Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2017 November 15; 99(4): 854–858. doi:10.1016/j.ijrobp.2017.06.2463.

Intensive Care Unit Outcomes Among Patients With Cancer After Palliative Radiation Therapy

Jacqueline M Kruser, MD, MS¹, Sunpreet S Rakhra, MD², Ryan M Sacotte, BS³, Firas H Wehbe, MD, PhD⁴, Alfred W Rademaker, PhD^{4,5}, Richard G Wunderink, MD¹, and Tim J Kruser, MD²

¹Department of Medicine, Division of Pulmonary and Critical Care Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

²Department of Radiation Oncology, Northwestern University Feinberg School of Medicine and The Robert H. Lurie Comprehensive Cancer Center, Chicago, IL

³Northwestern University Feinberg School of Medicine, Chicago, IL

⁴Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

⁵Northwestern University Cancer Biostatistics Core, Chicago, IL

Abstract

Purpose—To inform goals of care discussions at the time of palliative radiation therapy (RT) consultation, we sought to characterize intensive care unit (ICU) outcomes for patients treated with palliative RT compared to all other patients with metastatic cancer admitted to the ICU.

Methods—We conducted a retrospective cohort study of patients with metastatic cancer admitted to an ICU in a tertiary medical center from January 2010—September 2015. We compared in-hospital mortality between patients who received palliative RT in the 12 months prior to admission with all other patients with metastatic cancer. We used multivariable logistic regression to evaluate the association between receipt of palliative RT and in-hospital mortality, adjusting for patient characteristics and acute illness severity.

Results—Among 1,424 patients with metastatic cancer, 11.3% (n=161) received palliative RT prior to ICU admission. In-hospital mortality was 36.7% for palliative RT patients compared to 16.6% for other patients with metastatic cancer ($p<0.001$). Receipt of palliative RT was associated with increased in-hospital mortality (OR 2.08, 95% CI 1.34—3.21, $p=0.001$), after adjusting for patient characteristics and severity of critical illness. Only 34 (21.1%) patients treated with palliative RT received additional cancer-directed treatment after ICU admission.

Correspondence and Request for Reprints: Tim J Kruser, MD, 251 East Huron Street, Galter Pavilion LC-178, Chicago, Illinois 60611, tkruser@nm.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of Interest

The authors have no conflicts of interests to declare.

Conclusions—For patients with metastatic cancer, prior treatment with palliative RT is associated with increased in-hospital mortality after ICU admission. Nearly half of patients previously treated with palliative RT either died during hospitalization or were discharged with hospice care, and few received further cancer-directed therapy. Palliative RT referral may represent an opportunity to discuss end-of-life treatment preferences with patients and families.

Introduction

Palliative radiation oncology referral represents a distinct juncture for patients with advanced cancer, typically occurring at a time of disease or symptom progression. As part of the Choosing Wisely Campaign, the American Society for Radiation Oncology recently urged physicians to initiate goals of care (GOC) discussions and consider palliative care referral for all patients receiving palliative radiation therapy (RT).¹ A central feature of GOC discussions near end of life is patients' preferences for the use of life-sustaining treatments and intensive care unit (ICU) admission in the event of an acute, serious illness. However, little is known about ICU outcomes for patients with cancer previously treated with palliative RT.

The purpose of this study was to characterize ICU outcomes for patients treated with palliative RT prior to ICU admission, in effort to inform GOC discussions at the time of palliative RT consultation.

Materials and Methods

Study Design

Using a clinical data warehouse of all patients treated at the study site, an algorithm of International Classification of Diseases, Ninth Revision codes was used to retrospectively identify all patients with a diagnosis of metastatic cancer (196.xx, 197.xx, 198.xx) who were admitted to an ICU at a tertiary care medical center from January 2010—September 2015.^{2–4} We used Current Procedural Terminology (CPT) codes⁵ to identify patients who received any RT up to 12 months prior to ICU admission. Two study investigators reviewed clinical radiation oncology notes and the radiation oncology record and verify system (Mosaik®, Elekta, Stockholm, Sweden) of each radiation case to confirm the palliative intent and confirm site of palliative radiation. Reviewers excluded patients who received curative-intent radiation.

Measures and Covariates

The primary outcome measure was in-hospital mortality. We collected demographic characteristics, primary cancer/tumor site, and variables characterizing the ICU admission including the Sequential Organ Failure Assessment (SOFA) score after 24 hours of ICU admission,^{6–8} receipt of mechanical ventilation, type of ICU, and hospital discharge disposition. Investigators reviewed the EHR to determine whether patients treated with palliative RT received any additional cancer-directed therapy after ICU admission.

