Early and Midtreatment Mortality in Palliative Radiotherapy: Emphasizing Patient Selection in High-Quality End-of-Life Care

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ABSTRACT

Background: Palliative radiotherapy (RT) is effective, but some patients die during treatment or too soon afterward to experience benefit. This study investigates end-of-life RT patterns to inform shared decision-making and facilitate treatment consistent with palliative goals. **Materials and Methods:** All patients who died ≤ 6 months after initiating palliative RT at an academic cancer center between 2015 and 2018 were identified. Associations with time-to-death, early mortality (≤ 30 days), and midtreatment mortality were analyzed. **Results:** In total, 1,620 patients died ≤ 6 months from palliative RT initiation, including 574 (34%) deaths at ≤ 30 days and 222 (14%) midtreatment. Median survival was 43 days from RT start (95% CI, 41–45) and varied by site ($P < .001$), ranging from 36 (head and neck) to 53 days (dermal/soft tissue). On multivariable analysis, earlier time-to-death was associated with osseous (hazard ratio [HR], 1.33; $P < .001$) and head and neck (HR, 1.45; $P < .001$) sites, multiple RT courses ≤ 6 months (HR, 1.65; $P < .001$), and multisite treatments (HR, 1.40; $P = .008$), whereas stereotactic technique (HR, 0.77; $P < .001$) and more recent treatment year (HR, 0.82; $P < .001$) were associated with longer survival. No difference in time to death was noted among patients prescribed conventional RT in 1 to 10 versus > 10 fractions (median, 40 vs 47 days; $P = .272$), although the latter entailed longer courses. The 30-day mortality group included 335 (58%) inpatients, who were 27% more likely to die midtreatment ($P = .031$). On multivariable analysis, midtreatment mortality among these inpatients was associated with thoracic (odds ratio [OR], 2.95; $P = .002$) and central nervous system (CNS; OR, 2.44; $P = .002$) indications, > 5 -fraction courses (OR, 3.27; $P < .001$), and performance status of 3 to 4 (OR, 1.63; $P = .050$). Conversely, palliative/supportive care consultation was associated with decreased midtreatment mortality (OR, 0.60; $P = .045$). **Conclusions:** Earlier referrals and hypofractionated courses (≤ 5 –10 treatments) should be routinely considered for palliative RT indications, given the short life expectancies of patients at this stage in their disease course. Providers should exercise caution for emergent thoracic and CNS indications among inpatients with poor prognoses due to high midtreatment mortality.

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Background

Radiotherapy (RT) is an effective palliative tool for symptoms due to cancer, such as pain,^{1,2} neurologic compromise,³ mass effect,⁴ or bleeding,⁵ and remains an important mainstay of end-of-life (EoL) oncologic care. Although palliative RT is effective, some patients may not live long enough to experience its intended benefit. Prior reports of RT at EoL indicate a high proportion of patients die shortly after or during palliative RT.^{6–10} A large systematic review of 18 studies found that palliative RT utilization rates during the last month of life were up to 10% in all patients dying of cancer,¹¹ and another study reported that an estimated 1 in 5 patients who received RT in their final 30 days of life spent > 10 of those days receiving treatment.¹² Separate institutions have indicated that only half of patients undergoing RT at EoL even complete these treatments courses before death.^{13,14} There are also concerns regarding a shift toward more advanced RT technologies for these patients.^{15,16}

Utilization of palliative care is complex and driven by multiple stakeholder perspectives and expectations, including those of consulting and referring providers, patients, and patients' families. The significant proportion of patients dying shortly after or during RT stems from difficulties in predicting life expectancies accurately for terminally ill patients.^{17,18} Provider tendencies to overestimate survival lead to challenges with tailoring palliative regimens and can result in disproportionately

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extensive treatments.^{19–23} Furthermore, such patients are often discharged to their referring providers for follow-up after completion of RT. Taken together, these practice trends call for more data to help guide physician decision-making and improve the quality of RT at EoL.

Therefore, this study examines patterns of early and midtreatment mortality for patients undergoing palliative RT at a large academic cancer center. This investigation is one of the largest institutional series to date, encompassing a wide range of tumor histologies, disease sites, RT prescriptions, and treatment indications, thereby contributing to prior reports in the literature. In addition to describing patterns of RT at EoL, this work evaluates specific clinical factors associated with early and midtreatment mortality, with the goal of helping guide formal communication in EoL care and shared decision-making strategies for terminally ill patients with cancer.

