National Multi-Center Observational Retrospective Study to Understand Treatment Patterns and Outcomes for Stage III Non-Small Cell Lung Cancer Patients in Turkey: Turkish Society for Radiation Oncology Study, STONE Trial

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ABSTRACT

This study investigated treatment patterns and outcomes in patients with inoperable stage III non-small cell lung cancer (NSCLC) treated with radiotherapy (RT) in Turkey. We included 492 patients with stage III NSCLC in this multi-center retrospective study. Patient demographics, clinical characteristics, and clinical treatment patterns from the time of the initial diagnosis to disease progression were recorded. Additionally, the prognostic factors predicting overall survival (OS) and progression-free survival (PFS) were analyzed. For the initial treatment, 429 patients (89.2%) received chemotherapy and RT, whereas 53 patients (10.8%) were treated only with RT. The first disease progression occurred in 288 patients (58.4%) at 9.3 months (median) after the initial treatment, and 64.6% received treatment after first progression. The second disease progression occurred in 30 patients, and 20 patients (66.7%) received treatment. Median OS and PFS were 27.0 months and 13.4 months, respectively. Age ($p< 0.001$), stage ($p= 0.04$), poor performance score (PS) ($p= 0.03$) and RT doses ($p= 0.002$) were independent predictors for OS and PFS in our multivariate analysis. Additional significant predictors for OS in the multivariate analysis were gender ($p= 0.004$), treatment period (0.02), and irradiation technique ($p= 0.02$). Disease progression occurred in nearly 58% of the patients, and one-third of these patients remained untreated during the disease progression. These findings indicate a need for additional treatment options in patients with unresectable stage III NSCLC with high-risk features, namely older age, stage IIIB disease, poor PS, and lower RT doses.

Keywords: Lung cancer, Stage III, Treatment patterns, Chemotherapy, Radiotherapy

INTRODUCTION

Lung cancer is the leading cause of cancer death worldwide in both sexes.[1] Most patients with lung cancer are diagnosed with non-small cell lung cancer (NSCLC), and approximately 20%–25% of all NSCLC patients diagnosed at stage III disease typically have unresectable disease.[2,3] Due to the heterogeneous characteristics of stage III disease, namely large tumors that invade surrounding tissues without lymph node metastasis or small tumors with large lymph nodes, a diverse 5-year survival rate ranging from 15% to 35% has been observed.[4]

The recommended strategy for unresectable stage III NSCLC patients is concurrent chemoradiotherapy (CRT); however, the treatment strategies vary according to the tumor location and patient performance.[5-7] Although there have been no major improvements in treatment options, updated treatment guidelines recommend consolidation therapy as an adjuvant treatment after CRT in patients without disease progression.[8,9] However, patient populations in clinical trials may not represent current practice, because clinical trials select certain populations of patients. Therefore, understanding the national treatment patterns and outcomes is important to define treatment guidelines and examine nonadherence. Moreover, the treatment outcomes of NSCLC patients who are treated within a community setting may represent the real-world data. Our findings may thus inform future projects in terms of better defined treatment modalities for improving patient outcomes, including new therapeutic approaches, such as immunotherapy and stereotactic radiotherapy (SBRT).

The understanding of real-world treatment patterns and patient outcomes for patients with unresectable stage III NSCLC is limited. The few studies that evaluated treatment strategies in stage III patients presented variable results, which may be due to the treating physicians' decisions, patient performance, or effects of the social security system.[10-13] Rapidly changing treatment strategies for locally advanced NSCLC reflect the need to collect information about new treatment options systematically for these patients. In this multi-center study conducted in Turkey, we investigated contemporary treatment patterns of patients with primary stage III NSCLC at the time of the initial diagnosis and during the first and second progressions. Additionally the prognostic factors for overall survival (OS) and progression-free survival (PFS) in patients with unresectable stage III NSCLC were analyzed in order to characterize patients that may benefit from consolidative treatment.

