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Clinical Factors Associated with 30-Day Mortality Among Patients Undergoing Brain Metastases Radiotherapy

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Running Title: Factors for 30-DM after RT for Brain Metastases

Data Sharing Statement*: The data that support the findings of this study are not publicly available due to patient privacy and ethical restrictions. De-identified data may be available upon request to the corresponding author.*

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Abstract

Background:

Existing brain metastases prognostic models do not identify patients at risk of very poor survival after radiotherapy (RT). Identifying patient and disease risk factors for 30-day mortality after RT (30-DM) may help identify patients who would not benefit from RT.

Methods:

All patients who received stereotactic radiosurgery (SRS) or whole brain RT (WBRT) for brain metastases from 1/1/2017- 9/30/2020 at a single tertiary care center were included. Variables regarding demographics, systemic and intracranial disease characteristics, symptoms, radiotherapy, palliative care, and death were recorded. 30-DM was defined as death within 30 days of radiotherapy completion. The Kaplan-Meier method was used to estimate median overall survival. Univariate and multivariable logistic regression models were used to assess associations between demographic, tumor, and treatment factors and 30-DM.

Results:

636 patients with brain metastases were treated with either WBRT (n=117) or SRS (n=519). The most common primary sites were non-small cell lung (46.7%) and breast (19.8%) cancer. Median survival time was 6 months (95% CI 5-7 months). 75/636 patients (11.7%) died within 30 days of RT. On multivariable analysis, progressive intrathoracic disease (HR 4.67, 95% CI 2.06-10.60, p=0.002), progressive liver/adrenal metastases (HR 2.20, 95% CI 1.16-3.68, p=0.02), and inpatient status (HR 4.51, 95% CI 1.78-11.42, p=0.002) were associated with dying within

30 days of RT. Higher Karnofsky Performance Score (KPS) (HR 0.95, 95% CI 0.93-0.97, p<0.001), synchronous brain metastases at time of initial diagnosis (HR 0.45, 95% CI 0.21-0.96, p=0.04), and OPC utilization (HR 0.45, 95% CI 0.20-1.00, p=0.05) were associated with survival past 30 days of RT.

Conclusions:

Multiple factors including lower KPS, progressive intrathoracic disease, progressive liver/adrenal metastases, and inpatient status were associated with 30-DM after RT. Higher KPS, brain metastases at initial diagnosis, and outpatient palliative care utilization were associated with survival beyond 30 days. These data may aid in identifying which patients may benefit from brain metastasis-directed radiotherapy.

Introduction

Radiation therapy (RT) for brain metastases is commonly utilized to increase intracranial disease control and palliate neurologic symptoms. However, brain RT administered at the end of life (EOL) may have limited clinical utility in poor prognosis patients, and can contribute to side effects and negatively impact quality of life [1]. In other fields of oncology, the receipt of aggressive therapy such as chemotherapy at the EOL (i.e. within 14 days of death) is established as an indicator of lower quality care [2]. Within radiation oncology, there are no such consensus quality utilization metrics guiding the use of RT at EOL. Consensus guidelines have proposed that 30-day mortality (30-DM) after radiation may be an indicator to judge the appropriate use of palliative RT [3-5], however this benchmark has not been explored among patients receiving RT for brain metastases.

Accurate prognostication of patients with brain metastases is necessary to appropriately select patients who may benefit from brain RT. However, no existing brain metastases prognostic models have identified patient or disease factors which portend very poor survival limited to 30 days [6, 7].

We conducted a large, modern, retrospective analysis at an academic medical center specializing in the care of patients with brain metastases to characterize the incidence of 30-DM after brain RT. Patient and disease characteristics (such as performance status, systemic disease, inpatient status, intracranial disease features) associated with 30-DM were identified in this patient population.

Methods

Patient Selection

This study was reviewed and approved by the XXX Institutional Review Board (IRB #XXX). All patients who received stereotactic radiosurgery (SRS) or whole brain radiotherapy (WBRT) for brain metastases from 1/1/2017- 9/30/2020 were identified through the radiation oncology departmental database and verified through the XXX (Cancer Institute) database. For the purposes of this study SRS included both single-fraction treatments and up to five fractions of hypofractionated stereotactic radiation therapy. Patients were excluded if they received prophylactic cranial irradiation (PCI), had a diagnosis of lymphoma or acute lymphoblastic leukemia, or had less than 30 days of follow up.

