Prevalence, Treatment Patterns, and Survival by Age in Patients Diagnosed with Metastatic Non-Small Cell Lung Cancer (mNSCLC) and Brain Metastases (BM) in the United States (US)

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Background

- Of 220,000 patients diagnosed with non-small cell lung cancer annually, 57% present with metastatic disease (mNSCLC). The 5-year mNSCLC survival rate is 7%.[1]
- Estimates of brain metastases (BM) incidence among NSCLC patients range from 10% to 30% generally and over 40% for patients with mutations such as $KRAS^{G12C}$.[2-7]
- BM are resistant to treatment by most chemotherapeutic drugs, attributed to the inability of drugs to cross the blood-brain barrier, particularly for patients with microscopic metastases.[8,9]
- BM may indicate poor prognosis, with evidence of low overall and progression-free survival with an increased chance of neurological deterioration.[10-11]

Objective

- To estimate the prevalence, treatment modalities, and survival by age in patients diagnosed with mNSCLC and BM in the US.

Methods

Data

Surveillance, Epidemiology, and End Results (SEER, 2016-2019), which includes patient demographic and mortality data for 27% of all cancer registries in the US, inclusive of details about the cancer (location, stage, grade, histology, and initial course of cancer-directed therapy).

Inclusion and Exclusion Criteria

Patients diagnosed with cancer of the lung and bronchus between January 1, 2016-December 31, 2019, and ≥18 years old, with mNSCLC identified at diagnosis were included. Excluded patients were those diagnosed at autopsy, without known age at diagnosis, missing follow-up information for survival analyses, or patients with small cell lung cancer (histology codes 8002, and 8041-8045).

Outcome Variables

- Type of metastasis by age.
- Treatment modalities (e.g., surgery, radiation, systemic therapy) among patients with BM.
- Survival measured from diagnosis to death by treatment modality.

Statistical Approach

- Estimate of the proportion of mNSCLC patients with BM at diagnosis for each age cohort.
- Description of demographic and clinical characteristics by BM status at diagnosis, as well as treatment type among patients with BM by age.
- Comparison of mNSCLC patients with and without BM.
- Cox proportional hazards models were applied to identify demographic and clinical factors associated with risk of death.

Table 1. Patient Characteristics

Variable	mNSCLC *with* BM	mNSCLC *without* BM	All mNSCLC patients
	N = 16,508 (26.3%)	N = 46,252 (73.7%)	N = 62,760 (100%)
	% (N) or Mean (SD)	% (N) or Mean (SD)	% (N) or Mean (SD)
Age at Diagnosis (years)	66.2 (10.4)	70.6 (11.0)	69.4 (11.0)
Male (%)	51.2% (8,452)	54.4% (25,174)	53.6% (33,626)
White (%)	75.0% (12,387)	77.6% (35,893)	76.9% (48,280)
Histology			
Squamous (%)	12.0% (1,979)	21.4% (9,893)	18.9% (11,872)
Adenocarcinoma (%)	71.2% (11,753)	62.1% (28,739)	64.5% (40,492)
All Other (%)	16.8% (2,776)	16.5% (7,620)	16.6% (10,396)
Mean Time to Treatment (mo.)	1.2 (1.0)	1.6 (1.3)	1.5 (1.2)

Table 2. Metastatic Site at Diagnosis and Treatment Modality by Presence of Brain Metastases

Variable	mNSCLC *with* BM	mNSCLC *without* BM	All mNSCLC patients
	N = 16,508	N = 46,252	N = 62,760
	% (N)	% (N)	% (N)
Metastatic Site(s) at Diagnosis			
Brain	100.0% (16,508)	0.0% (0)	26.3% (16,508)
Liver	18.6% (3,069)	17.9% (8,292)	18.1% (11,361)
Bone	38.7% (6,390)	40.8% (18,874)	40.3% (25,264)
Lung	25.6% (4,219)	32.4% (14,984)	30.6% (19,203)
Other Known Site	30.2% (4,990)	43.4% (20,057)	39.9% (25,047)
Initial Treatment Modality			
Surgery*	2.6% (424)	3.3% (1,520)	3.1% (1,944)
Systemic + Radiation	42.7% (7,047)	16.6% (7,668)	23.4% (14,715)
Systemic w/o Radiation	8.9% (1,466)	30.2% (13,984)	24.6% (15,450)
Radiation Alone	28.7% (4,731)	11.2% (5,164)	15.8% (9,895)
None/Unknown	19.8% (3,264)	42.0% (19,436)	36.2% (22,700)

* The 'Surgery' category is not mutually exclusive as surgery patients may also receive systemic and/or radiation therapy

Limitations

- Metastatic disease reported at diagnosis only; no restaging.
- Minimal data availability for radiation and systemic therapy. Reported as "yes" vs. "no or unknown" which may lead to underestimates of treatment frequency and an inability to compare treatments directly.
- Timeframe reported in SEER data. Treatments available and prognosis have evolved as new mNSCLC treatments became available after 2019.