Analysis

We performed univariate logistic regression to identify individual variables associated with in-hospital mortality. We conducted multivariable logistic regression and included variables with a p value of <0.10 on univariate analysis or those variables considered clinically relevant to in-hospital mortality. A two-tailed p-value of <0.05 defined statistical significance. All statistical analyses were performed using STATA (Version 14; StataCorp LP, College Station, TX).

Results

A total of 1,424 patients with metastatic cancer were admitted to an ICU from 2010–2015. A total of 161 patients (11.3%) received palliative RT within 12 months prior to ICU admission. Demographic characteristics were similar between patients treated and not treated with palliative RT (Table 1). The distribution of primary cancer/tumor types differed between patients treated and not treated with palliative RT ($p < 0.001$) (Table 1). Patients received palliative radiation therapy to the following sites (including patients with more than one site of radiation): bone (55.0%), brain (41.0%), lung (5.9%) and other (5.5%). The median radiation dose was 30 gray (range 3 to 60), and the median number of radiation fractions was 10 (range 1 to 30). Patients treated with palliative RT were more likely to receive mechanical ventilation (24.8% versus 15.7%, $p = 0.003$, Table 2) and to be admitted to the Medical or Neurosciences/Spine ICU ($p < 0.001$). ICU length of stay and SOFA scores were similar between the two groups.

In-hospital mortality was significantly higher for patients previously treated with palliative RT (36.4% versus 16.6%, $p < 0.001$) (Table 2). In the multivariable analysis, prior palliative RT was associated with in-hospital mortality (OR 2.08, 95% CI 1.34–3.21, $p = 0.001$) after adjusting for covariates (Table 3). Other variables associated with in-hospital mortality were mechanical ventilation, SOFA score, and type of ICU (Table 3). Patient sex and year of ICU admission were evaluated in the univariate analysis but were excluded from the multivariable model based on the univariate results.

Among the 161 patients who received palliative RT, 41.6% ($n = 67$) were discharged home, 13.0% ($n = 21$) were discharged to a post-acute facility, and 9.3% ($n = 15$) were discharged to hospice (Figure 1); discharge disposition differed significantly by palliative RT status ($p < 0.001$). Thirty-four (21.1%) of the patients treated with palliative RT received any additional cancer-directed therapy after ICU admission. Two patients (1.2%) received additional cancer surgery, 10 patients (6.2%) received additional RT, and 28 patients (17.4%) received additional chemotherapy.

Discussion

To our knowledge, this study provides the first description of outcomes of patients with metastatic cancer admitted to the ICU previously treated with palliative RT. Patients previously treated with palliative RT have significantly increased in-hospital mortality (36.4%) after ICU admission compared to other patients with metastatic cancer (16.6%) and are less likely to return home, more likely to transition to hospice care, and rarely receive

additional cancer-directed therapies. These findings suggest that a history of palliative radiation treatment is a marker of advanced disease and is associated with higher mortality in the event of acute critical illness.

For oncologists, these findings highlight a previously unrecognized opportunity in the trajectory of cancer care to discuss prognosis, goals of care, and treatment preferences. Prior research has established a survival and quality of life benefit of early palliative care in patients with metastatic lung cancer, in addition to less aggressive end-of-life care utilization.⁹ The results of this study build on this prior research and suggest that the timeframe of referral for palliative radiation treatment may be an important, easily identified event that could trigger a discussion about palliative care, prognosis, and patient treatment preferences.

Critical illness often requires urgent intervention without extensive opportunity to discuss expected outcomes. The palliative RT consultation may serve as an upstream time point that could afford a patient and family the opportunity to consider prognosis, GOC, and treatment preferences *before* the acute onset of illness. Our data describe the range of possible ICU and oncologic outcomes for patients treated with palliative RT and are therefore useful to radiation oncologists, palliative care physicians, and intensivists during GOC discussions. We favor an “all-hands on deck” approach to end-of-life care planning including radiation oncologists, palliative care specialists, and medical oncologists; we believe our findings should embolden radiation oncologists to participate regularly in this important aspect of oncologic care.

Alternative explanations may exist for the observed mortality difference in this study. Patients who receive palliative radiation may have already engaged in palliative care and goals of care discussions prior to ICU admission; thus, the higher mortality could result from patients opting for less invasive care based on established end-of-life care preferences. However, more patients in the palliative radiation cohort received mechanical ventilation (Table 2), suggesting that lower intensity end-of-life care is less likely to account for the observed mortality difference.

