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Clinical Investigation

# Age Disparity in Palliative Radiation Therapy Among Patients With Advanced Cancer



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## Summary

Radiation in the palliative setting plays a critical role in reducing symptoms and improving the quality of life in patients with metastatic cancer. This study demonstrates substantial age disparity with palliative radiation therapy that extends beyond age-related differences in patient and tumor characteristics, as well as differences in patient survival. Extra effort should be made to give older patients

**Purpose/Objective:** Palliative radiation therapy represents an important treatment option among patients with advanced cancer, although research shows decreased use among older patients. This study evaluated age-related patterns of palliative radiation use among an elderly Medicare population.

**Methods and Materials:** We identified 63,221 patients with metastatic lung, breast, prostate, or colorectal cancer diagnosed between 2000 and 2007 from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. Receipt of palliative radiation therapy was extracted from Medicare claims. Multivariate Poisson regression analysis determined residual age-related disparity in the receipt of palliative radiation therapy after controlling for confounding covariates including age-related differences in patient and demographic covariates, length of life, and patient preferences for aggressive cancer therapy.

**Results:** The use of radiation decreased steadily with increasing patient age. Forty-two percent of patients aged 66 to 69 received palliative radiation therapy. Rates of palliative radiation decreased to 38%, 32%, 24%, and 14% among patients aged 70 to 74, 75 to 79, 80 to 84, and over 85, respectively. Multivariate analysis found that

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the opportunity to receive this quality of life-enhancing treatment at the end of life.

confounding covariates attenuated these findings, although the decreased relative rate of palliative radiation therapy among the elderly remained clinically and statistically significant. On multivariate analysis, compared to patients 66 to 69 years old, those aged 70 to 74, 75 to 79, 80 to 84, and over 85 had a 7%, 15%, 25%, and 44% decreased rate of receiving palliative radiation, respectively (all  $P < .0001$ ).

**Conclusions:** Age disparity with palliative radiation therapy exists among older cancer patients. Further research should strive to identify barriers to palliative radiation among the elderly, and extra effort should be made to give older patients the opportunity to receive this quality of life-enhancing treatment at the end of life. © 2014 Elsevier Inc.

## Introduction

Palliative radiation therapy represents a standard treatment option in cases of advanced cancer to improve patient quality of life. Among its many indications in the palliative setting, radiation therapy can decrease pain from tumor metastases, improve neurologic function from brain or spine metastases, or help relieve compressive or obstructive symptoms caused by tumor bulk. Numerous prospective clinical trials spanning decades have shown the value of this important treatment modality (1-3).

Despite the proven benefit of palliative radiation, multiple studies have found decreased use among the elderly (4-7). The underlying causes remain unclear, although many potential confounding factors could influence this age-related disparity in palliative radiation therapy. Older patients often have more comorbidity, shorter survival, and less proclivity to receive aggressive cancer care, all of which could impact a patient's decision or ability to receive palliative radiation therapy. To date, research has not assessed the use of palliative radiation therapy adjusting for these confounding factors. The purpose of this study was to define the age-related patterns of palliative radiation therapy in a population-based cohort, with a specific focus on identifying and adjusting for confounding factors.

## Methods and Materials

### Dataset

To evaluate the patterns of palliative radiation therapy among the elderly we used data from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. SEER consists of U.S. cancer registries that track cancer diagnoses for approximately 28% of the U.S. population. The Medicare program provides health insurance for U.S. residents over the age of 65. The SEER-Medicare linkage contains healthcare claims data for Medicare patients within SEER. This dataset allows for population-based longitudinal tracking of healthcare delivery across the United States. This research was found to be exempt from institutional review board approval.

### Study cohort

This study included patients with lung, breast, prostate, or colorectal cancer, which represent the 4 most common types of cancer diagnosed in the United States (8). Our initial query identified 115,834 patients between 2000 and 2007 with stage IV cancer at diagnosis. We sequentially excluded those with multiple primary cancer diagnoses (13%), as well as those with disease diagnosed on death certificate or autopsy only (0.2%). This study accounted for differences in survival time as well as aggressiveness of care at end of life, and to allow for complete patient follow-up, we excluded the small fraction of patients alive at the end of the study period (7%). Finally, we excluded patients with incomplete data, including noncontinuous Medicare part A or part B (6%) or enrollment in part C (26%) from 12 months prior to diagnosis through death. The final study cohort included 63,221 patients. The median age of excluded patients was slightly higher than those in the final study cohort (76 years vs 75 years, respectively).

