

Thirty-day Mortality in Palliative Radiotherapy: A Retrospective Cohort Analysis in a Single Center

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Abstract. *Background/Aim:* Palliative radiotherapy is a critical component of cancer care aimed at symptom management and enhancing the quality of life of patients with advanced cancer. Balancing symptom relief and potential risks is pivotal in clinical decision-making. This study explored the 30-day mortality (30-DM) rate after palliative radiotherapy in a single-center setting to shed light on potential prognostic factors and safety considerations. *Patients and Methods:* This retrospective cohort study included patients who underwent palliative radiotherapy for various indications between March 2020 and February 2023. Data were retrieved from electronic medical records and analyzed according to ethical guidelines. The primary outcome measure was 30-DM rate, and multivariate logistic regression analysis was conducted to identify the independent predictors of 30-DM. *Results:* A total of 931 palliative radiotherapy sessions were administered to 601 patients, with a median of one session per patient. The cohort had a median age of 70 years, predominantly men (58%), and featured diverse primary cancer types, with lung cancer being the most prevalent (15.8%). The 30-DM rate was 12.9%. Multivariate analysis identified Karnofsky Performance Status (KPS) as the sole

independent prognostic factor significantly associated with 30-DM. *Conclusion:* This study provides valuable insights into 30-DM rates following palliative radiotherapy. Future research should focus on prospective multicenter investigations with larger cohorts and comprehensive data collection, ultimately leading to improved risk prediction models for personalized treatment decisions in palliative radiotherapy.

Palliative radiotherapy focuses on the management of symptoms and improvement of quality of life in patients with advanced cancer (1). The primary goal is to alleviate pain, reduce tumor burden, and relieve other symptoms caused by cancer, such as bleeding, obstruction, and neurological deficits (2). The use of palliative radiotherapy is determined on a case-by-case basis, considering the patient's overall condition, the location and extent of the tumor, and the nature of the symptoms. Sullivan *et al.* suggested that appropriate palliative care was associated not only with symptom palliation but also survival benefits among patients with advanced lung cancer (3).

For symptom palliation achieved through radiotherapy for bone metastasis, the onset of effects requires several weeks (4). Therefore, estimating patient prognosis becomes important. However, clinicians often overestimate the survival of patients with advanced cancer (5), resulting in inadequate utilization of palliative and end-of-life care. Guadagnolo *et al.* analyzed data from over 200,000 patients with cancer to evaluate the use of palliative radiation therapy in the last month of life. Nearly 18% of patients who received RT spent more than 10 days undergoing treatment (6). Sborov *et al.* reported that inaccurate survival predictions by oncologists lead to excessive care for patients with advanced cancer (7).

In clinical decision making, 30-day mortality (30-DM) is a pivotal metric (8). This study elucidated the incidence of 30-DM after palliative radiotherapy at a single cancer center. The study also aimed to examine the independent prognostic factors for 30-DM, providing valuable insights into the potential risks associated with palliative radiotherapy.

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Key Words: Palliative radiotherapy, symptom management, quality of life, prognostic factors, single-fraction.