This study has several limitations. We conducted a single-center, retrospective study in a large, urban tertiary care center. As such, generalizability may be limited to similar institutions. To the best of our knowledge, there is no previously published or validated method to identify patients treated with palliative RT using administrative data. Thus, to identify exposure to palliative RT, we developed a novel strategy combining ICD-9 and CPT codes, and confirmation with manual chart review. This strategy may have failed to identify all patients who had received palliative RT (e.g., patients who had received treatment outside of the study healthcare system), but this limitation would most likely bias our findings toward the null result. Chemotherapy utilization in the period prior to ICU admission was not assessed and may be a confounding factor. Additionally, the radiated and non-radiated groups differed in terms of primary malignancies and type of ICU admission. These differences likely reflect of the patterns of metastatic spread (and resultant palliative RT utilization) in gastrointestinal versus breast and lung tumors; the variation in palliative RT utilization based on underlying malignancy in this study is consistent with previously

published observations.¹⁰ For example, patients with brain metastases are more likely to be admitted to a neurosciences ICU and have had prior palliative brain-directed radiotherapy, whereas patients with liver metastases rarely receive palliative radiation but are more likely to be admitted to a surgical ICU with an abdominal surgical condition.

Conclusions

In critically ill patients with metastatic cancer, a history of previous treatment with palliative RT is associated with increased risk of in-hospital mortality. These results point to the timeframe of palliative radiation consultation as an important opportunity to address goals of care, prognosis, and end-of-life treatment preferences with patients and their families.

Acknowledgments

Research Funding:

Jacqueline M Kruser's work for this manuscript was supported by the US Agency for Healthcare Research and Quality (T-32 HS 000078). Firas H Wehbe's work for this manuscript was supported, in part, by the National Cancer Institute. Tim J Kruser received funding to support this research from the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

References

1. ASTRO releases second list of five radiation oncology treatments to question, as part of national Choosing Wisely® campaign. 2014. at <http://www.choosingwisely.org/astro-releases-second-list/>.
2. Nordstrom BL, Whyte JL, Stolar M, Mercaldi C, Kallich JD. Identification of metastatic cancer in claims data. *Pharmacoepidemiol Drug Saf.* 2012; 21(Suppl 2):21–8.
3. Nordstrom BL, Simeone JC, Malley KG, et al. Validation of Claims Algorithms for Progression to Metastatic Cancer in Patients with Breast, Non-small Cell Lung, and Colorectal Cancer. *Front Oncol.* 2016; 6:18. [PubMed: 26870695]
4. Whyte JL, Engel-Nitz NM, Teitelbaum A, Gomez Rey G, Kallich JD. An Evaluation of Algorithms for Identifying Metastatic Breast, Lung, or Colorectal Cancer in Administrative Claims Data. *Med Care.* 2015; 53:e49–57. [PubMed: 23524464]
5. Guadagnolo BA, Liao KP, Elting L, Giordano S, Buchholz TA, Shih YC. Use of radiation therapy in the last 30 days of life among a large population-based cohort of elderly patients in the United States. *J Clin Oncol.* 2013; 31:80–7. [PubMed: 23169520]
6. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996; 22:707–10. [PubMed: 8844239]
7. Vincent JL, de Mendonca A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on “sepsis-related problems” of the European Society of Intensive Care Medicine. *Crit Care Med.* 1998; 26:1793–800. [PubMed: 9824069]
8. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. *JAMA.* 2001; 286:1754–8. [PubMed: 11594901]
9. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *NEJM.* 2010; 363:733–42. [PubMed: 20818875]
10. Murphy JD, Nelson LM, Chang DT, Mell LK, Le QT. Patterns of care in palliative radiotherapy: a population-based study. *J Oncol Pract.* 2013; 9:e220–7. [PubMed: 23943892]

Summary

We characterized ICU outcomes for patients who received palliative radiation prior to ICU admission, in comparison to all metastatic cancer patients admitted to the ICU. Patients who received palliative RT are twice as likely to die during their ICU stay as other metastatic cancer patients, and infrequently receive further cancer care after severe, acute illness. These findings support the palliative RT consultation as a time to discuss goals of care, including end-of-life treatment preferences.

Figure 1. Hospital discharge disposition. When comparing discharge disposition by palliative radiation status using Fisher's Exact Test, $p < 0.001$.

Table 1

Demographic characteristics of patients with metastatic cancer admitted to the ICU.