### Study endpoints

This study's primary endpoint was the receipt of palliative radiation therapy in patients with metastatic cancer. This primary endpoint was ascertained from Medicare claims data by using the daily radiation treatment and weekly management Healthcare Common Procedure Coding System (HCPCS) codes (77371-77373, 77417, 77419-77420, 77425, 77427, 77430-77432, 77435, 77401-77416, 77418, 77422-77423, 77470, 77499, 77520, 77522-77523, 77525, G0173-G0174, G0243, G0251, and G0338-G03340). These radiation codes encompass external beam treatments including 2-dimensional (2D), 3D conformal, intensity modulated radiation therapy, and stereotactic radiation therapy. A course of radiation was defined as a cluster of radiation claims without a break of more than 14 days. Cancer patients often receive multiple courses of radiation, and we assumed that a break in radiation codes of 14 days or more indicated multiple separate courses. Length of an individual course of radiation was defined as the time difference between the first and last radiation claims.

**Table 1** Patient characteristics according to age

Characteristic	Percentage of patients in age (yrs) ranges				
	66-69 (n=11,749)	70-74 (n=15,688)	75-79 (n=15,707)	80-84 (n=11,666)	≥85 (n=8431)
<b>Year of diagnosis</b>					
2000	11	12	12	11	11
2001	11	13	12	11	11
2002	12	13	12	13	11
2003	13	13	13	12	12
2004	14	13	14	14	14
2005	14	13	13	14	14
2006	13	12	13	13	14
2007	12	11	11	12	14
<b>Primary tumor origin</b>					
Lung	73	72	69	61	47
Breast	5	5	5	6	8
Prostate	6	7	8	11	16
Colorectal	16	17	18	22	29
<b>Sex</b>					
Male	57	55	53	50	46
Female	43	45	47	50	54
<b>Race</b>					
White	83	84	84	85	85
Black	12	10	9	8	9
Other	5	6	7	7	6
<b>Marital status</b>					
Married	54	53	50	44	31
Other	46	47	50	56	69
<b>Charlson comorbidity score</b>					
0	55	50	48	47	48
1	26	28	27	28	27
2	10	12	14	14	13
≥3	9	10	11	12	12
<b>Median income</b>					
Bottom quintile	22	21	20	19	18
2nd quintile	21	20	20	20	19
3rd quintile	20	20	20	20	20
4th quintile	19	19	21	20	21
Top quintile	18	19	20	21	22
<b>Geographic region</b>					
East	19	23	24	25	26
Midwest	16	16	16	16	16
South	25	22	20	18	17
West	40	39	40	41	42
<b>Metropolitan area</b>					
Yes	81	82	84	85	85
No	19	18	16	15	15
<b>Density of radiation oncologists (per 1000 square miles)</b>					
<1	26	24	22	20	19
1-10	29	29	28	28	27
11-20	10	10	11	12	12
21-30	8	8	9	9	10
31-40	9	9	10	10	12
≥40	18	19	20	21	21
<b>Aggressiveness of care composite score</b>					
0	52	53	55	59	63
1	18	19	18	18	18
≥2	30	28	26	23	19
<b>Treated with chemotherapy</b>					
Yes	58	53	46	35	21
No	42	47	54	65	79

Bone and brain metastases represent 2 of the most common indications for palliative radiation, and we sought to evaluate these sites further. The ninth revision of the International Classification of Diseases (ICD-9) diagnosis codes from radiation billing claims were used to identify patients treated with bone or brain metastases. ICD-9 diagnosis codes 196 through 198 refer to secondary or metastatic neoplasms, with specific codes for bone (198.5) and brain metastases (198.3) (9). We assumed that patients were treated for bone or brain metastases when the corresponding ICD-9 code was present, in the absence of another metastatic neoplasm ICD-9 diagnosis codes.