Materials and Methods

Data Sources and Patient Population

All patients who died within 6 months of starting RT at a large academic cancer center between January 1, 2015, and December 31, 2018, were identified through several databases: institutional daily inpatient reports, separate departmental lists, tumor registries, and state registries. These databases were consolidated, with systematic removal of duplicate entries and verification of patients within the electronic medical record. This study protocol was approved by the Institutional Review Board at the University of Texas MD Anderson Cancer Center. Palliative intent was an inclusion criterion, with definitive cases excluded from analysis.

Various clinical factors were collected, including age, treatment service, number of radiation fractions, RT technique, diagnosis, treatment site, indication, inpatient status, number of RT courses within the 6 months preceding death, number of simultaneous treatment sites, and treatment dates. Inpatient status was defined with respect to the date of CT simulation and/or first RT fraction. Performance status (PS) was recorded using 3 different scales: Karnofsky performance score (KPS), ECOG, and the Lansky score for pediatric patients. These were translated into a single PS index for analysis (range, 0–4, analogous to ECOG), using empirically derived and validated interconversion systems.^{24–26}

For treatment sites, vertebral bodies were categorized as osseous. Central nervous system (CNS) site encompassed intracranial disease, leptomeningeal or intramedullary cord involvement, and symptomatic perineural invasion (eg, cranial nerve involvement from skull base tumor) but did not include extrinsic cord compressions alone. Multiple sites (>1) were defined with respect to separate fields/isocenters treated at the

same time within the last course of RT, although these could still be classified under the same anatomic category (eg, femur and humeral bone metastases). At the same time, treatment sites were not mutually exclusive with respect to patient-level coding: for simultaneous sites, each treated region would be noted (eg, both thoracic and bone). Overlapping regions were similarly handled (eg, skull base tumor with symptomatic perineural involvement coded as CNS, bone, and head and neck simultaneously, yet representing a single treatment site or isocenter).

Statistical Analyses

The primary outcomes were time to death (computed from RT start), early mortality (defined as death within 30 days from RT start), and midtreatment mortality (with RT cessation before course completion). Midtreatment mortality included early cessation for discharge to hospice care if the patient died within 1 week of initiating RT; such patients were unlikely to continue RT at our institution after hospice transition. Notably, these endpoints were not mutually exclusive; all patients who died midtreatment also experienced early mortality (within 30 days from RT). For patients who received multiple RT courses within the 6 months preceding death, outcomes were calculated in reference to the last (most recent) treatment course.

The Kaplan-Meier method was used for survival time analysis, with log-rank tests to evaluate differences among groups. Univariate and multivariable Cox proportional hazards analyses were also conducted to identify clinical associations with time to death, generating hazard ratios (HRs) with 95% confidence intervals. For midtreatment mortality, univariate and multivariable logistic regression analyses were used to identify associations with clinical variables, generating odds ratios (ORs) with 95% confidence intervals. Variables were also compared among groups by use of the Mann-Whitney U test for continuous variables and chi-square test for categorical variables. Statistical analyses were performed using SPSS Statistics, version 24 (IBM Corp). For all tests, a *P* value $\leq .050$ was considered statistically significant.

Results

Patient Characteristics

Among 20,534 total RT courses delivered at our large academic center during this time frame (including definitive or palliative intent), a total of 1,912 patients were identified as having died within 6 months of initiating RT. Removal of 292 patients treated with definitive intent resulted in 1,620 study patients treated with palliative RT for analysis, with a median age of 63 years (interquartile range [IQR], 53–70 years) at time of death. Only 18 patients (1%) were aged <18 years. Primary histology included lung (33%), gastrointestinal (13%), breast (10%),

Table 1. Patient Characteristics Who Died ≤6 Months From Palliative RT and Survival Duration (n=1,620)