Data Collection

Variables regarding patient demographics, disease, radiographic brain metastases characteristics, symptoms at time of radiotherapy consult, radiotherapy details, and death were retrospectively recorded utilizing the institutional EPIC medical record (Epic Systems Corporation, Verona, Wisconsin) and radiation therapy planning software (ARIA, Varian Medical Centers).
Study data were collected and stored in REDCap [8, 9].

Statistical Analysis

30-day mortality (30-DM) was defined as death within 30 days of radiotherapy end date; all patients studied were followed a minimum of 30 days from end of radiotherapy.
Univariate and multivariable logistic regression models were used to assess associations between demographic, tumor, and treatment factors and 30-DM. Potential predictors included:age, sex, race, lung as primary site, presence of brain metastases at initial diagnosis, size of largest brain metastasis, number of brain metastases present, presence of hemorrhagic component, presence of leptomeningeal disease, presence of midline shift , presence of intrathoracic disease, presence of liver or adrenal metastases, presence of spinal metastases, ongoing use of systemic therapy, Karnofsky Performance Status (KPS), seizures, altered mentation, cranial neuropathy, motor or sensory deficit, headache, place of radiation therapy, palliative care utilization, steroid use, hospice use, radiotherapy technique (WBRT; SRS).

Pre-treatment patient and disease characteristics that are clinically relevant were included in the multivariable model. Logistic regression models were conducted among all patients and secondary analyses were conducted among patients with lung and non-lung primary disease

sites. The Kaplan-Meier method was used to estimate median overall survival. Cox regression was used to estimate hazard ratios and associated confidence interval estimates for overall survival. Identification of a patient subset at high risk for 30-DM was explored using recursive partitioning with cross validation (rpart and caret packages, R) [10, 11]. All tests were two-tailed, and *P* value of <0.05 was considered to be statistically significant. All statistical analyses were performed using SAS (version 9.4, Cary NC).

Results

Patient, disease, and treatment characteristics

636 patients were treated with either whole brain radiation therapy (WBRT) (n=117) or stereotactic radiosurgery (SRS) (n=519) for brain metastases in the study period. Median age of the patients was 61 years. 56.0% were female. The most common primary sites were non-small cell lung (46.7%) and breast (19.8%) cancer. Median survival time for all patients was 6 months (95% CI 5-7 months). 75 (11.7%) patients died within 30 days of radiation treatment. Patient, treatment, and disease characteristics, overall and by those who did and did not die within 30 days of RT, are listed in Table 1. Patients who died within 30 days had worse Karnofsky Performance Status (KPS) (median score 50 versus 80). A higher proportion of those who died within 30 days of RT had innumerable brain metastases (45.3% vs 10.7%) and had ongoing systemic therapy at radiation therapy consultation (52.0% vs 23.5%).

Regarding disease characteristics, a higher proportion of those who died within 30 days had leptomeningeal disease (16.0% vs 5.0%), progressive intrathoracic disease (86.7% vs 49.7%), progressive liver/adrenal metastases (60% vs 24.2%), and progressive spinal metastases

(57.3% vs 18.7%). Other characteristics of those who died within 30 days were those symptomatic from seizures (12.0% vs 4.1%), cranial neuropathies (32.0% vs 8.7%), motor/sensory deficits (50.7% vs 28.9%), altered mentation (60.0% vs 26.2%), and headaches (48.0% vs 29.6%). Steroid use at radiation oncology consultation was more common in this group as well (68.0% vs 48.3%).

Regarding treatment, a higher proportion of those who died within 30 days were treated with WBRT versus SRS (46.7% vs 14.6%), were treated as inpatients (38.7% vs 3.4%), and did not complete their radiation (24.0% vs 1.2%).