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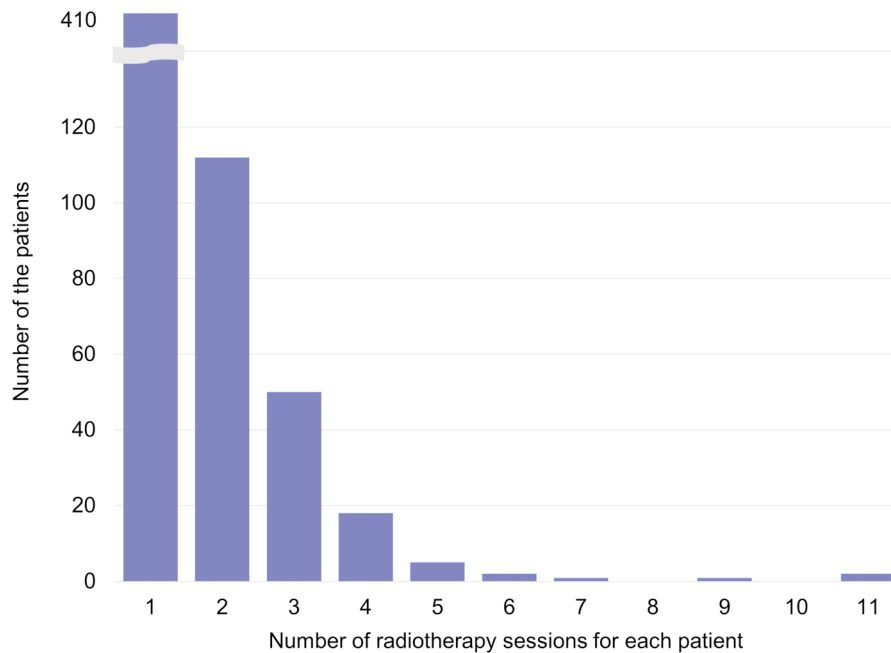


Figure 1. Histogram of the sessions for each patient and the number of the patients.

Patients and Methods

This study was conducted at a single center and involved patients who received repeated palliative radiotherapy for various indications. The inclusion criteria were patients with advanced cancer who underwent at least one session of palliative radiotherapy between March 2020 and February 2023. Patients with incomplete medical records or those lost to follow-up were excluded. The medical records of eligible patients were retrieved from the hospital's electronic database, and relevant data were extracted for analysis. The study was conducted in compliance with the ethical guidelines and was approved by the institutional review board of the ethics committee (Number: 3372-6). Patient data were anonymized and kept confidential throughout the study. The requirement for informed consent was waived due to the retrospective nature of this study.

The main outcome measure in this study was the 30-DM rate following palliative radiotherapy. Subgroup analyses were performed to explore the potential factors associated with increased mortality rates. Univariate and multivariate logistic regression analyses were conducted to determine the independent predictors of 30-DM after adjusting for potential confounders. Statistical significance was set at $p < 0.05$.

Results

In this comprehensive analysis of 931 palliative radiotherapy sessions administered to 601 patients, it was observed that the median number of palliative radiotherapy sessions per patient was one, although one patient received up to 11 sessions (Figure

1). The clinical characteristics of the patients are summarized in Table I. The study cohort had a median age of 70 years (range=3-98 years), with a sex distribution slightly skewed towards men (58% men, 42% women), and the most prevalent primary cancer types were the lungs (15.8%), followed by esophagus (6.6%), prostate (6.0%), and lymphoma (5.9%).

Survival analysis revealed a 30-DM rate of 12.9% in the present study [95% confidence interval (CI)=10.3-16.0%] (Figure 2). We further analyzed the associations between various factors and mortality rates using multivariate logistic regression analysis (Table II). Univariate analysis indicated that KPS [hazard ratio (HR)=6.335; 95%CI=4.822-8.321; $p < 0.001$] and radiotherapy fractionation (HR=0.627; 95%CI=0.496-0.793; $p < 0.001$) were significant prognostic factors associated with increased risk of mortality rate. After multivariate analysis, only KPS still remained an independent prognostic factor (HR=6.249; 95%CI=4.733-8.251; $p < 0.001$).

Among the 70 patients who passed away within 30 days of their last radiotherapy session, it is noteworthy that 36 patients (51.6%) had received a single radiotherapy session, while 15 patients (21.4%) were originally planned for a session consisting of 10 fractions; however, only six patients managed to complete the initially planned radiotherapy treatment. This highlights the challenges and complexities of delivering radiotherapy in a palliative care context and underscores the importance of tailoring treatment regimens to individual patient circumstances.

Table I. Patient clinical characteristics at last palliative radiotherapy in 601 patients in this study.