PATIENTS AND METHODS

Patient Selection

The clinical data of 492 patients treated between 2013 and 2017 were collected from a geographically diverse set of 10 community oncology centers in Turkey. The inclusion criteria were ≥18 years old, primary diagnosis of NSCLC confirmed by pathology, and presenting with clinical stage III disease according to the American Joint Committee on Cancer (AJCC) staging system. Patients who initiated the first-line treatment were eligible for the study. Additionally, the medical records of all the patients were available at the participating site. They reflected at least 9 months of follow-up from the index date unless the patient had died within the first 9 months of diagnosis. We excluded patients with a concomitant cancer at the time of diagnosis (except for non-metastatic non-melanoma skin cancers or in situ or benign neoplasms) and patients who had surgery before or after radiotherapy (RT). The patient performance was scored according to the Eastern Cooperative Oncology Group (ECOG) performance score (PS).

Data Collection

All the data were collected from the patients' files and treatment charts from each institution, and the final data were collated by the primary investigator in October 2019 for a central analysis. Each center that participated in this study enrolled 50 patients. Initially, we analyzed data from 554 patients and excluded 62 patients because they had undergone surgery for lung cancer. The final analysis included 492 patients with inoperable stage III NSCLC who were treated with RT.

Table 1. Patient and tumor characteristics for the entire cohort of patients with squamous cell carcinoma (SCC) and adenocarcinoma histologies

Variable	Entire cohort n (%)	SCC n (%)	Adenocarcinoma n (%)	p
Age (years, median)	64 (40–90)	65 (42–90)	63 (40–85)	0.22
Tumor size (cm, mean)	5.2±2.1	5.2±2.2	5.1±2.1	0.49
Gender				
Male	435 (88.4)	267 (91.1)	168 (84.4)	0.03
Female	57 (11.6)	26 (8.9)	31 (15.6)	
Smoking status				
Never	33 (6.7)	9 (3.1)	24 (12.1)	<0.001
Current	181 (36.8)	120 (41.0)	61 (30.7)	
Past	278 (56.5)	164 (55.9)	114 (57.2)	
ECOG PS				
0	203 (41.3)	118 (40.3)	85 (42.7)	0.82
1	246 (50.0)	148 (50.5)	98 (49.2)	
≥ 2	43 (8.7)	27 (9.2)	16 (8.1)	
Treatment period				
2013 - 2015	331 (67.3)	192 (65.5)	139 (69.8)	0.33
2016 - 2017	161 (32.7)	101 (34.5)	60 (30.2)	
T stage				
T1	32 (6.5)	13 (4.4)	19 (9.5)	0.24
T2	120 (24.4)	64 (21.8)	56 (28.1)	
T3	172 (35.0)	106 (36.3)	66 (33.2)	
T4	268 (34.1)	110 (37.5)	58 (29.2)	
N stage				
N1	73 (14.8)	47 (16.0)	26 (13.1)	0.44
N2	333 (67.7)	197 (67.3)	136 (68.3)	
N3	86 (17.5)	49 (16.7)	37 (18.6)	
Stage				
IIIA	311 (63.2)	180 (61.4)	131 (65.8)	0.34
IIIB	181 (36.8)	113 (38.6)	68 (34.2)	
Treatment				
CCRT	393 (79.9)	229 (78.2)	161 (80.9)	0.63
Seq CT + RT	46 (9.3)	31 (10.5)	16 (8.0)	
RT alone	53 (10.8)	33 (11.3)	22 (11.1)	
RT technique				
3DCRT	282 (57.3)	171 (58.4)	111 (55.8)	0.61
IMRT	144 (29.3)	82 (28.0)	62 (31.1)	
VMAT	66 (13.4)	40 (13.6)	26 (13.1)	

Abbreviations: *SCC= squamous cell carcinoma, ECOG PS= Eastern Cooperative Oncology Group performance status, CCRT= concurrent chemoradiotherapy, seq= sequential, CT= chemotherapy, RT= radiotherapy, 3DCRT= three dimensional conformal radiotherapy, IMRT= intensity modulated radiotherapy, VMAT= volumetric modulated arc therapy*

Treatment Patterns

The initial treatment included chemotherapy and RT delivered either sequentially or concurrently. These treatment patterns were analyzed for the first treatment period and during the first and second progression periods. We defined the first progression interval as the time between the end of the first treatment and the first progression. The second progression interval was calculated as the time between the first and second progressions. The treatment regimens were documented for patients who received treatment during the progression periods.

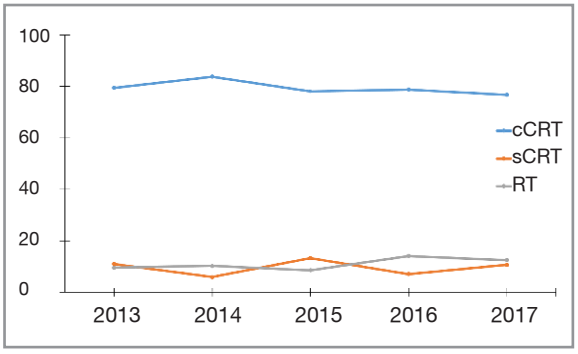

Figure 1. Annual treatment choice for stage III non-small cell lung cancer patients between 2013 and 2017

Ethics approval and consent to participate: This study was approved by the Baskent University Institutional Review Board (Project no: KA19/51). Local approvals were procured from all departments where required.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 software (SPSS for Windows, IBM Corp., Armonk, NY, USA). Descriptive methods were used for defining patient characteristics, treatment patterns, and treatment sequences, and these methods were conducted independently for the first treatment and the first and second progression intervals. The primary endpoints were OS and PFS. The Chi-squared (χ^2) test or Student's t-test was used to analyze the differences in the clinical and pathological factors between patients with squamous cell carcinoma (SCC) and adenocarcinoma. The time-to-death or progression was calculated as the period from the date of diagnosis to the date of death or the first clinical or imaging evidence of disease recurrence. Both OS and PFS rates were estimated by the Kaplan–Meier method. The Chi-squared test or Student's t-test was used for univariate analysis. Multivariate analysis was performed using a Cox proportional hazards model, with hazard ratio (HRs) and 95% confidence intervals (95% CIs) estimated using significant factors in the univariate analysis. A value of $p< 0.05$ was considered statistically significant.

RESULTS

Patients' Characteristics

The patients' and tumors' characteristics are summarized in Table 1. The median age at diagnosis was 64 years (range: 40–90 years). Most patients were male and were either past or current smokers. The predominant histology was SCC, and most of the patients had stage IIIA disease. There were no significant differences in clinicopathological characteristics between the patients with SCC and those with adenocarcinoma histology, except for gender and smoking habits. The incidence of adenocarcinoma histology was significantly higher in the female compared to the male population and in non-smokers compared to current or past smokers (Table 1).