## Study covariates

Patient and demographic-related variables obtained from SEER include age, race, sex, marital status, year of diagnosis, geographic location, and median household income. Geographic regions were grouped into East (Connecticut and New Jersey), Midwest (Detroit and Iowa), South (Atlanta, rural Georgia, Kentucky, and Louisiana), and West (San Francisco, Hawaii, New Mexico, Seattle, Utah, San Jose, Los Angeles, and greater California). Median household income was determined from the 2000 census, using census tract data preferentially rather than ZIP code data, and using race- and age-adjusted data preferentially rather than unadjusted data. The proximity of patient to radiation facility was estimated from the number of radiation oncologists per 1000 square miles in the county where the patient resided, as determined from the Area Resource File (10).

This study focused on potential confounding factors that could impact the relationship between age and palliative radiation therapy. Specifically, we focused on patient comorbidity, length of life, and patient tendency toward aggressiveness of care, as we hypothesized that these covariates would vary by patient age and could potentially independently impact the use of palliative radiation therapy. Comorbidity during the 12 months prior to diagnosis was determined from Medicare data by using the Charlson comorbidity index (11) adapted by Deyo et al (12). Length of life, or survival time, was defined as the time from diagnosis through death. Patient tendency toward aggressiveness of care is not explicitly captured in Medicare data; therefore, we used proxy covariates to estimate how receptive a patient would be toward receiving active cancer-directed treatment. Specific measures of aggressiveness included either receipt of chemotherapy at any point after diagnosis or the use of aggressive end-of-life measures. The use of chemotherapy was defined as described elsewhere (13). The use of aggressive care at the end of life (14) was defined as a composite covariate that included any of the following: receiving chemotherapy within 14 days of death, starting a new chemotherapy agent in the last month of life, visiting the emergency room or staying in a hospital more than once in the last month of life, being admitted to an

intensive care unit or spending more than 2 weeks in a hospital in the last month of life, or dying in an acute care hospital.

## Statistical analysis

Continuous covariates such as age were reclassified into categorical covariates. Age was categorized into 5-year increments to allow demonstration of age-specific trends in palliative radiation. Patients over 85 years of age were included in a single category due to small patient numbers. The association of age and palliative radiation therapy was determined with a Poisson regression with robust error estimation (15). We constructed sequential multivariate Poisson regression models to examine potential confounding covariates which impact the age disparity associated with palliative radiation. We selected clinically relevant covariates a priori to enter into the multivariate model. We used a Poisson regression rather than a conventional logistic regression because Poisson regressions have the advantage of producing relative risks, which can be more interpretable than odds ratios. Reported *P* values were all 2-sided and were determined to be significant if less than .05. All analyses were conducted with SAS, version 9.4, software (SAS Institute, Cary, NC).

## Results

Patient characteristics for the 63,221 patients stratified by age are presented in Table 1. We found significant age-related differences among patient characteristics ( $\chi^2$  test,  $P < .05$  for comparison between age and each characteristic in Table 1). Compared to the younger cohort, older patients were less likely to have lung cancer and more likely to have breast, prostate, or colorectal cancer. Older patients were more likely to be female, unmarried, live in metropolitan areas, and have higher comorbidity scores. Older patients were less likely to be treated with chemotherapy and were less likely to have aggressive cancer care at the end of life. The median survival was shorter for older patients than for younger patients. The median survival for patients 66 to 69 was 6 months compared to 3 months for those 85 and older.

Across the whole study cohort, 19,836 patients (31%) received palliative radiation therapy. The rates of palliative radiation therapy decreased steadily with age (Table 2). Among those 66 to 69 years of age, 42% received palliative radiation therapy, which decreased to 14% among patients 85 years and older. The declining trend in the use of palliative radiation therapy was relatively consistent and statistically significant across a wide array of patient covariates (Table 2, *P* value for declining trend,  $< .05$ , for each patient subgroup). Among those treated with chemotherapy, 46% received palliative radiation compared to those not treated with chemotherapy, where 19% received palliative radiation. We found a decreasing rate of palliative