Results

Patient Characteristics

- Of a total of 175,690 NSCLC patients, 62,760 met all eligibility criteria. (Table 1)
- mNSCLC patients with BM were younger (66.2y vs. 70.6y), less likely to be male (51.2% vs. 54.4%) or white (75.0% vs. 77.6%) compared to those without BM. Additionally, while only 16.7% of patients with squamous mNSCLC had BM, 29.0% of adenocarcinoma patients had BM. (Table 1)
- Prevalence of BM was 38% among patients aged <45y and 11% among those aged 85-100y. BM had the steepest decline in incidence by age vs. other metastasis sites. (Figure 1)
- Of all BM patients, 5,855 had BM alone, with no other metastases present. The most observed metastatic site in combination with the brain was bone (N=1,946), followed by "other" sites, lung, and liver, respectively. (Not shown)

Treatment Modalities

- Patients with BM were more likely to receive systemic therapy with radiation (42.7% vs. 16.6%), but less likely to receive systemic therapy without radiation (8.9% vs. 30.2%) compared to patients without BM (Table 2).
- Treatment modality selected among BM patients varied by age. Use of systemic therapy among patients with BM declined with increasing age, from around 86% of those <45y to about 42% of those aged 85-100y. Conversely, use of radiation alone rose from 13% to 58%. (Figure 2)

Survival

- Risk of death was 20% higher in patients with BM compared to those without BM (hazard ratio=1.20, 95% CI 1.18-1.23).
- BM patients receiving systemic therapy had a higher median overall survival (mOS) than radiation alone, both for those <65 (mOS: 13 months (mo) vs. 2 mo) and ≥ 65 (mOS: 9 mo vs. 2 mo).

Figure 1. Prevalence of Metastases By Site & Age

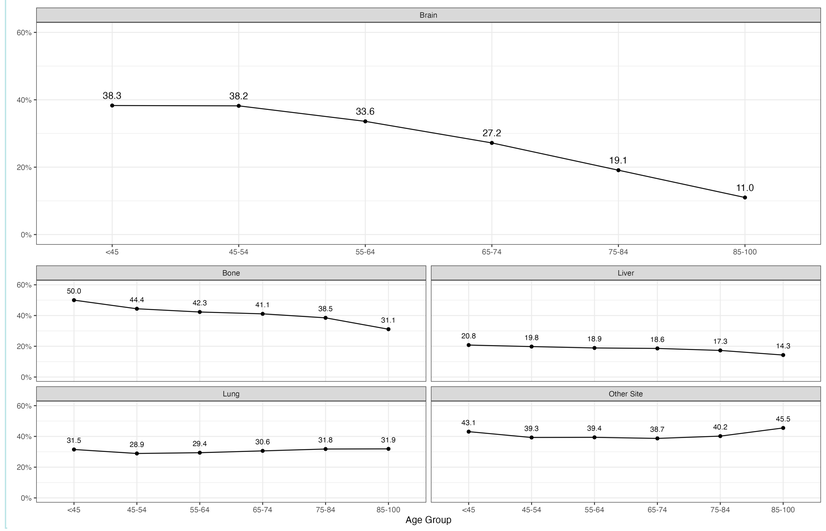
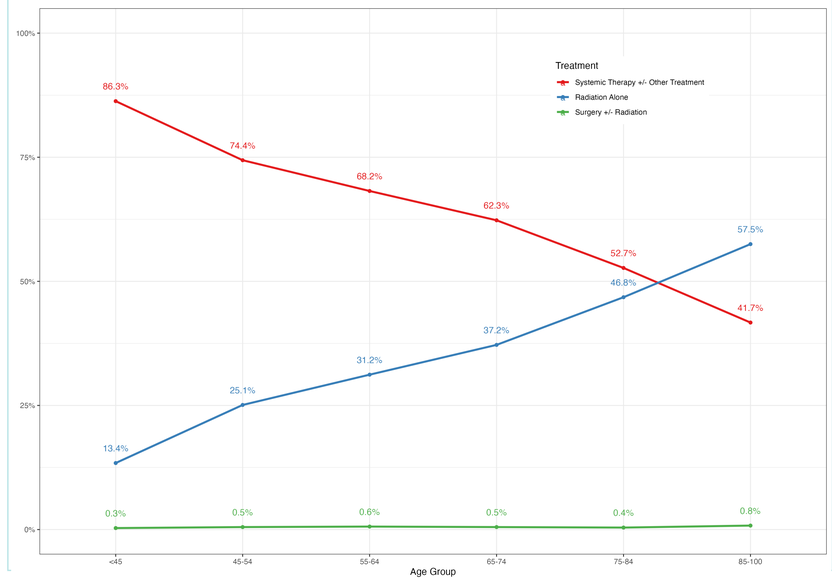


Figure 2. Treatment Modality by Age Group in Treated Population with Brain Metastases



Summary

- **Among patients with mNSCLC, brain metastases are more common among younger patients and those with adenocarcinoma histology.**
- **Use of systemic therapy among patients with BM decreases with age; use radiation alone increases with age. Survival is greatest among BM patients receiving systemic therapy.**
- **Future research should look to identify specific treatment options that improve and optimize survival as well as reduce the humanistic burden for patients with BM. BM screening patterns by age should also be assessed.**

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