	Patients Treated With Palliative Radiation N = 161	Patients Not Treated With Palliative Radiation N=1,263	
	Number of Patients (%)	Number of Patients (%)	p-value
Age			p=0.204 *
< 40	10 (6.2)	78 (6.2)	
40–49	22 (13.7)	121 (9.6)	
50–59	43 (26.7)	267 (21.1)	
60–69	44 (27.3)	369 (29.2)	
70–79	28 (17.4)	281 (22.3)	
80–100	14 (8.7)	147 (11.6)	
Female Sex	82 (50.9)	691 (54.7)	p=0.365 *
Race/Ethnicity			p=0.130 †
Asian	4 (2.5)	35 (2.8)	
Black or African American	33 (20.5)	190 (15.0)	
Hispanic or Latino	14 (8.7)	71 (5.6)	
Non-Hispanic White	85 (52.8)	707 (56.0)	
Other	25 (15.5)	260 (20.6)	
Primary Cancer or Tumor Type			p<0.001 *
Gastrointestinal	15 (9.3)	341 (27.0)	
Breast	34 (21.1)	182 (14.4)	
Lung	34 (21.0)	159 (12.6)	
Renal/Bladder	7 (4.4)	120 (9.5)	
Gynecologic	2 (1.2)	86 (6.8)	
Head and Neck	4 (2.5)	38 (3.0)	
Multiple Myeloma/Hematologic	24 (14.9)	40 (3.2)	
Lymphoma	3 (1.9)	29 (2.3)	
Melanoma and other skin	14 (8.7)	47 (3.7)	
Prostate	7 (4.4)	40 (3.2)	
Thyroid	9 (5.6)	29 (2.3)	
Central Nervous System	0 (0.0)	23 (1.8)	
Other	8 (5.0)	129 (10.2)	

* Pearson's Chi Squared

† Fisher's Exact

Table 2

In-hospital mortality and ICU admission characteristics.

	All Patients with Metastatic Cancer N =1,424	Patients Treated With Palliative Radiation N = 161	Patients Not Treated With Palliative Radiation N=1,263	p-value
In-Hospital Mortality, %	18.9	36.7	16.6	p<0.001 *
Type of ICU, number (%)				p<0.001 *
Medical	561 (39.4)	96 (59.3)	465 (36.8)	
Surgical	355 (24.9)	7 (4.4)	348 (27.6)	
Neurosciences and Spine	276 (19.4)	42 (26.1)	234 (18.5)	
Cardiothoracic and Transplant	125 (8.8)	7 (4.4)	118 (9.3)	
Coronary Care Unit	107 (7.5)	9 (5.6)	98 (7.8)	
Treated with Mechanical Ventilation, number (%)	238 (16.7)	40 (24.8)	198 (15.7)	p=0.003 *
ICU Length of Stay, median days (IQR)	2 (1–3)	2 (1–4)	2 (1–3)	p=0.626 †
SOFA Score, median (IQR)	2 (0–4)	2 (0–4)	2 (0–3)	p=0.041 †

* Pearson's Chi-squared test

† Mann-Whitney two-sample test

Table 3

Multivariable regression model for odds of in-hospital mortality.

	Odds Ratio of In-Hospital Mortality	95 % Confidence Interval	p-value
Palliative Radiation Therapy			
No	1.00 (reference)		
Yes	2.08	1.34–3.21	0.001
Age			
< 60	1.00 (reference)		
60–80	1.15	0.81–1.63	0.443
>80	1.13	0.66–1.93	0.668
Race/Ethnicity			
Non-Hispanic White	1.00 (reference)		
Hispanic	1.07	0.56–2.04	0.839
Asian	1.34	0.58–3.11	0.500
Black	0.96	0.62–1.49	0.854
Other	0.81	0.53–1.24	0.336
Primary Cancer or Tumor Type			
Gastrointestinal	1.00 (reference)		
Breast	1.01	0.60–1.70	0.973
Lung	1.28	0.77–2.12	0.337
Other	0.73	0.48–1.09	0.119
Mechanical Ventilation			
No	1.00 (reference)		
Yes	7.29	5.14–10.35	<0.001
Initial SOFA Score			
per 1 point increase in SOFA	1.17	1.09–1.25	<0.001
Type of ICU			
Medical	1.00 (reference)		
Coronary Care Unit	0.32	0.16–0.66	0.002
Neurosciences and Spine	0.35	0.22–0.55	<0.001
Surgical	0.18	0.11–0.31	<0.001
Cardiothoracic and Transplant	0.25	0.13–0.48	<0.001