Factors Associated with Overall Survival

Among the entire cohort of 636 patients, higher KPS (HR 0.98, 95% CI 0.97-0.98, $p<0.001$) and synchronous brain metastases detected at time of initial diagnosis of the primary cancer (HR 0.72, 95% CI 0.57-0.91, $p=0.006$) were associated with increased overall survival (Supplementary Table 1). On multivariable analysis across all patients, older age (HR 1.01, 95% CI 1.00-1.02, $p=0.008$) greater number of brain metastases ($p=0.02$), progressive intrathoracic disease (HR 1.38, 95% CI 1.11-1.71, $p=0.004$), progressive liver/adrenal metastases (HR 1.46, 95% CI 1.17-1.82, $p=0.001$), and inpatient status (HR 1.77, 95% CI 1.19-2.61, $p=0.004$) were all associated with decreased overall survival. Lung versus non-lung primary disease site, presence of leptomeningeal disease, neurologic symptoms and use of outpatient palliative care were not associated with overall survival.

Factors Associated with Death within 30 Days of RT

Results of univariate analyses testing factors for associations with 30-DM are presented in Table 2.

Multivariable analyses of factors associated with 30-DM are presented in Table 3 and overall survival are presented in Supplementary Table 1, respectively. On multivariable analysis, progressive intrathoracic disease (OR 4.67, 95% CI 2.06-10.60, p=0.002), progressive liver/adrenal metastases (OR 2.20, 95% CI 1.16-3.68, p=0.02), and inpatient status (OR 4.51, 95% CI 1.78-11.42, p=0.002) were all associated with dying within 30 days of radiation. Conversely, higher KPS (OR 0.95, 95% CI 0.93-0.97, p<0.001), synchronous brain metastases detected at time of initial diagnosis of the primary cancer (OR 0.45, 95% CI 0.21-0.96, p=0.04), and outpatient palliative care utilization (OR 0.45, 95% CI 0.20-1.00, p=0.05) were associated with survival past 30 days of RT. Age, lung versus non-lung primary disease site, number of metastases, presence of leptomeningeal disease, and presence of neurologic symptoms were not associated with death within 30 days (Table 3).

30-DM after RT was further analyzed within lung and non-lung histology patient subsets (Table 3). For those with non-lung primaries, synchronous brain metastases detected at time of initial diagnosis of the primary cancer were not associated with favorable survival beyond 30 days. Additionally, progressive liver/adrenal metastases and inpatient status were not associated with 30-DM among those with non-lung histologies. For patients with lung primaries, age, number of brain metastases, leptomeningeal disease, and presence of neurologic symptoms were not significantly associated with 30-DM.

Palliative Care Utilization and End of Life Care

Among all patients receiving RT for brain metastases, 446 patients were deceased at the time of this retrospective analysis. Characteristics regarding palliative care utilization and end of life care in these patients are presented in Table 4. 122/446 (27%) of patients had utilized outpatient palliative care at the time of death. A higher proportion of those who utilized outpatient palliative care had a hospice referral (81.1% vs 50.0%, $p<0.001$). Those who utilized outpatient palliative care had a lower proportion of hospital/ER deaths (6.6% vs 15.1%) and a higher proportion of home hospice deaths (65.6% vs 39.8%). No clinically meaningful patient classification for high risk of 30-DM was found by recursive partitioning in this dataset.

Discussion

In this analysis of 636 patients with brain metastases treated with SRS or WBRT, 11.7% died within 30 days of their radiation treatment (RT). Factors associated with 30-day mortality (30-DM) included poor performance status by KPS score, progressive intrathoracic or liver/adrenal metastases, number of brain metastases, inpatient status, and metachronous brain metastases. Patients included in this study were evaluated and treated in the modern era, with current practices of MR imaging and SRS treatment when appropriate, at a tertiary center specializing in the multidisciplinary care of patients with brain metastases.

Cancer treatments offered near the end of life may not appreciably improve a patient's quality of life, while contributing to toxicity, increasing time spent in medical facilities, and adding costs to patients and health systems. Accordingly, the use of chemotherapy near the end of life been a quality measure of interest proposed by the American Society of Clinical Oncology and the National Quality Forum, and adopted by Center for Medicare & Medicaid Services for implementation [12]. Within radiation oncology, the UK Royal College of Physicians

recommended a less than 20% rate of 30-DM for patients undergoing palliative RT [3]. Data detailing short term mortality of patients undergoing brain RT is necessary to develop and implement similar radiation oncology quality metrics within the US.