Variables	Number (Percentage)
Age: Median [Range]	70 [3-98]
Sex	
Male	347 (58%)
Female	254 (42%)
Karnofsky Performance Status	
90	91 (15%)
80	199 (33%)
70	147 (24%)
60	83 (14%)
50	61 (10%)
40	20 (3%)
Radiotherapy fractionation scheme	
30 Gy in 10 fractions	216 (36%)
20 Gy in 5 fractions	200 (33%)
8 Gy in 1 fraction	132 (22%)
39 Gy in 13 fractions	14 (2%)
20 Gy in 4 fractions	7 (1%)
Others	32 (5%)
Primary disease	
Lung cancer	95 (16%)
Esophageal cancer	40 (7%)
Prostate cancer	36 (6%)
Non-Hodgkin's lymphoma	33 (5%)
Stomach cancer	31 (5%)
Breast cancer	27 (4%)
Others	339 (56%)
Site of irradiation	
Distant metastasis	401 (67%)
Primary site	150 (25%)
Regional lymph node	30 (5%)
Others	20 (3%)

Discussion

This retrospective cohort analysis aimed to investigate the 30-DM rate after palliative radiotherapy at a single center. Palliative radiotherapy plays a crucial role in alleviating symptoms and improving the quality of life of patients with advanced and incurable cancer. However, the balance between providing symptomatic relief and ensuring patient safety remains a critical concern. Patients with a limited life expectancy and a compromised performance status might not derive a net advantage from undergoing palliative radiotherapy (9). There is a pressing need for endeavors directed towards the improvement and precision of the criteria employed for determining the appropriate timing of radiotherapy initiation (10). Furthermore, when administering palliative radiotherapy, the implementation of a customized care framework guided by a multidisciplinary healthcare team becomes imperative for enhancing both survival rates and the overall quality of life for these patients (11).

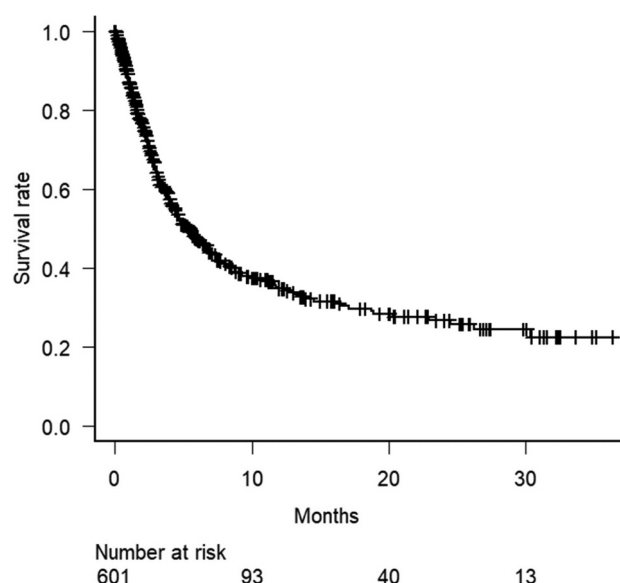


Figure 2. Kaplan–Meier curves for survival in patients who underwent palliative radiotherapy in our institution.

Our study identified a 30-DM rate in patients who received palliative radiotherapy at our center that was comparable to that reported in recently published studies. Spencer *et al.* reported that 30-DM following palliative radiotherapy was 12.9% in a large United Kingdom cancer center. They investigated the factors influencing this rate, considering its significance as a clinical indicator (12). Vázquez *et al.* conducted a retrospective cohort study of 708 patients receiving palliative radiation therapy in 2018 and 2019 that reported a 30-DM rate of 17.5% (13). Kutzko *et al.* conducted a comprehensive literature search from 1980 to 2020 and included various studies that reported the 30-DM in patients with advanced cancer receiving palliative radiotherapy. Their meta-analysis of 42 studies involving 88,516 patients revealed that 16% of patients with advanced cancer died within 30 days of receiving palliative radiotherapy (14).

