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ORIGINAL ARTICLE

Outcomes of Radiotherapy and Chemoradiotherapy in Patients Aged ≥70 Years with Stage III Non-Small Cell Lung Cancer: A Retrospective Single-Center Analysis

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OBJECTIVE

The aim of the study is to evaluate overall survival (OS) and radiation pneumonitis (RP) in patients aged ≥70 years with stage III non-small cell lung cancer (NSCLC) treated with definitive radiotherapy (RT) or concurrent chemoradiotherapy (CRT).

METHODS

A retrospective analysis included 104 patients. Clinical, dosimetric, and treatment-related factors were assessed. Survival was analyzed using Kaplan–Meier and Cox regression models.

RESULTS

Median OS was 21 months (95% confidence interval: 17–24). Univariate analysis showed associations between OS and Karnofsky Performance Status, tumor volume, total mean lung dose (tMLD), histopathology, chemotherapy use and regimen, RP grade, and RT response. Multivariate analysis identified planning target volume, tMLD, RT response, and RP as independent predictors of OS. RP severity was significantly associated with comorbidities, lymph node location, chemotherapy regimen, and higher lung dose-volume parameters (tV50–60, iV45–60).

CONCLUSION

OS in elderly stage III NSCLC patients is influenced by tumor response and lung dosimetry. RP independently worsens survival. Treatment decisions should rely on functional status rather than age, and concurrent CRT is feasible in selected patients.

Keywords: Concurrent chemoradiotherapy; definitive radiotherapy; geriatric patients; non-small cell lung cancer; overall survival.

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INTRODUCTION

Lung cancer is one of the most common malignancies in the elderly population and has the highest mortality rate.[1] Approximately 85% of lung cancer patients have non-small cell lung cancer (NSCLC), and about 25% of these patients are in the locally advanced stage. [2] Due to the median age at diagnosis being over 70 years, a significant portion of NSCLC patients are in the geriatric patient group. Looking at the entire NSCLC patient group, more than 50% of patients are over 65 years old, and 30–40% are over 70 years old.[3] This situation makes the question of how and under what conditions curative approaches in the treatment

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of stage III NSCLC can be applied in the geriatric patient population even more clinically important.

At present, treatment for stage III NSCLC involves multimodal approaches aimed at curative outcomes, but common comorbidities in patients aged 70 and over, and age-related physiological reserve loss, lead to clinical uncertainties regarding patient tolerance of standard treatment approaches and the risk of treatment-related toxicity.[4,5] Therefore, treatment decisions in geriatric NSCLC patients should be carefully evaluated not only in terms of oncological efficacy but also in terms of treatment tolerance and toxicity risk.

The median age of patients diagnosed with lung cancer is 71 years, and although a significant proportion of patients diagnosed with lung cancer are in the geriatric group, these patients are often excluded from clinical trials, making it difficult to provide evidence-based treatment to the elderly population.[6] Furthermore, the exclusion of elderly patients from studies may lead to inadequate treatment in this age group due to concerns about potential toxicity. As expected, physiological reserve decreases with aging, and the incidence of many comorbid diseases and the use of multiple drugs increase. Such factors can also hinder elderly patients from tolerating standard treatment. However, treatment decisions for elderly patients should not be made solely based on chronological age; the expected lifespan, patient preferences, functional age, and additional diseases should be considered, and the expected benefit and potential side effects of the treatment should be evaluated together.[7]

Treatment decisions for elderly lung cancer patients have mostly been derived from retrospective studies or subgroup analyses of randomized trials. Some of these studies have shown that elderly patients benefit from chemoradiotherapy (CRT), while others have shown no difference in oncological outcomes between CRT and radiotherapy (RT).[8,9] This makes treatment selection difficult for clinicians.

In this study, overall survival (OS) outcomes and factors affecting OS were evaluated in patients aged ≥70 years with stage III NSCLC diagnosed with definitive RT and concurrent CRT, and the development of radiation-induced pneumonia was investigated.

MATERIALS AND METHODS

Patients

This retrospective study evaluated 104 geriatric patients diagnosed with stage III NSCLC who received definitive RT or CRT between January 2014 and December 2024. Inclusion criteria were age 70 years or older at diagnosis, histopathological diagnosis of NSCLC, TNM stage III, Karnofsky performance status (KPS) ≥60, completion of RT or CRT, and attendance at regular follow-up appointments. Patients with multiple primary tumors or missing clinical, treatment, dosimetric, or follow-up data required for the analyses were excluded from the study. Follow-up data were censored on June 30, 2025. The median follow-up duration, measured from the 1st day of RT to the date of death or last clinical follow-up, was 19 months (range, 3–94 months). OS was defined as the time from diagnosis to death or the last follow-up date. None of the patients received consolidation durvalumab during the study period, and chemotherapy administered before or after definitive RT/CRT (induction or sequential regimens) was not separately categorized in the present analysis.