In prior studies of patients receiving any palliative RT, rates of 30-DM ranged from 10-24% [4, 13-15]. One recent study of patients with brain metastases from any primary reported a 30-DM of 28% [16]. We observed a lower rate of 30-DM in our cohort, possibly due to inclusion of those receiving SRS to limited intracranial metastases representing a better prognosis population. The 30-DM rate for those receiving SRS was 7.7%, suggesting that patients are appropriately being selected for SRS at our center. Among the 117 patients receiving WBRT, however, the rate of 30-DM was considerably higher at 29.9%. The high short-term mortality in the population selected for WBRT highlights the importance of weighing the expected benefits of WBRT with the toxicity of treatment. As previously established by the QUARTZ trial, the optimal treatment for select poor performance patients with brain metastases ineligible for SRS/surgery may be best supportive care alone as neither survival or quality of life were significantly improved with the addition of WBRT [17]. A patient centered discussion of the potential benefits of brain metastasis directed therapy including improvement in neurologic symptoms such as headaches, weakness, dizziness, seizures should be balanced with possible side effects from the treatment including fatigue, drowsiness, and nausea. An understanding of prognosis may help patients and their families clarify their goals of care and make these difficult treatment decisions near the end of life.

Identification of patients with brain metastases and poor prognoses, however, is an ongoing challenge. There are several prognostic models available for patients with brain metastases including the RTOG recursive partitioning analysis (RPA), Score Index for

Radiosurgery in Brain Metastases (SIR), and diagnosis-specific Graded Prognostic Assessment (dsGPA) [6, 7, 18, 19]. The most unfavorable prognosis patients in these models are estimated to have median survival of 2-3 months. However, no existing brain metastases-specific models further identify patients whose survival is limited to less than 1 month.

Prior prognostic score indices and smaller retrospective analyses have demonstrated poor performance status and extracranial disease are important indicators of poor prognosis [6, 7, 18-20]. In one recent study inclusive of 100 patients treated with radiation for brain metastases, extracranial disease progression (measured by blood test results and imaging) was a significant predictor for 30 DM [16]. Consistent with this observation, lower KPS and extracranial disease were associated with 30 DM in our analysis. These factors highlight the importance of evaluating a patient's intracranial disease in the context of their systemic progression and performance status. Notably, a patient's inpatient status was significantly associated with 30-DM suggesting palliative brain RT, particularly WBRT, for hospitalized patients should be offered judiciously since many may not benefit from this treatment. To our knowledge, hospitalization is not considered in any prognostic indices for those with brain metastases, and likely should be. Although age is frequently identified as a prognostic factor for survival, older age was not associated with imminent death within 30 days in this study.

As indicated by other studies, disease histology likely influences the prognostic importance of various clinical factors [18]. Among patients with metastatic lung cancer, synchronous brain metastases were associated with survival beyond 30 days. Innumerable brain metastases were associated with 30-DM among patients with non-lung histologies, however not lung histologies. These differences may reflect relative improvements in prognoses for lung cancer patients with brain metastases resulting from emerging systemic therapies. This also

highlights the continued need to revisit prognostic factors in the modern era given evolving diagnostic and therapeutic advances in the management of brain metastases.

Use of outpatient palliative care (OPC) was associated with significantly decreased mortality in the 30-day post-RT period. This finding reflects the results of several studies which demonstrate that early palliative care utilization in patients with advanced cancer is associated with improved survival [21-23]. Another possibility is that patients engaging with OPC services may be more appropriately selected for RT intervention. We observed that OPC was infrequently utilized (27%) in this population of patients with brain metastases. A higher proportion of those who utilized palliative care were referred to hospice and died on home hospice. A lower proportion of those who utilized OPC died in the hospital, emergency room, or at home without hospice. Although the correlation of these end-of-life outcomes are difficult to assess in a retrospective study, it is likely that early OPC influences care delivery at the end of life and this should be the topic of further investigation in patients with brain metastases [24].

One of the strengths of this study is that it was conducted at a multidisciplinary center in the modern era (2017-2020), incorporating common utilization of immune checkpoint and molecularly targeted therapies – likely making these data more generalizable than older studies. Given robust follow-up and consistent documentation at our center, we detail several clinical factors including extracranial disease, intracranial disease features, and hospitalization which may influence mortality in this population. Limitations of this study include the retrospective nature, selection bias, heterogeneity of the population given inclusion of multiple primary disease sites, and the small number of deaths within 30 days. Additionally, patients who were considered for but did not receive radiation therapy are not included in this study. Molecular

profiling of tumors has been utilized in prior prognostic brain metastases models however was not available in this study [25].

