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Palliative radiation therapy in the last 30 days of life: A systematic review

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ABSTRACT

Purpose: To investigate the utilization of palliative radiation therapy (RT), predictors for the use of RT, and symptom palliation following RT during the last 30 days of life through systemic review of literature.

Materials/methods: A systematic search of available medical literature databases was performed on patients receiving palliative RT in the last 30 days of life. A total of 18 studies were evaluated.

Results: The overall palliative RT utilization rates during the last month of life were in the range of 5–10% among patients who died of cancer and 9–15.3% of patients who received palliative RT. The most commonly used regimen was 30 Gy in 10 fractions (36–90%). Single fraction RT utilization ranged from 0% to 59%. ECOG performance status 3–4 was significantly associated with patients receiving RT in the last 30 days of life and shorter survival. Twenty-six percent of patients who survived less than 1 month were reported to show symptom palliation following RT.

Conclusion: Palliative RT was performed in approximately 10% of patients who died of cancer near their end of life, with the most commonly used regimen of 30 Gy in 10 fractions. This study suggests that greater use of shorter or single fraction regimens may be beneficial, especially in patients with poor performance status.

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Radiation therapy (RT) is one of the pivotal treatment options in the palliative management of symptomatic disease from advanced cancer. While palliative RT undoubtedly benefits patients with cancer in various stages of the disease, its use during the last month of life has recently been questioned, both in terms of symptom improvement and survival [1–4]. When survival is short, palliative RT may have minimal clinical benefit for patients, delay referral to hospice, and impede optimal end-of-life (EOL) planning and care delivery [5]. It is well-recognized that even experienced oncologists tend to overestimate patient prognosis [4,6,7]. As radiation oncologists incorporate life expectancy estimates into treatment decision-making, including selection of dose-fractionation prescription [8], overestimation of life expectancy may contribute to inappropriate use of longer fractionation regimens. This subjects patients and caregivers to longer active treatment at the EOL [4]. Little is known regarding the frequency of palliative RT use and

patterns of palliative RT in the last 30 days of life, despite its frequent utilization.

The primary aim of the present study was to investigate the utilization of palliative RT, fractionation schedules, predictors for, and efficacy of palliative RT during the last 30 days of life through a systematic review of published literature. Results from this study would help build guidelines for palliative RT in patients at their EOL.

Methods

Online literature search of PubMed, CINAHL, and the Cochrane Review databases was performed to identify all original articles from January 1960 to December 2016. The search terms queried were 'palliative radiation' or 'palliative radiotherapy' and 'end-of-life', 'last 30 days', 'last 1 month', 'terminally ill', and 'hospice'. The reference sections of the selected papers were manually searched for relevant publications.

For this systematic review, we included studies published in English and reporting (1) RT utilization in the last 30 days of life (death within 1 month of completing RT), (2) risk variables associated with receiving RT during the last 30 days of life, and/or (3) the efficacy of RT in the last 30 days of life. Editorials and commentaries were excluded. Articles were screened on the basis

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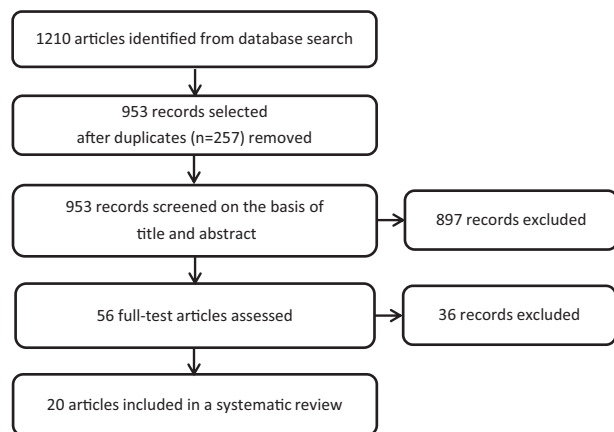


Fig. 1. The PRISMA flow diagram.

of title and abstract, and then selected through reading the complete articles by two authors (Fig. 1). Independent data extraction from articles was made by two authors using predefined data template.

A comprehensive systematic review using the PISMA guideline was conducted. However, a formal meta-analysis was not feasible because of the heterogeneity of patient cohort in published studies and the lack of minimal standards in reporting results.