Variable	Sites n (%)	Time-to-Death HR (95% CI)	Univariate P Value ^a	Time-to-Death HR (95% CI)	Multivariable P Value ^a
Treatment site					
CNS (vs non-CNS)	523 (32)	1.03 (0.93–1.14)	.588		
Bone (vs nonbone)	496 (31)	1.36 (1.22–1.51)	<.001	1.33 (1.19–1.48)	<.001
Thoracic (vs nonthoracic)	275 (17)	0.87 (0.77–0.99)	.038		
Abdominopelvic	198 (12)	0.87 (0.75–1.01)	.065		
Head and neck	115 (7)	1.51 (1.25–1.82)	<.001	1.45 (1.19–1.77)	<.001
Dermal/Soft tissue	104 (6)	0.78 (0.64–0.96)	.016		
Liver (vs nonliver)	24 (1.5)	0.88 (0.59–1.32)	.528		
Primary histology					
Lung (vs nonlung)	534 (33)	1.06 (0.96–1.18)	.270		
Gastrointestinal	206 (13)	1.08 (0.94–1.24)	.289		
Breast (vs nonbreast)	156 (10)	0.99 (0.84–1.17)	.895		
Hematologic	144 (9)	1.14 (0.96–1.35)	.138		
Genitourinary	114 (7)	0.88 (0.73–1.06)	.176		
Head and neck	92 (6)	1.06 (0.85–1.30)	.619		
Gynecologic	75 (5)	0.79 (0.63–1.00)	.052		
RT modality					
Stereotactic	231 (14)	0.74 (0.65–0.86)	<.001	0.77 (0.67–0.89)	<.001
Standard RT	1,389 (86)				
Standard RT fractions					
11–26 (3D/IMRT)	193 (14)	0.92 (0.79–1.07)	.277		
1–10 (2D/3D)	1,196 (86)				
Treatment year					
2017–2018	749 (46)	0.84 (0.76–0.93)	.001	0.82 (0.74–0.91)	<.001
2015–2016	871 (54)				
RT in last 6 mo					
2–5 courses	277 (17)	1.64 (1.44–1.87)	<.001	1.65 (1.44–1.88)	<.001
1 course	1,343 (83)				
Number of sites treated					
2–3	66 (4)	1.77 (1.38–2.26)	<.001	1.40 (1.09–1.80)	.008
1	1,554 (96)				
Patient age					
71–97 y (vs <50 y)	388 (24)	0.98 (0.84–1.13)	.749		
50–70 y (vs <50 y)	928 (57)	0.93 (0.82–1.06)	.273		
2–49 y	304 (19)				

Abbreviations: CNS, central nervous system; HR, hazard ratio; IMRT, intensity-modulated radiotherapy; RT, radiotherapy.

^aCox proportional hazards for univariate and multivariable analyses of associations.

hematologic (9%), genitourinary (7%), head and neck (6%), and gynecologic (5%) cancers (Table 1). Anatomic treatment sites included CNS (32%), bone (31%), thoracic (17%), abdominopelvic (12%), head and neck (7%), dermal/soft tissue (6%), and liver (1.5%). Treatment indications among patients with hematologic cancers (n=144) included (with overlapping regions) osseous sites in 42% (eg, multiple myeloma), dermal/soft tissue

nodules in 21%, CNS disease in 20%, head and neck sites in 17%, and abdominopelvic sites in 11%.

Treatment Details

Multiple sites (2–3) were treated during the last RT course of 66 patients (4%), whereas 277 patients (17%) received multiple RT courses (2–5) within the 6 months preceding death. Of the last RT courses, 231 (14%) involved

stereotactic technique, 79% of which were for brain metastases and 13% were for osseous sites (11% vertebrae). Among patients receiving conventional (nonstereotactic) RT ($n=1,389$), the median number of fractions was 10 (IQR, 5–10) per last treatment course. With respect to hypofractionation, osseous (40%), head and neck (39%), dermal/soft tissue (31%), and abdominopelvic (28%) sites were more likely to be treated with ≤ 5 fractions, whereas thoracic (17%) and CNS (10%) sites were more often prescribed longer fractionation schemes ($P<.001$). However, an increase in ≤ 5 -fraction courses was seen over time, from 24% in 2015–2016 up to 30% in 2017–2018 ($P=.010$).