Thoracic computed tomography (CT), 18F-fluorodeoxyglucose positron emission tomography-CT (18F-FDG-PET-CT), and brain magnetic resonance imaging were ordered for staging.

Tumor staging was performed according to the TNM classification system valid at the time of diagnosis. For uniformity, all patients were retrospectively reclassified according to the 8th edition of the TNM staging system for lung cancer.[10] Staging, treatment decision, and post-treatment response evaluation were performed multidisciplinarily at the Lung Oncology Council. OS was defined as the time from diagnosis to death or the last follow-up date. Treatment response evaluation was performed according to the response evaluation criteria in solid tumors version 1.1 (RECIST 1.1) using the first CT images obtained within the first 6 months after completion of RT.[11]

Radiation pneumonitis (RP) was classified according to the Radiation Therapy Oncology Group (RTOG) grading systems. Patients were graded in terms of their need for clinical support, along with imaging and examination findings.[12] Patients with a preliminary diagnosis of RP were again evaluated multidisciplinarily in the Lung Cancer Board.

This study was approved by the Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee (Decision No. 70, decision date: January 06, 2026).

The study was conducted in accordance with the principles of the Declaration of Helsinki.

Treatment

Patients were immobilized in a supine position with their hands above their heads on a T-bar/Wingboard. Images with a thickness of 2–3 mm were obtained be-

tween the cricoid cartilage and the upper border of the L2 vertebra using Siemens Somatom Definition AS (Siemens Healthineers) and GE Discovery RT (GE Healthcare) CT devices. Diagnostic Thoracic CT and 18F-FDG-PET-CT were fused with planning CT.

Gross tumor volume (GTV) was contoured for the tumor, based on the post-CT volume in patients receiving chemotherapy (ChT) before definitive RT. Lymph node GTV (GTV_nod) was defined based on the pre-treatment volume in patients receiving ChT. For clinical target volume (CTV), a margin of 0.6 cm was given for squamous cell carcinoma (SCC) and 0.8 cm for adenocarcinoma (ACC); 0.5 cm was added to the GTV_nod volume. CTV_node and CTV_tumor volumes were combined to create CTV_total, and a 0.5 cm margin was added to CTV_total for the planning target volume (PTV). Treatment planning in all patients was performed using intensity-modulated RT or volumetric modulated arc therapy techniques, and treatments were administered under image-guided RT. Treatment planning was performed using the Varian Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA, USA) and the Anisotropic Analytical Algorithm. Patients were treated with Varian Trilogy and Varian TrueBeam linear accelerators (Varian Medical Systems).

Most patients received conventionally fractionated RT (60–66 Gy). In selected elderly patients, a hypofractionated regimen of 45 Gy in 15 fractions was used according to multidisciplinary clinical judgment.

Platinum-based regimens were used as concurrent ChT. The chemotherapy regimen consisted of weekly cisplatin (40 mg/m^2) or carboplatin (AUC 2) + paclitaxel (50 mg/m^2). Before the decision for concurrent ChT, patients were evaluated based on numerous parameters including blood values, additional comorbidities, cardiomyopathy, medications used, and smoking history. Consultations were requested from relevant departments (cardiology, gastroenterology, nephrology, etc.) for patients deemed necessary.

Patients receiving only RT were seen in the outpatient clinic at least once a week during their RT treatment. Patients receiving concurrent ChT were evaluated in the outpatient clinic at least three times a week. Blood values were recorded before and after concurrent ChT, and close monitoring was performed during the application of concurrent ChT.

Variables İncluded in the Analysis

The variables evaluated were age, gender, KPS, smoking history, history of chronic disease, histopathological subtype, tumor location, central or peripheral tumor location, tumor size, location of pathological lymphadenopathy (LAP), pathological LAP level (single level, multilevel, or none), T stage, N stage, TNM stage, presence of concurrent ChT, concurrent ChT regimen, GTV, PTV, RT dose, RP grade, total lung volumes receiving ≥5–60 Gy dose (tV5–V60), total mean lung dose (tMLD), ipsilateral lung volumes receiving ≥5–60 Gy dose (iV5–V60), ipsilateral mean lung dose (iMLD), contralateral lung volumes receiving ≥5–60 Gy dose (cV5–cV60), and contralateral mean lung dose (kMLD).