**Table 2** Fraction of patients receiving palliative RT stratified by age

Characteristic	Percentage of patients in age (yrs) ranges				
	66-69	70-74	75-79	80-84	≥85
All patients	42	38	32	24	14
Year of diagnosis					
2000	42	36	31	22	13
2001	43	38	35	24	14
2002	46	36	31	23	16
2003	41	40	32	25	15
2004	42	39	32	24	13
2005	42	39	31	25	14
2006	41	36	29	26	16
2007	43	35	31	25	14
Primary tumor origin					
Lung	48	43	36	30	19
Breast	44	38	36	25	18
Prostate	46	41	36	26	18
Colorectal	16	13	10	7	4
Sex					
Male	41	37	32	25	16
Female	44	38	30	23	13
Race					
White	43	38	32	25	15
Black	36	30	26	18	10
Other	41	38	31	26	14
Marital status					
Married	45	41	35	27	18
Other	38	34	28	22	13
Charlson comorbidity score					
0	44	40	34	26	16
1	43	39	33	25	14
2	37	33	28	21	12
≥3	31	27	23	21	12
Median income					
Bottom quintile	37	32	27	20	12
2nd quintile	41	36	31	25	14
3rd quintile	42	38	31	23	14
4th quintile	45	41	32	27	16
Top quintile	47	41	35	26	16
Geographic region					
East	45	39	33	24	16
Midwest	44	37	31	22	12
South	43	37	31	25	13
West	40	37	31	25	15
Metropolitan area					
Yes	42	38	32	24	15
No	42	37	31	24	12
Density of radiation oncologists (per 1000 square miles)					
<1	42	37	31	22	12
1-10	43	39	32	25	15
11-20	41	40	31	26	16
21-30	43	39	31	24	14
31-40	40	35	33	26	17
≥40	42	37	31	23	14
Aggressiveness of care composite score					
0	45	41	34	26	16
1	44	35	29	22	12
≥2	37	32	27	21	13

*(continued)***Table 2** (*continued*)

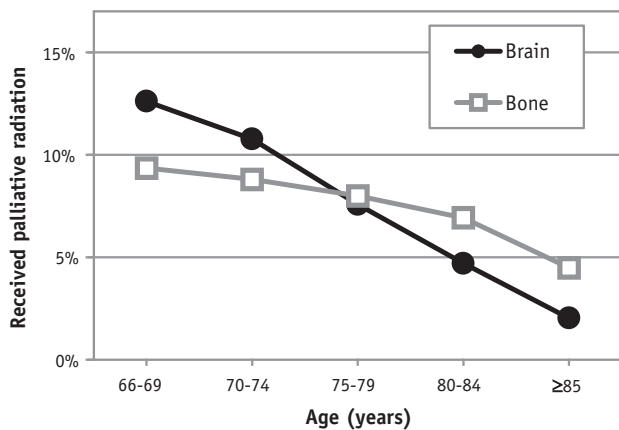
Characteristic	Percentage of patients in age (yrs) ranges				
	66-69	70-74	75-79	80-84	≥85
Treated with chemotherapy					
Yes	55	50	44	36	27
No	25	23	21	18	11

radiation with increasing age both in patients receiving and in those not receiving chemotherapy (Table 2).

We next evaluated age-related differences in specific attributes of palliative radiation. Among those who received palliative radiation, younger patients were more likely to receive longer courses of radiation. The median length of a course of radiation was 18 days (interquartile range, 12-30 days) for those aged 66 to 69, which decreased to 16 days (interquartile range, 11-28 days) for those 85 and over. The average patient received 1.25 courses of radiation per year of life after diagnosis, although younger patients were more likely to receive more than 1 course of radiation therapy. Of patients 66 to 69 years old, 27% received more than 1 course of palliative radiation, which steadily decreased to 15% among those 85 or older.

Further evaluation of the specific indication for radiation revealed specific age-related trends. Among those who received palliative radiation therapy, 6123 subjects received radiation for bone metastases, and 5730 received radiation for brain metastases. While the use of bone and brain radiation decreased with increasing age, the declining use of brain radiation was more pronounced (Fig. 1). With radiation for bone metastases, the use among patients aged 66 to 69 was 9%, which decreased to 4% among those over 85. With radiation for brain metastases, the use among patients aged 66 to 69 was 13%, which decreased to 2% among those over 85.