Survival Time From RT Start

Among all patients dying within 6 months of palliative RT initiation, median survival was 43 days (95% CI, 40.6–45.4) from RT start. Survival duration varied significantly by treatment site (log-rank, $P<.001$): 53 days for dermal/soft tissue (95% CI, 44–62), 47 days for thoracic (95% CI, 41–53), 47 days for CNS (95% CI, 42–52), 46 days for abdominopelvic (95% CI, 37–55), 38 days for bone (95% CI, 33–43), and 36 days for head and neck (95% CI, 32–40) (Figure 1). For patients treated with conventional RT techniques ($n=1,389$), no significant difference was noted in survival time among those prescribed >10 versus 1 to 10 RT fractions (log-rank, $P=.272$; median, 47 [95% CI, 48–56] vs 40 days [95% CI, 38–42], respectively) (Figure 2). On multivariable analysis, multisite treatments (HR, 1.40; $P=.008$), multiple RT courses within 6 months (HR, 1.65; $P<.001$), and treatment of osseous (HR, 1.33; $P<.001$) and head and neck sites (HR, 1.45; $P<.001$) were associated with shorter time to death, whereas stereotactic techniques (HR, 0.77; $P<.001$) and more recent treatment period (2017–2018; HR, 0.82; $P<.001$) were associated with longer survival duration (Table 1).

Early Mortality Within 30 Days From RT Start

Of the 1,620 study patients, 574 (35%) died within 30 days, at a median of 18 days from RT start (95% CI, 16.7–19.3); median PS was 2 (IQR, 2–3). The proportion of patients dying within 30 days varied significantly per treatment site ($P<.001$): bone (43%), head and neck (39%), CNS (32%), abdominopelvic (30%), thoracic (24.5%), and dermal/soft tissue (22%) (Figure 1B), yet no differences were noted with respect to primary tumor histology ($P=.07$). Compared with the remaining 1,046 patients, neither prescribed fractions ($P=.130$) nor patient age ($P=.123$) were significantly different; however, fewer of the patients treated with conventional RT techniques who died within 30 days were treated with stereotactic technique (10% vs 17%; $P<.001$). Patients within the early mortality group treated for thoracic disease ($n=74$) presented nonexclusively with dyspnea

Figure 1. (A) Median time-to-death by treatment site among patients who died ≤ 6 months from palliative RT. (B) Proportion of patients dying within 30 days of RT initiation by anatomic site. Although separated for presentation, patients who died midtreatment (green) also fall into the early mortality group (orange). Abbreviations: CNS, central nervous system; RT, radiotherapy.

(66%; due to airway compromise or obstruction), cough (22%; 12% with hemoptysis), chest pain (19%), and/or superior vena cava syndrome (12%).

Midtreatment Mortality Among All Patients

Among the 1,620 study patients, 222 (14%) died midway through RT before course completion, at a median 15 days (IQR, 14–16) after RT initiation. On multivariable analysis controlling for potential confounders (Table 2), treatment of multiple sites (OR, 2.16; $P=.009$), longer RT courses (>10 fractions; OR, 2.02; $P<.001$), and CNS site (OR, 1.93; $P<.001$) were associated with midtreatment mortality, whereas breast histology (OR, 0.49; $P=.018$) and abdominopelvic site (OR, 0.54; $P=.026$) were associated with decreased likelihood of death during treatment. Notably, neither age nor multiple RT courses within 6 months were significant factors on analysis.

Figure 2. Survival time from RT start for patients who died ≤ 6 months from palliative RT and were treated with standard techniques ($N=1,389$). Patients treated with stereotactic techniques were excluded from this analysis ($n=231$).

Abbreviation: RT, radiotherapy.

Midtreatment Mortality Among Inpatients

Of the 574 patients dying within 30 days, 335 (58%) underwent CT-simulation and/or first fraction of RT during hospital admission. Compared with outpatients who died within 30 days, admitted patients also had poorer PS (3–4; 55% vs 24%; $P<.001$) and were more likely to die midtreatment (42% vs 33.5%; $P=.031$), although no difference in prescribed fractions was noted with respect to admission ($P=.152$). Among these 335 inpatients, multivariable analysis demonstrated that thoracic sites (OR, 2.95; $P=.002$), CNS sites (OR, 2.44; $P=.002$), longer RT courses (>5 fractions; OR, 3.27; $P<.001$), and poor PS (3–4; OR, 1.63; $P=.050$) were variables associated with midtreatment death (Table 3). After chart review, 29 of the 50 inpatient thoracic cases (58%) and 52 of the 98 inpatient CNS cases (53%) died before RT completion. However, palliative/supportive care consultation, which took place for 61% of inpatients, was associated with decreased midtreatment mortality (OR, 0.60; $P=.045$). In addition, increased service referrals were observed over time, from 52% in 2015–2016 up to 69% in 2017–2018 ($P=.002$).