Statistics

IBM Statistical Package for the Social Sciences for Windows 21.0 and MEDCAL 20.106 were used for data analysis. Shapiro–Wilk's test was used to determine the normality of the distribution of variables. Parametric and non-parametric tests were used to compare groups. One-way analysis of variance and Kruskal–Wallis tests were used to compare groups. Post hoc tests were used to identify different groups. Mann–Whitney U test was used to determine the difference between the medians of two groups. Chi-square tests were used to analyze the created cross-tables. Kaplan–Meier test was used to compare median survival times, and the log-rank test was used to determine group differences. Univariate and multivariate stepwise Cox proportional hazards regression were used to determine the effects of prognostic variables on survival time. For summarizing the data, number (%) statistics were used for qualitative data, and Mean±SD or Median (Q1; Q3) statistics were used for quantitative data. $P<0.05$ was considered statistically significant.

RESULTS

The median age was 74 (min: 70, max: 85). The median KPS was 80 (min: 60, max: 100). 100 patients (96.2%) were male and 4 (3.8%) were female. Seventy (67.3%) patients had a history of chronic disease, while 34 (32.7%) patients did not have a history of chronic disease. The median RT dose was 60 Gy (min: 45, max: 68), and 60 (57.7%) patients received concurrent ChT. Patient, tumor, and treatment characteristics are summarized in Table 1.

The rate of concurrent ChT was statistically significantly higher in patients with higher KPS ($p<0.001$). The median KPS was 80 (Q1–Q3: 80–90) in patients receiving concurrent ChT, while the median KPS was 70 (Q1–Q3: 70–80) in patients not receiving ChT. A box-plot graph showing the relationship between KPS and concurrent ChT is presented in Figure 1.

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Table 1 Patient, tumor, and treatment characteristics

Features	n (%) / Median (min, max)	Features	n (%) / Median (min, max)
Age	74 (70–85)	Mediastinal	29 (27.9)
Karnofsky performance status	80 (60–100)	Hilar+mediastinal	45 (43.3)
Gender		Hilar+mediastinal+supraclavicular	3 (2.9)
Female	4 (3.8)	Lymph node level involvement	
Male	100 (96.2)	None	15 (14.4)
History of smoking		Single-level	31(29.8)
+	100 (96.2)	Multilevel	58 (55.8)
–	4 (3.8)	T Stage	
Chronic comorbidity		T2	10 (9.6)
+	70 (67.3)	T3	24 (23.1)
–	34 (32.7)	T4	70 (67.3)
Histopathology		N Stage	
Squamous cell carcinoma	75(72.1)	N0	16 (15.4)
Adenocarcinoma	29 (27.9)	N1	11 (10.6)
Tumor Location		N2	60 (57.7)
Right lower lobe	19 (18.3)	N3	17 (16.3)
Right middle lobe	10 (9.6)	TNM Stage	
Right upper lobe	34 (32.7)	3A	35 (33.7)
Left lower lobe	15 (14.4)	3B	55 (52.9)
Left upper lobe	26 (25)	3C	14 (13.5)
Tumor size (cm)	5.7 (2–16)	Radiation dose (Gy)	60 (45–68)
GTV (cc)	99 (4–1581)	Concurrent chemotherapy	
PTV(cc)	302 (43–2334)	+	60 (57.7)
Tumor location		–	44 (42.3)
Peripheral	35 (33.7)	Concurrent chemotherapy regimen	
Central	69 (66.3)	None	44 (42.3)
Pathological lymph node location		Cisplatin-based	27 (26.0)
None	15(14.4)	Carboplatin–paclitaxel	33 (31.7)
Hilar	12 (11.5)		

PTV: Planning target volume; GTV: Gross tumor volume.

A statistically significant inverse relationship was found between age and KPS with KPS decreasing significantly as age increased ($p<0.05$).

Based on thoracic CT assessments performed within the first 6 months after RT, partial response (PR) was detected in 48 patients (46.2%), stable disease in 32 patients (30.7%), and progression in 24 patients (23.1%).

OS

The median OS in the entire patient group determined by the Kaplan–Meier method was 21 months (95% CI: 17–24). The mean survival was found to be 31 months (95% CI: 26–37). At the last follow-up, 22 patients (21.2%) were alive and 82 patients (78.8%) were deceased. The Kaplan–Meier curve for OS is shown in Figure 2. The 1-, 2-, and 5-year OS rates were 79.2%, 49.0%, and 22.9%,

Univariate Cox Regression Analysis Results

In the univariate Cox regression analysis, higher KPS was found to be significantly associated with better OS (HR: 0.97; 95% CI: 0.94–0.99; p=0.018). Conversely, increased GTV shortened OS and increased the risk of all-cause mortality (HR=1.002, 95% CI: 1.001–1.003, p=0.001); this risk corresponds to approximately a 2% increased risk for every 10 cc increase in GTV (HR≈1.02). Similarly, increased PTV was found to be associated with worsening OS (HR: 1.001; 95% CI: 1.000–1.002; p=0.001). This effect indicates that every