Next, we sought to determine if potentially confounding covariates impacted the age-related differences in the receipt of palliative radiation. We addressed this question with a multivariate analysis (Table 3). The unadjusted relative rate of palliative radiation decreased steadily with advancing age. Compared to patients 66 to 69 years old, those aged 70 to 74, 75 to 79, 80 to 84, and over 85 had an 11%, 25%, 42%, and 66% decreased rate of receiving palliative radiation, respectively (all,  $P < .0001$ ). Adjusting for patient comorbidity, survival time, and aggressiveness of care all attenuated the relative rate of palliative radiation therapy, although patient demographics and patient geography including the density of radiation oncologist per square mile did not appear to impact the age-related disparity in palliative radiation therapy. After we controlled for all known confounders, the age-related discrepancy in palliative radiation among the elderly remained substantial. Compared to patients 66 to 69 years old, those aged 70 to 74, 75 to 79, 80 to 84, and over 85 had



**Fig. 1.** Palliative radiation indication stratified by patient age. The figure demonstrates use of palliative radiation according to patient age and indication for radiation. Indications for radiation therapy were defined from ICD-9 diagnosis codes from radiation billing claims within Medicare and include bone metastases (gray squares) and brain metastases (black circles).

a 7%, 15%, 25%, and 44% decreased rate of receiving palliative radiation, respectively (all,  $P < .0001$ ).

Finally, we conducted a subset analysis of healthy patients without comorbidity, who received chemotherapy and lived at least 6 months ( $n = 10,834$ ). Multivariate analysis of this subset, controlling for all known confounders, found similar results. On multivariate analysis, among this favorable subset of patients compared to patients aged 66 to 69 years old, those aged 70 to 74, 75 to 79, 80 to 84, and over 85 had an 8%, 14%, 27%, and 39% decreased rate of receiving palliative radiation, respectively (all  $P < .0001$ ).

## Discussion

The principal finding of this study relates to the declining rates of palliative radiation therapy among elderly patients

with metastatic cancer. This analysis found that confounding covariates accounted for a portion of this age-related difference, although the final multivariate analysis shows a clinically relevant decrease in palliative radiation therapy among older patients. Furthermore, our findings of decreased radiation use among older patients held steady among a relatively healthier subset of patients who lived at least 6 months.

Many potential age-related barriers could impact a patient’s decision or ability to receive palliative radiation. Typical courses of radiation include outpatient daily treatments extending over several days or a few weeks. Older people may lack the ability or support system to get to treatment, and lack of transportation has proven to be a potential barrier to cancer care among the elderly in general (16). Of note, this study found that the median course of radiation stretched over 16 to 18 days, depending on patient age. The longer length of a course of radiation could impact a patient’s decision to pursue radiation or could impact a provider’s willingness to refer patients to a radiation oncologist. Increased use of shorter courses of treatment for certain indications such as bone metastases (1) could reduce barriers that prevent older patients who wish to receive radiation. Another factor to consider relates to physician bias. Physicians may consciously or subconsciously feel that older patients would not tolerate or be interested in palliative radiation therapy, which means that an informed discussion with patients might never take place. Increased physician education among referring physicians as well as radiation oncologists or more involvement of radiation oncology in the palliative care team could help increase utilization of palliative radiation therapy. Another important factor to consider is patient preference. Older patients may simply not want to receive palliative radiation therapy, which could mean that the age differences we see in this study simply reflect age-specific differences in patient choice. Although research has not evaluated patient preferences with respect to palliative