Discussion

This study is one of the largest institutional analyses investigating patterns of early and midtreatment mortality after palliative RT, encompassing a wide range of tumor histologies, disease sites, RT prescriptions, and treatment indications. Among the 1,620 patients who died ≤ 6 months from start of palliative RT at our institution, the most salient findings are as follows: (1) median survival ranges 1 to 2 months among these early patients, one-third of whom

die <30 days and one-seventh of whom die midtreatment; (2) extended RT courses are not associated with longer survival among these patients, but they impart longer treatment courses and carry a greater likelihood of midtreatment mortality; (3) inpatients with emergent thoracic or CNS indications are at high risk for midtreatment death; and (4) palliative/supportive care consultation is associated with decreased likelihood of mortality during treatment.

The high proportion of patients dying during or shortly after palliative RT initiation at this single institution is consistent with prior reports of RT at EoL,^{6–11,13,14} a pattern that stems from difficulties in predicting life expectancies accurately for terminally ill patients.^{17,18} Provider tendencies to overestimate survival lead to delayed patient referrals and challenges with tailoring palliative regimens, which can result in disproportionately extensive treatments.^{19–23} Therefore, these data call for additional efforts toward improving life expectancy assessments, perhaps through predictive modeling methods combining prognostic factors.^{27–37} Notable examples include the Chow,³³ NEAT,³⁸ and TEACHH³⁹ models, each with demonstrated utility for this setting. Consistent with these validated prognostic tools, our study found significant associations with respect to metastatic site, hospital admission, PS, and primary histology to a lesser extent. In addition, multisite treatments and receipt of multiple RT courses, as surrogates of metastatic disease burden, were also found to be associated with study endpoints.

Moreover, several practical conclusions may be derived from these data to help guide physician decision-making. For example, although palliative RT is effective, the limited survival among those who receive it indicates that RT is unlikely to impart a survival benefit among patients with poor prognoses, thus highlighting the importance of early patient referrals at symptom onset and appropriately tailoring RT prescriptions. To this end, our data demonstrate that extended RT courses were not associated with longer survival among patients receiving palliative care who died within 6 months from standard RT, although they were associated with longer treatment durations and greater likelihood of midtreatment mortality among such patients. Although select patients with stage IV disease may benefit from advanced modalities^{40–43} (as demonstrated by the longer survival observed for our stereotactic cohort), in general, shorter hypofractionated courses (≤ 5 –10 treatments) and standard complexity techniques should be prioritized among palliative cases to minimize treatment duration.

These findings are consistent with the ASTRO Choosing Wisely guidelines for EoL RT,^{2,44,45} which advocate for shorter palliative courses among patients with limited life expectancies. Our study reassuringly demonstrates increased use of ≤ 5 -fraction prescriptions over time; however, these courses were most often assigned for

Table 2. Characteristics of All Patients Who Died ≤6 Months From Palliative RT (n=1,620)