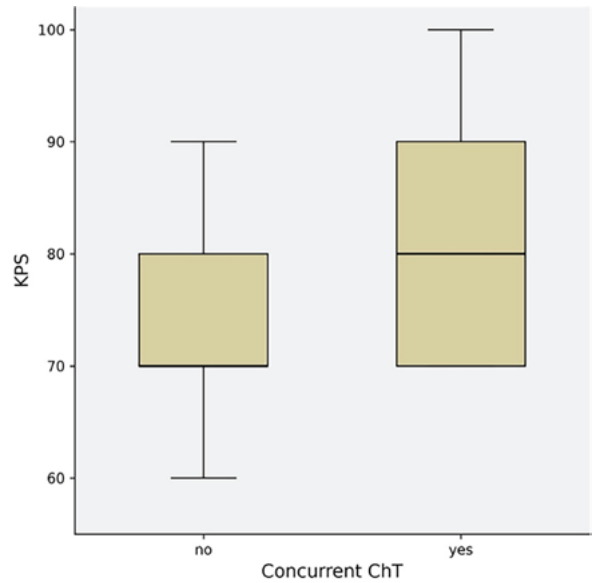


Fig. 1. Box-and-whisker plot showing the distribution of values.

10 cc increase in PTV corresponds to approximately a 1% increase in mortality risk (HR≈1.01).

Increased tMLD was associated with worse OS (HR=1.001, 95% CI: 1.001–1.002, p=0.001). Each 1 Gy (100 cGy) increase in mean lung dose corresponds to approximately a 10.5% increase in mortality risk (HR≈1.105).

When histopathological subgroups were examined, the median OS was 20 months (95% CI: 15–24) in patients with SCC and 27 months (95% CI: 6–47) in those with ACC. In the geriatric group, patients with ACC histopathology had a statistically significantly longer OS (p=0.024).

Concurrent ChT resulted in a significant difference in OS (p=0.020). The median OS was 16 months (95% CI: 12–19) in patients not receiving concurrent ChT, while it was 25 months (95% CI: 19–30) in patients receiving concurrent ChT. The ChT regimen was also associated with OS (p=0.032). When comparing patient groups, the median OS was 16 months (95% CI: 12–19) in the group not receiving ChT, 23 months (95% CI: 14–31) in the cisplatin group, and 27 months (95% CI: 10–43) in the carboplatin-paclitaxel group.

The distribution of OS differed significantly according to RP grade groups (p<0.001). The median OS was 18 months (95% CI: 8–27) in patients without RP, 22 months (95% CI: 17–26 and 15–28, respectively) in patients with grade 1 and Grade 2 RP, 12 months (95% CI: 7–16) in those with Grade 3 RP, and 4 months in those with Grade 5 RP. OS decreased significantly in patients with Grade 3 and above RP.

The distributions of OS according to the CT assessment of RT response (RECIST) showed borderline differences (p=0.051). The median OS was 22 months in the stable response group (95% CI: 15–28), 18 months in the progressive response group (95% CI: 12–23), and 22 months in the PR group (95% CI: 15–28). The difference between groups was more pronounced when considering the mean OS, with 26 months in the stable group (95% CI: 19–32), 20 months in the progressive group (95% CI: 15–24), and 38 months in the PR group (95% CI: 28–48).

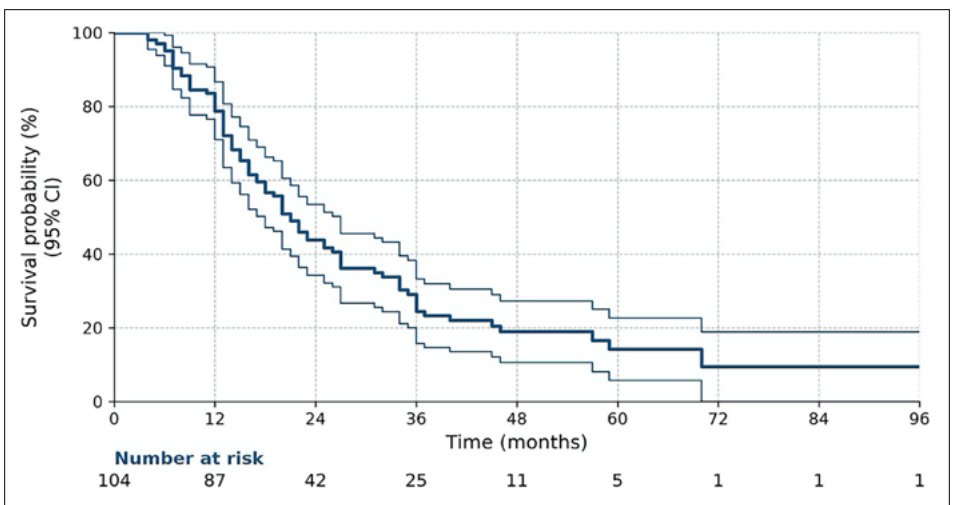


Fig. 2. Overall survival of patients aged ≥70 years with stage III non-small cell lung cancer (Kaplan–Meier analysis).

