singh Malik, Sushmita Pathy

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Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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