In summary, we identified multiple factors including performance status, extracranial disease, metachronous metastases, inpatient status, and outpatient palliative care utilization which were associated with 30-DM after brain RT. The importance and interaction of these individual factors, particularly in relation to primary disease site, are unknown. While the recursive partitioning analysis in this study was underpowered, future analyses including validation among a larger dataset across multiple centers will be useful in more precisely risk stratify patients who have a high likelihood of 30-DM.

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Tables

Table 1: Patient, Disease, Treatment Characteristics

	Death within 30 days (N=75)	Alive beyond 30 days (N=561)	Total (N=636)
***Age**	62 (27-81)	61 (11-89)	61 (11-89)
Sex			
Female	42 (56.0%)	314 (56.0%)	356 (56.0%)
Male	33 (44.0%)	246 (43.9%)	279 (43.9%)
Other	0 (0.0%)	1 (0.2%)	1 (0.2%)
Brain Metastases at Initial Diagnosis			
Yes	28 (37.3%)	216 (38.5%)	244 (38.4%)
No	47 (62.7%)	345 (61.5%)	392 (61.6%)
***Karnofsky Performance Status**	50 (20-100)	80 (20-100)	80 (20 -100)
Number of Brain Metastases			
1-5	36 (48.0%)	413 (73.6%)	449 (70.6%)
6-10	1 (1.3%)	59 (10.5%)	60 (9.4%)
11-40	4 (5.3%)	29 (5.2%)	33 (5.2%)
Innumerable	34 (45.3%)	60 (10.7%)	94 (14.8%)
***Size of Largest Brain Metastasis (cm)**	1.3 (0.2-6.5)	1.5 (0.1-6.3)	1.5 (0.1-6.5)
Technique			
WBRT	35 (46.7%)	82 (14.6%)	117 (18.4%)
SRS	40 (53.3%)	479 (85.4%)	519 (81.6%)
Brain Metastases Characteristics			
Hemorrhagic Component	10 (13.3%)	44 (7.8%)	54 (8.5%)
Leptomeningeal Disease	12 (16.0%)	28 (5.0%)	40 (6.3%)
Midline Shift/Herniation	9 (12.0%)	47 (8.4%)	56 (8.8%)
Extracranial Disease at Consultation			
Progressive Intrathoracic Disease	65 (86.7%)	279 (49.7%)	344 (54.1%)
Progressive Liver/Adrenal Metastases	45 (60.0%)	136 (24.2%)	181 (28.5%)
Spinal Metastases	43 (57.3%)	105 (18.7%)	148 (23.3%)
Systemic Therapy at Consultation			
Yes	39 (52.0%)	132 (23.5%)	171 (26.9%)
No	36 (48.0%)	429 (76.5%)	465 (73.1%)
Neurologic Symptoms at Consultation			
Seizures	9 (12.0%)	23 (4.1%)	32 (5.0%)
Cranial Neuropathies	24 (32.0%)	49 (8.7%)	73 (11.5%)
Motor/Sensory Deficits	38 (50.7%)	162 (28.9%)	200 (31.4%)

	Death within 30 days (N=75)	Alive beyond 30 days (N=561)	Total (N=636)
Presence of Altered Mentation	45 (60.0%)	147 (26.2%)	192 (30.2%)
Headaches	36 (48.0%)	166 (29.6%)	202 (31.8%)
Steroid Use at Consultation			
Yes	51 (68.0%)	271 (48.3%)	322 (50.6%)
No	24 (32.0%)	290 (51.7%)	314 (49.4%)
Place of Radiation			
Inpatient	29 (38.7%)	19 (3.4%)	48 (7.5%)
Outpatient	46 (61.3%)	542 (96.6%)	588 (92.5%)
Radiation Completion			
Yes	57 (76.0%)	554 (98.8%)	611 (96.1%)
No	18 (24.0%)	7 (1.2%)	25 (3.9%)
Outpatient Palliative Care Utilization			
Yes	12 (16.0%)	136 (24.2%)	148 (23.3%)
No	63 (84.0%)	425 (75.8%)	488 (76.7%)
Primary Site/Histology			
Breast	16 (21.3%)	111 (19.8%)	127 (19.8%)
Gastrointestinal	7 (9.3%)	32 (5.7%)	39 (6.1%)
Genitourinary	4 (5.3%)	31 (5.5%)	35 (5.5%)
Melanoma	2 (2.7%)	41 (7.3%)	43 (6.7%)
Non-Small Cell Lung	29 (38.7%)	268 (47.8%)	297 (46.7%)
Small Cell Lung	8 (10.7%)	35 (6.2%)	43 (6.7%)
Other	9 (12%)	43 (7.7%)	52 (8.2%)
Lung vs Not Lung Primary Site			
Lung	38 (50.7%)	311 (55.4%)	349 (54.9%)
Not Lung	37 (49.3%)	250 (44.6%)	287 (45.1%)