Variable	Sites n (%)	Midtreatment Death OR (95% CI)	Univariate P Value ^a	Midtreatment Death OR (95% CI)	Multivariable P Value ^a
Treatment site					
CNS (vs non-CNS)	523 (32)	1.27 (0.95–1.71)	.111	1.93 (1.39–2.67)	<.001
Bone (vs nonbone)	496 (31)	1.13 (0.84–1.53)	.431		
Thoracic (vs nonthoracic)	275 (17)	1.38 (0.97–1.96)	.074		
Abdominopelvic	198 (12)	0.56 (0.33–0.94)	.027	0.54 (0.32–0.93)	.026
Head and neck	115 (7)	1.95 (1.23–3.10)	.005		
Dermal/Soft tissue	104 (6)	0.81 (0.44–1.51)	.508		
Liver (vs nonliver)	24 (1.5)	0.54 (0.13–2.32)	.410		
Primary histology					
Lung (vs nonlung)	533 (33)	1.20 (0.89–1.61)	.230		
Gastrointestinal	205 (13)	0.86 (0.56–1.31)	.484		
Breast (vs nonbreast)	155 (10)	0.60 (0.34–1.05)	.074	0.49 (0.27–0.88)	.018
Hematologic	144 (9)	2.21 (1.47–3.34)	<.001		
Genitourinary	114 (7)	1.03 (0.60–1.78)	.915		
Head and neck	92 (6)	1.04 (0.57–1.90)	.902		
Gynecologic	75 (5)	0.64 (0.29–1.41)	.264		
RT modality					
Stereotactic	231 (14)	0.023 (0.01–0.17)	<.001		
Standard RT	1,389 (86)				
Standard RT fractions					
11–26 (3D/IMRT)	193 (14)	1.89 (1.31–2.73)	.001	2.02 (1.39–2.93)	<.001
1–10 (2D/3D)	1,196 (86)				
Treatment year					
2017–2018	749 (46)	1.01 (0.76–1.34)	.958		
2015–2016	871 (54)				
RT in last 6 mo					
2–5 courses	277 (17)	1.04 (0.72–1.51)	.842		
1 course	1,343 (83)				
Number of sites treated					
2–3	66 (4)	2.69 (1.55–4.68)	<.001	2.16 (1.21–3.87)	.009
1	1,554 (96)				
Patient age					
71–97 y (vs <50 y)	388 (24)	0.65 (0.42–1.01)	.055		
50–70 y (vs <50 y)	928 (57)	0.88 (0.62–1.27)	.503		
2–49 y	304 (19)				

Abbreviations: CNS, central nervous system; IMRT, intensity-modulated radiotherapy; OR, odds ratio; RT, radiotherapy.

^aLogistic regression for univariate and multivariable analyses of associations.

bone or head and neck, with most nonstereotactic CNS and thoracic sites still treated with longer courses. Although perhaps specific to our institution, this practice pattern could stem from a relative lack of data for certain anatomic sites. Multiple studies have demonstrated the noninferiority of shorter regimens for palliation,^{5,46–49} but these have largely focused on bone, head and neck,

and only recently abdominopelvic indications. Data on progressively hypofractionated courses (≤5 treatments) in other sites may encourage their increased use.

Additional study findings of clinical utility entailed the inpatient population with cancer. Hospital admission has been repeatedly associated with poor prognosis among patients receiving palliative RT^{6,7,9,10}; however, inpatient

Table 3. Characteristics of Inpatients Who Died Within 30 Days From Palliative RT (n=335)

Variable	Sites n (%)	Midtreatment Death OR (95% CI)	Univariate P Value ^a	Midtreatment Death OR (95% CI)	Multivariable P Value ^a
Treatment site					
Thoracic (vs nonthoracic)	50 (15)	2.10 (1.14–3.87)	.017	2.95 (1.49–5.81)	.002
Bone (vs nonbone)	156 (47)	0.52 (0.33–0.81)	.004		
CNS (vs non-CNS)	98 (29)	1.85 (1.15–2.97)	.012	2.44 (1.40–4.25)	.002
Head and neck	34 (10)	1.74 (1.07–2.83)	.025		
Abdominopelvic	36 (11)	0.65 (0.31–1.35)	.247		
Dermal/Soft tissue	18 (5)	1.38 (0.54–3.58)	.503		
Liver (vs nonliver)	6 (2)	0.68 (0.12–3.74)	.653		
Primary histology					
Lung (vs nonlung)	99 (30)	1.13 (0.70–1.81)	.622		
Hematologic	50 (15)	1.61 (0.79–3.27)	.192		
Gastrointestinal	42 (12)	0.62 (0.35–1.11)	.108		
Breast (vs nonbreast)	32 (10)	0.59 (0.27–1.29)	.184		
Genitourinary	22 (7)	1.39 (0.59–3.30)	.456		
Head and neck	15 (5)	0.90 (0.31–2.59)	.848		
Gynecologic	13 (4)	1.17 (0.39–3.57)	.779		
Treatment year					
2017–2018	161 (48)	0.94 (0.61–1.45)	.783		
2015–2016	174 (52)				
RT modality					
Stereotactic	13 (4)	NA	.998		
Standard RT	322 (96)				
Standard RT fractions					
6–22 (2D/3D/IMRT)	203 (63)	3.43 (2.09–5.61)	<.001	3.27 (1.92–5.57)	<.001
1–5 (2D/3D)	119 (37)				
RT in last 6 mo					
2–5 courses	277 (83)	0.51 (0.30–0.87)	.013		
1 course	1,343 (17)				
Number of sites treated					
2–3	26 (8)	1.40 (0.63–3.11)	.415		
1	309 (92)				
Performance status					
3–4	183 (55)	1.52 (0.98–2.36)	.062	1.63 (1.00–2.67)	.050
0–2	152 (45)				
Patient age					
71–90 y (vs <50 y)	67 (20)	0.73 (0.38–1.43)	.364		
50–70 y (vs <50 y)	183 (55)	1.33 (0.79–2.24)	.284		
2–49 y	85 (25)				
Palliative consultation					
Yes	204 (61)	0.62 (0.40–0.96)	.032	0.60 (0.37–0.99)	.045
No	131 (39)				