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Table 2 Univariate Cox proportional hazards regression analysis for overall survival

Variable	HR	%95 CI	p
KPS	0.970	0.94–0.990	0.018
PTV	1.001	1.000–1.002	0.001
GTV	1.002	1.001–1.003	0.001
tMLD	1.001	1.001–1.002	0.001
Histopathological subtype	---	---	0.024†
Concurrent ChT (yes/no)	---	---	0.020†
Concurrent ChT regimen	---	---	0.032†
RP	---	---	<0.001†
RT response (RECIST 1.1)	---	---	0.050†

†: Categorical variables were evaluated using the Kaplan–Meier method and log-rank test; global p-values are presented for these variables. HR: Hazard ratio; CI: Confidence interval; KPS: Karnofsky performance status; PTV: Planning target volume; GTV: Gross tumor volume; tMLD: Mean lung dose; ChT: Chemotherapy; RP: Radiation pneumonitis; RT: Radiotherapy; RECIST: Response evaluation criteria in solid tumors.

The univariate Cox regression analysis is summarized in Table 2.

Multivariate Cox Regression Analysis Results

In the multivariate Cox regression analysis, increased PTV was found to be independently associated with worsening OS (HR: 1.001; 95% CI: 1.000–1.002; p=0.026). Furthermore, tMLD was identified as an independent negative prognostic factor for OS (HR: 1.002; 95% CI: 1.001–1.002; p=0.001). RT response (RECIST) (p=0.021) and the presence of RP (p=0.031) were also found to be independently associated with OS in the multivariate analysis. In contrast, KPS and concurrent ChT administration did not maintain their statistical significance in the multivariate analysis (p>0.05). The multivariate Cox regression analysis is summarized in Table 3.

Toxicity

Out of a total of 104 patients, 54 (51.9%) developed Grade 0 RP, 45 (43.3%) developed Grade 1–2 RP, and 5 (4.8%) developed Grade ≥3 RP. The RP distribution graph is given in Figure 3. Among patients with severe RP, four experienced Grade 3 RP, one developed Grade 5 RP, and no Grade 4 events were observed.

23 (67.6%) patients without chronic disease had Grade 0, 11 (32.4%) had Grade 1–2 RP, and no patient had ≥Grade 3 RP. 31 (44.3%) patients with chronic disease had Grade 0, 34 (48.6%) had Grade 1–2, and 5 (7.1%) had ≥Grade 3 RP. A significant relationship was found between the presence of chronic disease and RP grade (p=0.048). Rates of Grade 1–2 and Grade ≥3 pneumonia are higher in patients with chronic disease, and Grade ≥3 pneumonia was observed only in patients with chronic disease (7.1% vs. 0%).

A significant association was found between pathological lymph node location and RP pneumonitis (p=0.015). RP rates were higher in patients with hilar/mediastinal LAP.

A significant association was found between ChT regimen and RP, with higher rates of Gr1–2 and Gr≥3 pneumonia in patients receiving carboplatin-paclitaxel (54.5% and 9.1%, respectively) (p=0.043).

Regarding total lung dosimetric characteristics, tV50 (p=0.026), tV55 (p=0.016), and tV60 (p=0.048)

Table 3 Multivariate Cox proportional hazards regression analysis for overall survival

Variable	HR	%95 CI	p
KPS	0.97	0.94–1.002	0.063
PTV	1.001	1.000–1.002	0.026
tMLD	1.002	1.001–1.002	0.001
Concurrent ChT (yes/no)	0.634	0.380–1.056	0.080
RP (overall)	---	---	<0.031†
Grade 0 RP	Reference	---	---
Grade 1–2 versus Grade 0 RP	0.649	0.402-1.048	0.077
Grade 3–5 versus Grade 0 RP	2.200	0.808-5.993	0.123
RT response (RECIST) (overall)	---	---	0.021†
Partial response	Reference	---	---
Stable disease versus partial response	1.636	0.886–3.020	0.116
Progressive disease versus partial response	0.731	0.424–1.260	0.259

†: For multicategorical variables (RECIST response and radiation pneumonitis), global p-values were calculated using the Wald test. The final multivariate model was constructed using the backward stepwise (Wald) method. HR: Hazard ratio; CI: Confidence interval; PTV: Planning target volume; tMLD: Total mean lung dose; KPS: Karnofsky performance status; ChT: Chemotherapy; RT: Radiotherapy; RECIST: Response evaluation criteria in solid tumors; RP: Radiation pneumonitis.