*Median (Range)

Table 2: Univariate Analyses of Clinical Factors associated with 30 Day Mortality (from last RT treatment)

	All patients (N=636)		Primary Site			
			Lung (N=349)		Not Lung (N=287)	
	OR (95 % CI)	p-value	OR (95 % CI)	p-value	OR (95 % CI)	p-value
Age	1.00 (0.99-1.02)	0.696	1.03 (0.99-1.06)	0.126	1.00 (0.97-1.02)	0.796
Karnofsky Performance Status	0.93 (0.91-0.94)	<0.001	0.93 (0.91-0.95)	<0.001	0.93 (0.91-0.95)	<0.001
Brain Metastases at Initial Diagnosis vs. Metachronous Presentation	0.95 (0.58-1.57)	0.845	1.07 (0.54-2.11)	0.849	0.99 (0.39-2.52)	0.978
Primary Site (Lung vs Not Lung)	0.83 (0.51-1.34)	0.436	-	-	-	-
Number of Brain Metastases		<0.001				<0.001
1-5	ref		ref		ref	
6-10	0.19 (0.03-1.45)		-	-	0.67 (0.08-5.37)	
11-40	6.50 (3.78-11.17)		3.18 (1.43-7.09)		0.96 (0.12-7.85)	
Innumerable	1.58 (0.53-4.75)		2.20 (0.59-8.27)		13.06 (5.83-29.26)	
Leptomeningeal Disease	3.63 (1.76-7.49)	<0.001	4.36 (1.04-18.20)	0.044	3.33 (1.40-7.95)	0.007
Progressive Intrathoracic Metastases	6.57 (3.32-13.05)	<0.001	6.44 (2.23-18.57)	0.001	7.50 (3.02-18.62)	<0.001
Progressive Liver/Adrenal Metastases	4.67 (2.84-7.74)	<0.001	5.52 (2.74-11.14)	<0.001	3.91 (1.91-8.01)	<0.001
Spinal Metastases	5.84 (3.52-9.66)	<0.001	4.59 (2.27-9.28)	<0.001	7.56 (3.57-16.03)	<0.001
Systemic Therapy at Consultation	0.28 (0.17-0.47)	<0.001	0.25 (0.13-0.50)	<0.001	0.31 (0.15-0.63)	0.001
Neurologic Symptoms						
Altered Mentation	4.23 (2.56-6.96)	<0.001	4.58 (2.29-9.19)	<0.001	3.85 (1.87-7.95)	<0.001
Seizure	3.19 (1.42-7.19)	0.005	0.81 (0.10-6.53)	0.846	5.03 (1.92-13.15)	0.001
Cranial Neuropathies	4.92 (2.79-8.67)	<0.001	5.26 (2.06-13.43)	<0.001	4.84 (2.30-10.19)	<0.001
Motor/Sensory Deficit	2.53 (1.55-4.12)	<0.001	1.81 (0.91-3.61)	0.090	3.56 (1.75-7.24)	<0.001
Headache	2.20 (1.35-3.58)	0.002	1.99 (1.00-3.94)	0.049	2.42 (1.20-4.86)	0.013
Any Neurologic Symptoms	2.26 (1.27-4.02)	0.006	1.79 (0.86-3.73)	0.123	3.12 (1.17-8.31)	0.023
Place of Radiation (Inpatient vs Outpatient)	17.98 (9.37-34.51)	<0.001	16.25 (6.81-38.77)	<0.001	21.13 (7.75-57-60)	<0.001
Outpatient Palliative Care Utilization	0.60 (0.31-1.14)	0.116	0.68 (0.29-1.59)	0.369	0.52 (0.19-1.39)	0.191