This finding emphasizes the importance of carefully assessing the potential risks and benefits of radiotherapy for patients in palliative care settings. In addition to age, KPS was the most important indicator of the mortality rate in our cohort. Clinicians must weigh the potential symptomatic relief against these risks, especially in patients with advanced age or significant comorbidities. Park *et al.* suggested that shorter or single-fraction regimens may be more beneficial, particularly for patients with a poor performance status (15). Recently, the European Society for Radiotherapy and Oncology strongly recommended single-fraction radiotherapy for uncomplicated painful bone metastases in their latest guideline (16). Even in complicated bone metastases, single-

Table II. Univariate and multivariate analyses of risk factors for mortality rate after palliative radiotherapy by the proportional hazard model.

Covariables		Univariate analysis			Multivariate analysis		
		Hazard ratio	95%CI	p-Value	Hazard ratio	95%CI	p-Value
Age	≤75 vs. >75 years old	1.033	0.810-1.316	0.795	1.015	0.793-1.298	0.907
Sex	Male vs. Female	0.864	0.685-1.091	0.219	1.046	0.826-1.324	0.711
Performance status	≥80 vs. <80	6.335	4.822-8.321	<0.001	6.249	4.733-8.251	<0.001
Treatment site	Distant metastasis vs. others	0.941	0.733-1.208	0.635	0.873	0.672-1.136	0.312
Radiotherapy fractionation	8 Gy/1 fr vs. others	0.627	0.496-0.793	<0.001	0.808	0.630-1.037	0.094

fraction radiotherapy is useful for neuropathic pain, pathological fractures, extraosseous tumor growth, and spinal cord compression (17). The global COVID-19 pandemic resulted in a decrease in the utilization of palliative radiotherapy requiring 10 or more treatment sessions (18).

This retrospective study has several limitations. First, the single-center design may limit the generalizability of our findings to a broader patient population. Variations in practice patterns and patient demographics in different healthcare settings may influence 30-DM rates following palliative radiotherapy. Second, the retrospective nature of the study introduced inherent biases and limitations in data collection. Missing data, incomplete medical records, and confounding variables may have affected the accuracy of our results. Third, our study did not assess the specific reasons for the 30-DM, such as treatment-related toxicities, disease progression, or other medical complications. A detailed analysis of these factors could provide deeper insight into the causes of mortality in this patient population.

In summary, our retrospective cohort analysis illuminated the intricate landscape of 30-DM rates after palliative radiotherapy at a single center. While reaffirming the indispensable role of palliative radiotherapy in managing symptoms in patients with advanced cancer, our findings underscore the importance of a judicious and tailored approach to treatment decision making. To advance our understanding, future research endeavors should be directed towards mitigating the limitations inherent in our study. Prospective multicenter investigations with larger sample sizes hold promise for furnishing more robust and widely applicable insights into the 30-DM rates following palliative radiotherapy. Comprehensive patient data encompassing treatment-related toxicities and assessments of quality of life should be integrated into these studies, thereby enriching our understanding of the multifaceted risk-benefit spectrum associated with this therapeutic modality.

Furthermore, the development of advanced risk-prediction models has emerged as a pivotal avenue for refining clinical practice. Such models, which meticulously amalgamate patient demographics, comorbidity profiles, treatment

specifics, and disease-related factors, have the potential to yield individualized risk assessments. Armed with these personalized insights, clinicians can engage in more nuanced and informed treatment decisions, ultimately improving the quality of care in palliative radiotherapy.

Conflicts of Interest

The Authors declare that they have no competing interests in relation to this study.

Authors' Contributions

The study was conceived and designed by A.K., and data were acquired by A.K., M.M., G.T., O.S., and H.Y. Data analysis and interpretation were performed by A.K., M.M., G.T., O.S., and H.Y., and the manuscript was drafted by A.K. The final manuscript was read and approved by all the Authors.

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Received September 4, 2023

Revised September 20, 2023

Accepted September 21, 2023