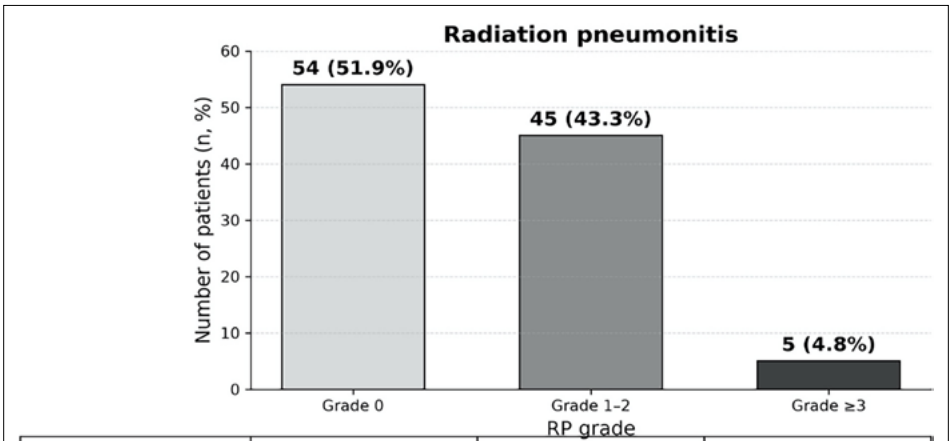


Fig. 3. Distribution of radiation pneumonitis grades (n=104).

showed significant differences, while no significant differences were found in tMLD and lower dose volumes. In post hoc analysis, values for all three parameters were found to be higher in the Grade 1–2 pneumonitis group compared to the non-pneumonitis (Grade 0) group (p=0.021 for tV50; p=0.013 for tV55; p=0.043 for tV60). No significant difference was observed between the Grade ≥3 pneumonia group and the other groups.

In the comparison of ipsilateral lung dosimetric values between RP grade groups, significant differences were found in iV45, iV50, iV55, and iV60 values (p=0.039, p=0.025, p=0.008, p=0.042, respectively); however, no significant difference was found at lower dose volumes and in terms of iMLD. Post hoc pairwise comparisons showed that significance stemmed from the difference between Grade 0 and Grade 1–2 groups (iV45 p=0.032; iV50 p=0.020; iV55 p=0.006; iV60 p=0.037); however, no significant difference was observed between Grade ≥3 and the other groups. Significant variables associated with RP are presented in Table 4.

DISCUSSION

Due to the increase in life expectancy, the number of patients diagnosed with lung cancer in the elderly group is also increasing, and the management of geriatric lung cancer patients is becoming increasingly important. However, the recommendations in the current international oncology guidelines are not directly applicable to this patient group. With advancing age, comorbid diseases such as diabetes, chronic

Table 4 Variables significantly associated with radiation pneumonitis

Variable	Grade 0 Median (IQR)	Grade 1–2 Median (IQR)	Grade ≥3 Median (IQR)	p
Chronic comorbidity	–	–	–	0.048
Pathological lymph node location	–	–	–	0.015
Concurrent ChT regimen	–	–	–	0.043
tV50	3.75 (3.65)	5.40 (4.40)	4.70 (2.55)	0.026
tV55	2.25 (2.93)	4.00 (3.40)	3.80 (1.65)	0.016
tV60	0.80 (2.23	1.60 (2.75)	0.70 (2.45)	0.048
iV45	10.60 (9.68)	14.70 (9.65)	13.80 (5.40)	0.039
iV50	7.20 (7.15)	11.70 (8.40)	11.20 (5.15)	0.025
iV55	4.95 (5.73)	8.00 (7.00)	8.90 (4.40)	0.008
iV60	2.00 (4.25)	3.50 (5.45)	**1.40 (5.15)**	0.042

ChT: concurrent chemotherapy; tV50, tV55, tV60: Percentage of total lung volume receiving ≥50 Gy, ≥55 Gy, and ≥60 Gy, respectively; iV45, iV50, iV55, iV60: percentage of ipsilateral lung volume receiving ≥45 Gy, ≥50 Gy, ≥55 Gy, and ≥60 Gy, respectively. (Values are presented as median (interquartile range, IQR). p-values were obtained using the Kruskal–Wallis test followed by post hoc pairwise comparisons where appropriate).