Table 3. Multivariable Analyses of Clinical Factors associated with 30 Day Mortality (from last RT treatment)

	All patients (N=636)		Primary Site*			
			Lung (N=349)		Not Lung (N=287)	
	OR (95 % CI)	**p-value**	**OR (95 % CI)**	**p-value**	**OR (95 % CI)**	**p-value**
Age	1.00 (0.98-1.03)	0.75	1.01 (0.96-1.06)	0.710	0.99 (0.96-1.03)	0.937
Karnofsky Performance Status	0.95 (0.93-0.97)	<0.001	0.96 (0.93-0.99)	0.004	0.96 (0.93-0.99)	0.012
Brain Metastases at Initial Diagnosis vs. Metachronous Presentation	0.45 (0.21-0.96)	0.04	0.29 (0.11-0.75)	0.01	1.23 (0.35-4.32)	0.744
Primary Site (Lung vs Not Lung)	1.31 (0.62-2.78)	0.48	-	-	-	
Number of Metastases		0.10		0.467		0.017
1-5	ref		ref		ref	
6-10	0.18 (0.02-1.43)		-		0.51 (0.06-4.63)	
11-40	2.05 (0.61-6.83)		3.43 (0.71-16.54)		1.13 (0.13-10.03)	
Innumerable	2.17 (1.00-4.68)		0.84 (0.25-2.77)		5.41 (1.76-16.63)	
Leptomeningeal disease	1.13 (0.35-3.68)	0.83	1.23 (0.11-13.34)	0.863	0.80 (0.21-3.07)	0.748
Progressive Intrathoracic Metastases	4.67 (2.06-10.60)	0.002	7.72 (2.10-27.67)	0.002	4.34 (1.41-13.39)	0.011
Progressive Liver/Adrenal Metastases	2.20 (1.16-4.16)	0.02	3.03 (1.25-7.38)	0.014	1.69 (0.63-4.55)	0.297
Any Neurologic Symptoms	0.73 (0.35-1.52)	0.40	0.87 (0.33-2.31)	0.776	0.71 (0.21-2.36)	0.576
Place of Radiation (Inpatient vs Outpatient)	4.51 (1.78-11.42)	0.002	10.63 (3.02-37.43)	<0.001	3.27 (0.81-13.26)	0.098
Outpatient Palliative Care Utilization	0.45 (0.20, 1.00)	0.05	-	-	-	=

*****The model containing outpatient palliative care utilization within the lung subgroup does not converge.

Table 4: Outpatient Palliative Care Utilization

	Outpatient Palliative Care Use			
	Yes (N=122)	No (N=324)	Total (N=446)	p value
Hospitalization within 30 days of death				0.045[1]
Yes	38 (31.1%)	119 (36.7%)	157 (35.2%)	
No	78 (63.9%)	170 (52.5%)	248 (55.6%)	
Missing	6 (4.9%)	35 (10.8%)	41 (9.2%)	
Referral To Hospice				<0.001[1]
Yes	99 (81.1%)	162 (50.0%)	261 (58.5%)	
No	23 (18.9%)	159 (49.1%)	182 (40.8%)	
Missing	0 (0.0%)	3 (0.9%)	3 (0.7%)	
Place of death				<0.001[1]
Hospital/Emergency Room	8 (6.6%)	49 (15.1%)	57 (12.8%)	
Inpatient Hospice	12 (9.8%)	26 (8.0%)	38 (8.5%)	
Home Hospice	80 (65.6%)	129 (39.8%)	209 (46.9%)	
Home (without hospice)	17 (13.9%)	102 (31.5%)	119 (26.7%)	
SNF	3 (2.5%)	8 (2.5%)	11 (2.5%)	
Unknown	2 (1.6%)	10 (3.1%)	12 (2.7%)	
***Days from RT Completion to Death**	128.5 (8.0-654.0)	101.0 (3.0-1248.0)	110.0 (3.0-1248.0)	0.216[2]

[1]Chi-Square
Where applicable, missing data were not used in generating p-values.
*Median (range)

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: