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**Original Article** 

# **Evaluation of Radiotherapy Practice in Patients** Aged over 80: A Retrospective Study

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### South Asian | Cancer

## Abstract



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#### **Keywords**

- older patients
- malignancy
- octogenarians
- overall survival
- radiotherapy

# Introduction

The elderly population is defined as individuals aged  $\geq 65$ years. The global burden of the elderly population is consistently increasing.<sup>1,2</sup> According to recent statistics, Turkey is among the countries with an increasing elderly population rate, and this increase is anticipated to continue. Population

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Background The study aims to evaluate the survival outcomes, survival-related prognostic factors, and treatment compliance in cancer patients aged  $\geq 80$  years treated with radiotherapy (RT).

Methods The records of 76 patients who received RT at a single center between August 2021 and May 2024 were retrospectively evaluated. Patient and tumor characteristics and treatment details were collected from medical records.

**Results** The median age of the patients was 83 years (range: 80–92 years). According to the purpose of RT, palliative (53.8%), definitive (18.4%), and adjuvant (15.8%) RT were most frequently administered, respectively. The median overall survival (OS) in all patients was 10 months. The median OS in patients receiving curative (definitive and adjuvant RT) and palliative RT was 25.1 and 7.2 months, respectively. Poor performance status (PS), leukocyte count prior to RT, compliance, and hospitalization status in the curative group and poor PS, RT compliance, hospitalization status, and new distant recurrence in the palliative group were associated with decreased OS. The majority of patients showed full compliance with the RT process (69.7%). The rate of full compliance with the treatment process was significantly higher in patients with good PS and receiving outpatient treatment. RT-related high-grade toxicity (grade 3–4) was not observed.

**Conclusion** This study demonstrates that RT can be used effectively and safely for both palliative and curative purposes in cancer patients aged  $\geq$ 80 years. The optimization of patient selection and ultimately improvement of treatment outcomes will be facilitated by the support of these results with multicenter studies.

> projections indicate that the elderly population rate is anticipated to reach 12.9% in 2030, 16.3% in 2040, 22.6% in 2060, and 25.6% in 2080.<sup>3</sup> The rise in the elderly population suggests that we should develop strategies to provide health care in the most effective manner. Otherwise, the aging population will face medical and sociodemographic challenges.

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When health problems of older people are considered, cancer occupies an important place. Cancer is accepted as a disease predominantly affecting the elderly. According to the U.S. National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program data, the median age at cancer diagnosis is 65 years for all types of cancer.<sup>4</sup> Cancer is the second most prevalent cause of mortality in this age group, following cardiac causes, and 60% of cancer cases appear for people over the age of 65 years.<sup>5</sup> By 2050, it is projected that 20.5% of all cancer diagnoses globally will occur in patients aged  $\geq$ 80 years.<sup>6</sup>

From a medical perspective, there is a race against time in terms of treatment for the elderly population. The presence of comorbidities, overall performance status (PS), and the additional challenges caused by cancer complicate the use of standard treatment algorithms for these patients. A significant number of patients are ineligible for surgical or systemic treatments due to these and similar reasons. Especially in these patients, radiotherapy (RT) is known as the prominent treatment modality due to its successful results, the minimum toxicity, and high tolerability. However, studies with strong evidence that could establish standardized treatment strategies, RT techniques, and tolerability, especially for older patients aged  $\geq$ 80 years, are very limited. The specific needs and challenges faced by elderly cancer patients necessitate dedicated studies in geriatric oncology. This study was designed considering the paucity of data on geriatric oncology in the literature, the importance of this age group, especially those aged  $\geq$ 80 years, which requires a much more sensitive approach in the health system, and the place of RT in treatment algorithms. Our objective is to offer a detailed evaluation of the overall survival (OS), treatment compliance, and toxicities in this age group following RT. Furthermore, by filling the existing knowledge gap, we hope that this study will contribute to the development of treatment guidelines that will assist in clinical decision-making for patients aged  $\geq$ 80 years.

## **Material and Methods**

## **Selection of Patients and General Characteristics**

This retrospective study was performed at a single center, using data obtained from medical records. The study protocol was approved by the Education Planning Board of our center. In addition, the University of Health Sciences Turkey, Hamidiye Scientific Research Ethics Committee approved the protocol of this study on October 17, 2024, with the meeting number 2024/12 and decision number 12/13, and found it ethically appropriate.

The study examined patients who received RT in our department as part of their cancer treatment between August 2021 and May 2024. The data recording system between these dates was scanned, and patients aged  $\geq$ 80 years were included in the study. Patients who younger than 80 years and who had missing information to be collected for the study were excluded from this study. These patients diagnosed with various malignancies received RT using different fractionation schemes based on the site of involvement and the treatment objectives.

#### **Examination of Clinical and Laboratory Parameters**

Data regarding patient demographics, tumor characteristics, treatment specifics, and clinical follow-up outcomes was collected. These data include age, gender, Eastern Cooperative Oncology Group (ECOG) PS,<sup>7</sup> comorbidities, tumor type and stage, treatment protocols, radiation doses, purpose of RT, RT compliance, RT-related side effects (used the Common Terminology Criteria for Adverse Events, version 5.0),<sup>8</sup> various pretreatment blood parameters (hemoglobin value, leukocyte count, and C-reactive protein level), hospitalization, surgical history, systemic treatment status, and survival outcomes.

The primary endpoint was determined as OS. OS was defined as the time from the start of RT to the date of death or last follow-up. Secondary endpoints were determined as treatment compliance and toxicity.

#### **Statistical Analysis**

IBM Statistical Package for the Social Sciences (SPSS) Statistics version 21 (IBM Corporation, Armonk, NY, United States) was used for statistical analysis. Categorical data are expressed with n (%), while numerical parameters are presented with median (min-max) or mean  $\pm$  standard deviation. The Kolmogorov–Smirnov test was used to examine whether the numerical data exhibited a normal distribution. A chi-squared test was used to determine differences in categorical variables between groups. Survival data were analyzed using Kaplan–Meier curves. Subgroup analyses were performed to assess possible associations between clinical outcomes and patient or tumor characteristics. Cox regression was utilized to perform multivariate survival analyses. A p-value of less than 0.05 was considered statistically significant.

#### Results

A total of 2,434 patient files were reviewed from the medical record archive and a total of 76 patients aged  $\geq$ 80 years were included in the study. The median age of the patients was 83 years (range: 80–92 years). A predominantly male (n = 44) cohort (male-to-female ratio: 1.37) was seen. Three or more comorbid diseases were present in 30.3% (n = 23) of the patients. The three most common primary cancers were colorectal (21.1%, n = 16), lung (18.4%, n = 14), and prostate cancer (18.4%, n = 14). According to gender, the most common cancers in men were prostate (31.8%, n = 14) and lung cancer (25%, n = 11), and the most common cancers in women were colorectal (34.4%, n = 11) and breast cancer (31.3%, n = 10). At first presentation, patients were most frequently in metastatic stage (58.3%, n = 42) and most frequently had bone metastasis (31%, n = 13).

The most common types of RT were palliative (53.8%, n = 41), definitive (18.4%, n = 14), and adjuvant (15.8%, n = 12). During RT, 23 (30.3%) patients were hospitalized for various reasons. As part of their oncological treatment, 20 patients (26.3%) underwent surgery, while 54 patients (71.1%) received various systemic treatments (most frequently 39.5% classical chemotherapy and 25% hormonotherapy; **Table 1**).

Table 1 Patient and treatmen	t characteristics
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Variables	Patient							
	n	%						
Sex								
Male Female	Iale44emale32							
ECOG performance status								
1 2 3 4	11 33 21 11	14.5 43.4 27.6 14.5						
Primary disease								
Lung Breast Prostate Colorectal Others	1418.41013.21418.41621.12228.9							
Stage								
1 2 3 4	6 11 13 42	8.3 15.3 18.1 58.3						
Site of metastasis <sup>a</sup>		•						
Bone Visceral Brain Mix	13 11 7 11	31.0 26.2 16.6 26.2						
Hemoglobin value <sup>b</sup> (g/dL): mean (min–max)	11.9 (7.5–16)							
Leukocyte count <sup>b</sup> (µL)	9,000 (1,400–31,000)							
CRP level <sup>b</sup> (mg/L): mean (min–max)	69.2 (0.6–267)							
Purpose of radiotherapy								
Palliative Definitive Adjuvant Neoadjuvant	41 14 12 9	53.8 18.4 15.8 11.8						
Oncological outcome								
Complete response Partial response Stable disease Progressive disease Not followed up	13 9 13 10 31	17.1 11.8 17.1 13.2 40.8						
Status								
Exitus Alive	41 35	53.9 46.1						

Abbreviations: CRP, C-reactive protein; ECOG, Eastern Cooperative Oncology Group.

<sup>a</sup>In metastatic patients.

<sup>b</sup>Two to 4 weeks before to radiotherapy.

The mean follow-up time post-RT was 8.6 months. Thirtyone patients (40.8%) could not be followed because of mortality during RT or immediately afterward. Among the 45 patients with accessible follow-up data, 22 (48.8%) exhib-



**Fig. 1** The Kaplan–Meier plot showing overall survival rates by curative and palliative treatment groups.

ited a complete oncological response or regression, whereas 10 patients (22.2%) showed a progression.

The median OS time for all the patients was 10 months. During the analysis, it was determined that the majority of the patients died (n = 41, 53.9%). The 1- and 2-year OS after RT for all patients was 47.5% (95% confidence interval [CI]: 41.6-53.6%) and 34.6% (95% CI: 26.8-42.4%), respectively. Patients treated with curative (definitive, neoadjuvant, and adjuvant RT) and palliative aims were assessed separately. The median, 6-month, and 2-year survival rates for the curative group were 25.1 months, 85.4%, and 72.2% and 7.2 months, 33.1%, and 6.5% were palliative groups, and the difference was significant (p < 0.000; **Fig. 1**). Subgroup analyses were performed on patient, tumor, and treatment characteristics to determine prognostic factors affecting OS in both groups. In the curative group, factors associated with worse survival in univariate analyses were poor PS (ECOG: 3-4; p < 0.000), leukocyte count before RT (p = 0.004), RT compliance (p = 0.004), and hospitalization status (p < 0.000). In multivariate analyses, poor PS (p = 0.001) remained significantly associated with survival. In the palliative group, factors associated with worse survival in univariate analyzes were poor PS (p < 0.000), RT compliance (p = 0.001), hospitalization status (p = 0.006), and new distant recurrence (p = 0.027). In multivariate analyses, new distant recurrence (p = 0.008) remained significantly associated with survival ( **Table 2**).

The majority of patients (69.7%, n = 53) showed full compliance with RT; however, 14 patients (18.4%) were unable to complete the planned treatment and 9 patients (11.8%) completed their treatment with a delay (prolonged treatment). Exitus (42.8%) and medical instability (42.8%) were the most common two reasons patients did not complete treatment, whereas technical problems (77.7%, n = 7) were the most common reason for prolonged treatment. Subgroup analyses related to patient and treatment characteristics were performed to identify prognostic factors associated with treatment compliance. Patient performance (p = 0.003) and hospitalization status (p < 0.000) were significantly associated

Univariate analysis	Treated with curative intent			Treated with palliative intent		
	p-value	HR	95% CI	p-value	HR	95% CI
ECOG PS 3-4 vs. 1-2	< 0.000	60.644	7.101–517.87	< 0.000	7.286	2.704-19.636
<b>Leukocyte count (µL)</b> > 8,000 vs. ≤8,000	0.004	1.112	1.355–9.090	0.027	5.500	1.004-30.116
RT compliance Incomplete vs. complete	0.004	6.172	1.497–2.564	0.001	3.636	1.587-8.333
Hospitalization Outpatient vs. inpatient	< 0.000	28.145	4.295–184.45	0.006	2.739	1.290-5.815
Multivariate analysis	Treated with curative intent			Treated with palliative intent		
Multivariate significant only for ECOG PS 3–4 vs. 1–2	0.001	287.45	1.889–4374.04			
Multivariate significant only for new distant recurrence				0.008	10.827	1.207–97.141

Table 2 Factors associated with mortality in patients receiving radiotherapy

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; PS, performance status.

with treatment compliance. Patients with good PS (ECOG: 1–2; 69.8 vs. 30.2%) and outpatients (83 vs. 17%) had higher compliance. The majority of patients (75%, n = 57) showed no acute toxicity following RT. Five patients (6.6%) had grade 1 toxicity, and 14 patients (18.4%) had grade 2 toxicity.

## Discussion

This study demonstrates that RT can be used effectively and safely for both palliative and curative purposes in cancer patients aged  $\geq$ 80 years. It was determined that the majority of the patients showed full compliance with the treatment process (69.7%, n = 53). The rate of full compliance with the treatment process was significantly higher in patients with good PS and in outpatients. RT-related high-grade toxicity (grade: 3–4) was not observed in this study population.

The elderly population around the world is increasing day by day.<sup>9</sup> Cancer constitutes one of the most important health problems of elderly individuals, with both its morbidities and socioeconomic effects. The evidence supporting oncological treatments in older patients remains inadequate due to their lack of representation in clinical trials. In terms of RT, much less data are available.<sup>10</sup> RT is an important treatment modality for elderly cancer patients, as modern techniques have minimized side effects and allowed shorter treatment hypofractionated regimens. In the present study, oncological outcomes, treatment tolerance, and compliance with the use of RT in elderly cancer patients in our clinic were investigated.

Pilleron et al published a study reporting the estimated global cancer incidence among those aged  $\geq$ 80 years and projections to 2050.<sup>6</sup> The study reported that in 2018, an estimated 2.3 million new cases of cancer (excluding non-melanoma skin cancers) were detected worldwide in adults aged  $\geq$ 80 years (13% of all cancer cases). The most common cancers in women were breast, lung, and colon cancers; the most common cancers in men were prostate, lung, and colon

cancer. In the current study, the most common cancers in men were prostate and lung cancers, and the most common cancers in women were colorectal and breast cancers. Another study examining cancer statistics for adults aged  $\geq$ 85 years reported that cancer is generally diagnosed at more advanced stages in this age group.<sup>11</sup> Accordingly, in breast and colorectal cancer, the incidence of local-stage disease at diagnosis in patients aged  $\geq$ 85 years is 10% lower compared with those aged 65 to 84 years. Similarly, in our study, more than half of the patients were in the metastatic stage at the time of presentation, and more than half of the treatments consisted of palliatives. Accordingly, clinicians should consider the diagnosis of cancer more frequently in older patients presenting with any complaint.

A study examining cancer incidence, mortality, and treatment data among individuals aged  $\geq$ 85 years in the United States demonstrated that cancer is the second most common cause of death in this population, following heart disease. The remaining lifetime risk of cancer mortality is reported as 14.4% for men and 9.6% for women. Again, in the same study, the most common causes of cancer deaths were prostate and lung cancers in men and lung and breast cancers in women.<sup>11</sup> A separate study assessing the clinical results and safety profile of RT in nonagenarians revealed OS rates of 55.4% at 1 year and 38.3% at 3 years. PS and primary site RT were reported as independent prognostic factors for OS.<sup>12</sup> The median OS for all patients in the current study was 10 months, with 1- and 2-year OS rates of 47.5 and 34.6%, respectively. Survival was better in patients who received curative treatment. PS, leukocyte count prior to RT, RT compliance, and hospitalization status were found to be associated with OS.

In most oncological treatment protocols, chronological age by itself is not a contraindication for curative treatment. Modern RT techniques, especially for early-stage and elderly cancer patients with contraindications to other therapies like surgery, can enable a successful treatment outcome.<sup>13,14</sup>

In our study, most of the patients with available follow-up data (48.8%) had complete oncological response or regression. Nevertheless, a majority of patients exhibiting a progressive disease (70%) experienced distant recurrence. These data once again highlight the crucial role that rapidly developing targeted systemic treatments and immunotherapies will play in providing systemic control for these patients.

There are many studies that show that RT is well tolerated by elderly cancer patients. Ikeda et al conducted a retrospective study on curative RT in elderly patients, reporting a treatment completion rate of 75% and highlighting the significance of family support.<sup>15</sup> Kocik et al investigated the feasibility of RT in a cohort of 93 nonagenarian patients. Of the patients, 85% completed the planned RT, whereas only 4% reported grade 3 or higher adverse events.<sup>16</sup> Similarly, in the current study, full compliance was seen in the majority of patients (69.7%). PS and hospitalization were found to be significantly associated with RT compliance. No grade 3 or higher adverse events were detected in our patients.

The primary limitation of this study is its retrospective nature, which may introduce unavoidable biases in data collection. The single-center design of the study restricts the generalizability of the findings. Furthermore, the absence of a control group and the heterogeneity in tumor types and treatment regimens make it difficult to conduct comparative analyses regarding the effectiveness of RT within the cohort. Further multicenter studies with larger sample sizes are required to confirm our results and provide stronger evidence.

In spite of these limitations, our study contains important data concerning the use of RT in patients aged  $\geq$ 80 years. The exclusion of patients in this age group in many studies in the literature makes the study much more valuable. The current data provided crucial information into survival outcomes, follow-up, and treatment compliance associated with RT in this age group, thus contributing significantly to the body of knowledge in this area.

In conclusion, our study demonstrates that RT can be used safely and effectively with patients aged  $\geq$ 80 years. Although the management of elderly cancer patients still presents many challenges for radiation oncologists, RT is an important treatment option for these patients with promising treatment responses and acceptable toxicity rates. In this growing patient population, research must be increased to improve patient selection and develop more effective treatments.

#### **Authors' Contributions**

The concept and design of the study were developed by H.D., İ.B., İ.A., M.C.K. Acquisition and analysis of data were done by H.D., İ.B., and İ.A. Drafting of the manuscript was

done by H.D., İ.B., and M.C.K. Critical review of the manuscript was done by H.D., İ.B., İ.A., and M.C.K.

## **Conflict of Interest**

None declared.

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