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lung diseases, and cardiovascular diseases are also frequently observed. At the same time, geriatric syndromes such as malnutrition and cognitive impairment are more common in this age group. Age-related physiological changes, comorbid diseases and the use of multiple drugs due to them, and malnutrition can alter the metabolism of ChT drugs and cause serious toxicity even at low doses. Exclusion of elderly patients from clinical trials leads to insufficient evidence-based treatment recommendations in this patient group. This causes clinicians to make treatment decisions based on chronological age. This situation can result in functionally fit patients receiving inadequate treatment. The main goal in treatment is to provide treatment with an appropriate therapeutic index, taking into account the patient's functional age.[13]

In our current study, a statistically significant inverse relationship was found between age and KPS, with KPS decreasing as age increases ($p<0.05$). In patients receiving concurrent chemotherapy, KPS was found to be statistically higher ($p<0.001$). In a study conducted by Logtenberg et al.,[14] concurrent or sequential ChT was evaluated in elderly patients, and similarly to our current study, statistically significantly more concurrent ChT was given to younger patients with higher performance scores ($p<0.001$). Functional age, as well as chronological age, actually affects the treatment decision. In conclusion, the patient's performance status must also be evaluated in the decision for concurrent chemotherapy. It should be considered that a patient with a higher KPS despite being older may tolerate concurrent ChT better than a younger patient with a lower KPS.

In our current study, the median OS was 21 months (95% CI: 17–24). The mean survival was found to be 31 months (95% CI: 26–37). The 1-, 2-, and 5-year OS rates were 79.2%, 49.0%, and 22.9%, respectively. In the literature, the median OS in stage III NSCLC receiving curative treatment ranges from 19 to 30 months.[15–17] In the study conducted by Driessen et al.[18] in elderly patients with stage III NSCLC, the median OS, as well as the 1- and 2-year OS rates, were 18 months (95% CI: 9.2–27), 57%, and 21%, respectively, in the concurrent CRT group. In contrast, in the RT -alone group, the median OS and the 1- and 2-year OS rates were 11 months (95% CI: 5.5–16), 49%, and 14%, respectively. In a review of patients diagnosed with stage III NSCLC, the 5-year OS was found to be 30%.[17] Although our study included a geriatric patient population, the median and long-term survival results obtained are consistent with the stage III NSCLC OS data reported in the literature, and it is seen that definitive RT and concurrent CRT for curative purposes may be an effective and feasible treatment option in functionally selected elderly patients. However, patients receiving concurrent CRT had significantly higher baseline KPS. Therefore, the observed survival difference between RT alone and concurrent CRT should be interpreted cautiously, as treatment-selection bias may have influenced this finding.

In this study, factors affecting overall OS in a geriatric patient group were evaluated using univariate and multivariate analyses; in the multivariate analysis, PTV, tMLD, response to RT (RECIST), and RP development were identified as independent determinants of OS. These findings demonstrate that in a geriatric patient group, OS is closely related not only to tumor biology and treatment response but also to treatment volume and lung dosimetric parameters.

Larger PTV volumes indicate both tumor and nodal disease burden and cause organs at risk to receive higher doses. In stage III disease, larger PTV volumes lead to higher lung doses, which increases the risk of pulmonary toxicity and reduces treatment tolerance, leading to poor oncological outcomes. In the RTOG 0617 study, PTV was also evaluated as a prognostic parameter.[19] In the study by Karin et al.,[20] a PTV >700 cc in stage III NSCLC treated with CRT was found to be associated with poor OS. In another study, tumor volume and primary tumor volume were found to statistically significantly affect OS in stage III NSCLC treated with CRT, but nodal volume alone did not.[21] In summary, regardless of T and N stages, OS is poor in large-volume tumors. Similarly, our study found that large tumor volume was associated with poor OS, with each 10 cc increase in PTV resulting in a 1% increase in mortality risk. Larger tumor volume causes an increase in MLD as expected. In stage III NSCLC, the negative impact of increased MLD on OS has been reported in the literature. In a retrospective study evaluating 468 patients diagnosed with stage III NSCLC and treated with RT, MLD was found to be an independent prognostic predictor for OS.[22] Similarly, in the study by Stervik et al.,[23] age and increased MLD were found to be associated with an increased risk of short-term respiratory-related mortality; this was indirectly associated with poor OS.

In our study, a significant relationship was found between RT response and OS. The literature also reports that RT response is closely related to survival; one study showed that the median OS was approximately 33.6 months in patients who achieved complete

response (CR)/PR, while the median OS was only 7.3 months in patients with progressive disease.[24]

Increased MLD with large PTV volumes facilitates RP development, reducing treatment tolerance. In our study, this interaction was thought to negatively affect OS in geriatric stage III NSCLC patients.