**Table 3** Multivariate analysis of palliative radiation therapy

Variable	Relative rate of palliative radiation (95% CI) by age ranges				
	66-69	70-74	75-79	80-84	≥85
Unadjusted	1.00	0.89 (0.86-0.92)	0.75 (0.72-0.77)	0.58 (0.55-0.60)	0.34 (0.32-0.36)
Prior model adjusted for primary tumor site	1.00	0.89 (0.87-0.92)	0.76 (0.74-0.78)	0.61 (0.58-0.63)	0.39 (0.36-0.41)
Prior model adjusted for geography*	1.00	0.89 (0.87-0.92)	0.76 (0.73-0.78)	0.60 (0.58-0.63)	0.38 (0.36-0.41)
Prior model adjusted for patient demographics†	1.00	0.89 (0.86-0.91)	0.76 (0.73-0.78)	0.61 (0.59-0.63)	0.40 (0.37-0.42)
Prior model adjusted for comorbidity‡	1.00	0.90 (0.87-0.92)	0.77 (0.75-0.80)	0.62 (0.60-0.65)	0.41 (0.38-0.43)
Prior model adjusted for survival time§	1.00	0.91 (0.89-0.94)	0.80 (0.78-0.83)	0.67 (0.64-0.69)	0.45 (0.43-0.48)
Prior model adjusted for aggressiveness of care	1.00	0.93 (0.91-0.96)	0.85 (0.82-0.87)	0.75 (0.73-0.78)	0.56 (0.53-0.59)

Abbreviation: CI = confidence interval.

This table represents sequentially constructed multivariate Poisson regression models.

\* Geography refers to geographic region, metropolitan area, and density of radiation oncologists.

† Patient demographics refer to sex, race, median income level, and year of diagnosis.

‡ Comorbidity refers to the Charlson comorbidity score.

§ Survival time refers to the time from diagnosis through death.

|| Aggressiveness of care covariates includes the aggressiveness at end-of-life score (defined in the methods) and the receipt of chemotherapy. All  $P$  values are  $< .0001$ .

radiation, studies surveying patient preference for chemotherapy do not find age-related differences (17). Ultimately, the underlying cause of age-related differences in palliative radiation therapy remains unknown, and future research should focus on identifying potentially surmountable barriers.

An important issue relevant to this study relates to the question of overall effectiveness of palliative radiation therapy among the elderly. Few reported studies compare the efficacy of palliative radiation across different age groups. With bone metastases, a secondary analysis of the Dutch bone metastases study found that patients over 75 had a 67% response rate to palliative bone metastases radiation, slightly lower than that for patients under 65 (78% response rate) (18). Although age is a well-documented adverse prognostic factor in patients with brain metastases (19), research has not thoroughly addressed whether the effectiveness or toxicity of brain radiation varies with patient age. If the efficacy or side effects of radiation depend on the age of the patient, then the declining use of radiation could be appropriate. Further study focusing on age-specific quality of life metrics with palliative radiation is warranted.

This observational population-based study has limitations worth mentioning. Our covariates of patient comorbidity, income level, proximity to radiation oncologist, all reflect estimates. Any age-related bias in these estimates could introduce residual confounding and impact our multivariate analysis. Additionally, our estimate of patient tendency toward aggressiveness of cancer care partly depends on measures of aggressive care at the end of life, which may not accurately reflect a patient's inclination toward receiving aggressive cancer care in general. Also, the administrative data in this project lacks patient-level detail; therefore, we cannot directly assess a medical chart to determine the clinical scenario, indication, or value of palliative radiation. Plus, we cannot account for possible age-specific differences in disease biology, disease presentation, and patterns of progression, any of which could explain the differences in the need for or willingness of a patient to receive palliative radiation therapy. Additionally, we cannot determine patient performance status, which could vary with age, and could potentially account for decreased rates of palliative radiation among the elderly. Another limitation relates to our inability to analyze patients with Medicare Part C, which represents patients enrolled in Health Maintenance Organizations (HMOs) which are not required to submit detailed Medicare claims. This lack of HMO patients leads to an inability to generalize our study findings to this cohort. Finally, as noted above, this study does not address patient preference, which limits our ability to determine whether these age-related differences in palliative radiation represent disparity. Although studies evaluating chemotherapy preference do not find age-specific differences (17), this question should be reassessed in the palliative radiation therapy setting.

## Conclusions

Despite these limitations, this study shows a substantial decrease in the use of palliative radiation therapy among older patients with metastatic cancer. Given the increasingly aging population, as well as the potential quality of life benefit with palliative radiation, future research should strive to define and overcome potential barriers to treatment.

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