Results

A total of 20 publications met our inclusion criteria were evaluated, of which 9 studies were from single institutions [4,9–16] and 11 studies from population registries (Table 1) [1–3,17–24]. The patient populations included in these studies varied significantly across different studies. Ten studies examined patients who died of cancer (Table 2) [1,3,9,10,17–21,23], 6 studies presented the frequency of palliative RT among patients receiving specifically palliative RT [2,4,11–13,22], and 2 studies evaluated for patients receiving any RT (Table 3) [14,15]. Most single institution studies examined patients who received palliative RT or any RT and most population based studies evaluated patients who died from cancer.

Utilization of RT during the last 30, 14, and 7 days of life

The overall palliative RT utilization rate in the last 30 days of life widely varied from 0.7% to 33% depending on the study cohort, region (country), and cancer type. The frequency of palliative RT use in the last 30 and 14 days of life ranged between 5% and 10% (mean \pm standard deviation [STDEV] = 7.5 \pm 2.1), and between 2.2% and 4.6% (mean \pm STDEV = 3.5 \pm 1.1) among patients who died from cancer, respectively (Table 2) [10,17,19,23]. The range of pal-

Table 1
Publications on palliative radiation therapy in the last 30 days of life.

Classification of articles	No. of articles	Country	No. of articles
Single Institution Study	9	China	1
		Germany	1
		Norway	3
		USA	4
Population Based Study	11	Dutch	1
		Norway	1
		Swiss	1
		Canada	3
		USA	5
		Total	20

liative RT use rates in the last 30 days of life was 9–15.3% (mean \pm STDEV = 12.1 \pm 3.2) among patients receiving palliative RT, and 6.2–7.2% among patients receiving any RT (Table 3) [4,11,12,14]. The frequency of RT use in the last 30 days for pediatric patients receiving any RT with protons and photons was 0.7% and 1.6%, respectively [15]. Palliative RT was most frequently utilized in patients with lung cancer (Tables 2 and 4) [1,3,9,11,14,17–19,22,23].

Regarding the proportion of time spent on treatment relative to the remaining life span, 33 (52%) of 63 patients who received RT within 30 days of death died during their treatment course, and 43 patients (69%) had their last treatment within 10 days before their death in a single institution study [16]. Half of the patients spent greater than 60% of their remaining life span on therapy in a population based study [4]. Two single intuition studies reported that 6 (10%) of 63 patients who died within 30 days of receiving RT and 12 (4%) of 339 patients whose final RT course was for bone metastases had their final RT on the days of their deaths [13,16].

Radiation treatment

All results associated with radiation treatment procedure are shown in Table 5. The most common indication for RT was metastatic disease, involving bone (33–54%), brain (11–42%), central airway (16%), or spine (11–14%) for all cancer type [4,12,17,23].

Ten fractions of RT was most commonly used (30–90%) [1,4,11,12]. Single fraction radiotherapy (SFRT) utilization ranged from 0% to 59% depending on the treatment center with reported rates of 8–9.4% in the US and 19–59% in Canada [3,13,17,22]. A study of a single institution in Germany showed that SFRT was never applied [4]. The proportions of patients receiving >10 fractions were 17–17.8%, 12%, and 11% in studies from the US, Canada, and Norway, respectively [1,3,13,17,23].

For RT technique, single field (74%) or 3-dimensional treatment planning (17%) was used in a population based study [17]. A study using the NCCN database of NSCLC reported that RT techniques used included conventional 2-dimensional RT (33%), 3-dimensional conformal RT (42%), intensity modulated RT (5%), stereotactic radiosurgery (37%), while 17% of cases did not report the RT technique [1].

The percentage of patients who did not complete RT was 53–82% [1,4,16,17,23]. The causes for not completing RT were poor performance status (47%), patient's death (17–27%), cancer progression, comorbidity, and patient/family preference [1,4,23].

Efficacy of palliative RT in the last month of life

Only 2 studies reported the efficacy of RT during the last month of life. Of 31 patients who died within 30 days after referral for palliative RT, despite palliative RT, condition worsened in 16 (51.6%) patients, and improved or remained stable in 8 (26%) patients. The remaining patients died before they could be assessed [4]. The Dutch Bone Metastasis Study observed that the efficacy of RT for painful bone metastases during the last 12 weeks of life varied by time from death; 25%, 52%, 65%, and 81% for 1–4, 5–8, 9–12, and >12 weeks from death, respectively. Longer survival was associated with higher response rate, while 26% of patients that survived less than 1 month showed symptom response [24].

Predictors for RT and prognostic variables

Table 6 demonstrates the predictors for the use of RT in the last month of life and prognostic variables. Among single institution studies, the patients who had Eastern Cooperative Oncology Group (ECOG) performance status (PS) 3–4, primary lung or bladder cancer, multiple metastases, and evidence of progressive disease

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