In the present study, RP was not observed in 51.9% of patients, while mild-to-moderate (Grade 1–2) RP was observed in 43.3% and Grade 3 and above RP in 4.8%. In a systematic review and meta-analysis conducted by Kuang et al.[25] with patients diagnosed with stage III NSCLC, the rate of Grade 3 and above RP was reported to range from 0 to 8.3%. Although our study only included geriatric patients, the Grade ≥3 RP rate of 4.8% was found to be consistent with the literature. The risk of radiation pneumonia is associated not only with dosimetric parameters but also with chronic comorbidities. Chronic diseases such as diabetes mellitus and chronic obstructive pulmonary disease have been reported to increase the risk of RP.[26,27] The increased risk of RP due to chronic comorbidities can be largely explained by the increase in the basal inflammatory background of the lung, endothelial/microvascular dysfunction, and decreased pulmonary reserve.[28]

The more frequent occurrence of comorbidities in geriatric patients often leads clinicians to adopt a more protective approach towards this patient group. Our findings suggest that carefully selected elderly patients may tolerate RT and CRT with acceptable toxicity. However, only patients who completed treatment and attended regular follow-up were included in this study.

The addition of concurrent ChT to RT is also known to increase the risk of RP.[29] In our study, concurrent ChT, especially when administered with the carboplatin-paclitaxel regimen, was found to be associated with a higher risk of developing RP. Therefore, this suggests that when planning concurrent treatment in the geriatric patient group, not only oncological efficacy but also pulmonary reserve and comorbidity profile, i.e., functional age, should be carefully evaluated. In our study, a significant relationship was found between the development of RP and high-dose lung volumes (tV50–60 and iV45–60), while no significant relationship was observed with MLD and low-dose volumes. Similar to our study, there are studies that identify high-dose volumes as a risk factor for the development of RP.[30,31] These findings suggest that cellular damage and associated local inflammation developing in high-dose lung portions may contribute to the development of RP. These findings may be particularly relevant in elderly patients because of age-related reductions in pulmonary reserve; however, this hypothesis requires confirmation in larger prospective studies.

In our study, significant associations between RP and high-dose lung dose–volume parameters were observed primarily between patients with Grade 0 and Grade 1–2 RP, whereas no statistically significant differences were identified between patients with Grade ≥3 RP and the other RP groups. Given the limited number of severe RP events, these findings should be considered exploratory and interpreted with caution. Although minimizing high-dose lung volumes during treatment planning remains a reasonable strategy whenever clinically feasible, the present study does not support the definition of elderly-specific lung dose constraints or specific threshold values.

Limitations of the Study

This study has several limitations. Its retrospective and single-center design may have resulted in patient selection and treatment decisions being based on institutional experience rather than standardized, contemporary geriatric guidelines. Furthermore, the lack of routine application of comprehensive geriatric assessment (CGA) parameters (such as frailty scores, cognitive status, and nutritional status) prevented a complete analysis of the difference between chronological age and functional age. Although KPS was used to assess functional status, it primarily reflects performance rather than the multidimensional concept of functional age. Established geriatric assessment approaches, including the Charlson Comorbidity Index, validated geriatric screening tools, and CGA, may provide a more comprehensive evaluation of physiological reserve, frailty, and treatment tolerance in older adults. Future prospective studies incorporating these assessments may improve patient selection and individualized treatment strategies in elderly patients with stage III NSCLC. In addition, RP and RECIST response were assessed after treatment initiation and were analyzed as fixed covariates in the survival analysis. Therefore, the observed associations between these post-treatment variables and OS may have been influenced by time-dependent (guaranteed-time) bias and should not be interpreted as evidence of an independent causal relationship. This consideration is particularly relevant for Grade 5 RP, which by definition represents treatment-related mortality. The presence of chronic disease was considered as a single variable, and chronic lung diseases, cardiovascular diseases, and diabetes mellitus could

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not be examined as separate subgroups. Finally, the small number of patients who developed severe RP (Grade ≥3, n=5) limited the statistical power of analyses involving severe toxicity. Therefore, findings related to severe RP should be interpreted cautiously and require validation in larger prospective cohorts.

CONCLUSION

The standard treatment approach for stage III NSCLC patients aged ≥70 years remains unclear. The limited elderly-specific prospective evidence leads to heterogeneity in treatment approaches for this age group, with treatment decisions often relying on clinician judgment. In the geriatric patient group, OS was found to be closely related not only to tumor response but also to treatment volume and lung dosimetric parameters. The development of RP stands out as an independent factor negatively affecting OS in the geriatric patient group. Higher high-dose lung volumes were associated with RP in this cohort. Therefore, minimizing high-dose lung exposure during treatment planning may be considered whenever clinically feasible. However, the present findings are exploratory and do not support the definition of elderly-specific dose constraints or specific threshold values. According to this study, definitive RT and concurrent ChT can be applied with close monitoring in functionally appropriate selected geriatric patients.

Ethics Committee Approval: The study was approved by the Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee (no: 70, date: 06/01/2026).

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