Abbreviations: CNS, central nervous system; IMRT, intensity-modulated radiotherapy; NA, not applicable; OR, odds ratio; RT, radiotherapy.

^aLogistic regression for univariate and multivariable analyses of associations.

consultation requests are common practice for radiation oncologists. Notably, our data indicate that emergent thoracic and CNS indications among inpatients are highly associated with midtreatment mortality and poor PS. Although RT in general can be an extremely useful tool for palliation of spine, brain, or thoracic metastases,^{44,50–53} these inpatient thoracic and CNS cases represented emergent scenarios known to impart poor survival among patients with end-stage cancer, such as airway compromise, severe hemoptysis, altered mental status, seizures, or symptomatic leptomeningeal disease.^{10,13} Our data indicate that such patients are more likely to die midtreatment before RT completion.

Therefore, although palliative RT in general is highly effective for a range of indications, with symptomatic improvement noted even among patients surviving >30 days,¹¹ providers, patients, and families should remain realistic about the potential benefits for emergent inpatient cases, particularly those with poor PS. At the very least, these circumstances should serve as clinical prompts for hospice referral and goals-of-care discussions with patients and families. In support of this, our study found that palliative/supportive care consultation was associated with decreased midtreatment mortality among inpatients, likely through facilitation of advanced planning conversations and coordination of hospice care transition. Although potentially specific to our institution, we also observed a reassuring increase in such referrals over time, suggesting that more providers recognize the benefit of supportive measures at EoL.

Conclusions

This study analyzes patterns of early and midtreatment mortality of patients who died within 6 months of palliative RT at a large academic cancer center. The major limitation of this work is its single-institution, retrospective nature, reflecting practice patterns specific to our group of >70 physicians. Here, palliative RT is largely driven by direct referrals from providers of other disciplines (eg, medical oncology, surgical oncology) who are also subspecialized to treating 1 to 2 disease sites. The observed tertiary cancer center outcomes may not be fully generalizable toward the distinct patient populations treated in community-based practice.

This work also shares inherent biases associated with studies of decedents,⁵⁴ and the 6-month time frame further selected for patients with particularly poor prognoses, limiting our ability to integrate the validated scoring indices of prior models.^{33,38,39} Extent of metastatic disease burden (a significant prognostic factor) was also not quantified via standardized method, with multisite treatments and receipt of multiple RT courses used as surrogate measures. Additional confounders include death from nonmalignant causes (eg, pancytopenia in the setting of hematologic malignancies). Furthermore, this study does not characterize or quantify the intent of therapy, whether goals of palliation (notably symptomatic improvement) were achieved, and the incidence or severity of toxicities (which can significantly impact quality of life in the palliative setting). The design also lacks examination of sociodemographic and cultural factors, which factor into the complexity of palliative care.

However, despite these limitations, our study benefits from being one of the largest series of its kind to date, encompassing a wide range of tumor histologies, disease sites, RT prescriptions, and treatment indications. Taken together, these data strongly advocate for the use of shorter hypofractionated treatment courses during palliative RT for terminally ill patients with cancer, and thereby help inform goals-of-care discussions and shared decision-making strategies to promote high-quality EoL cancer care.

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