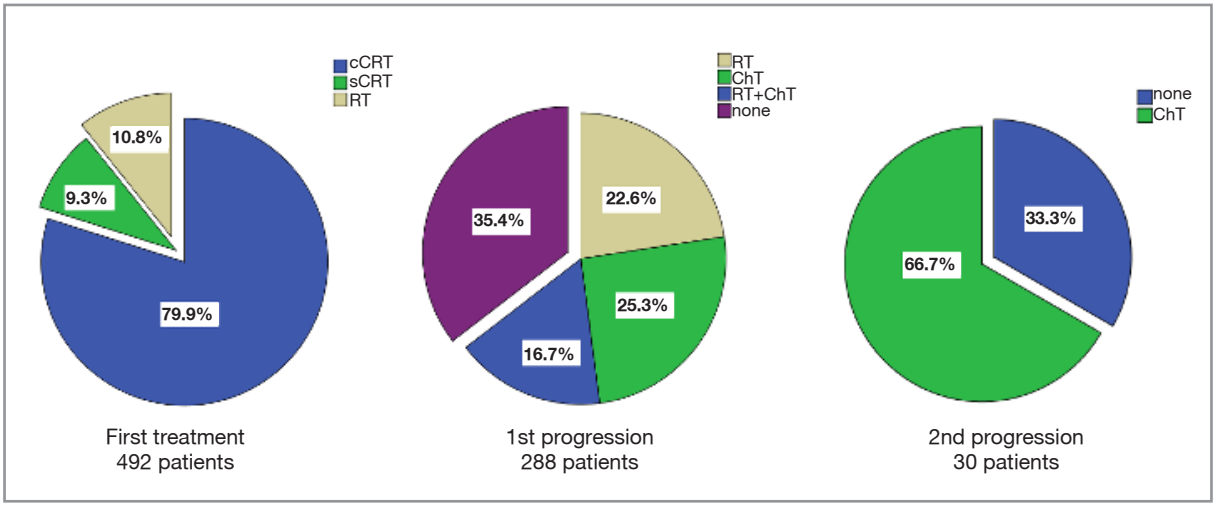

Figure 2. Pie graph showing treatment strategies at initial diagnosis and during the progression periods

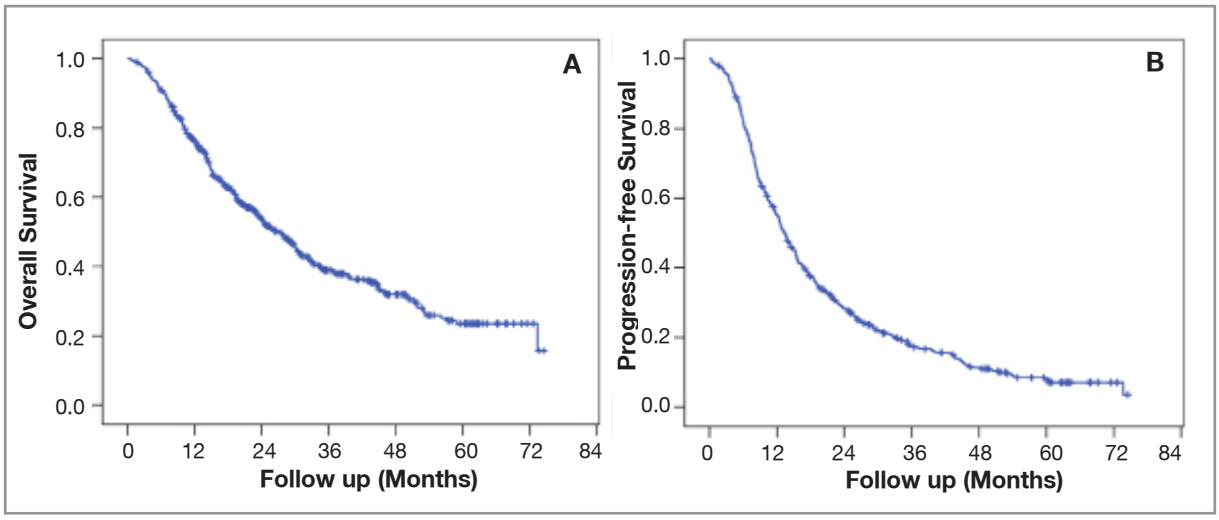

Figure 3. Kaplan–Meier graphics demonstrating overall survival (OS) and progression-free survival (PFS)

Molecular testing, mutation analyses, or both were performed in 123 patients (25.0%). Epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutation analyses were conducted in 85 (17.3%) and 70 patients (14.2%), respectively. Of the 70 patients analyzed, the EGFR mutation was seen in 12 patients (14.1%), and ALK mutation, in 3 patients (0.6%). Mutations in exons 18, 19, 20, and 21, which were analyzed in 88 patients, were observed in 4 (0.5%), 6 (0.7%), 2 (0.4%), and 2 patients (0.4%), respectively.

Treatment Patterns

All the patients received treatment for primary lung cancer. For the initial treatment, 429 patients (89.2%) received chemotherapy and RT, either concurrently (393 patients, 79.9%) or sequentially (46 patients, 9.3%), and 417 patients (84.6%) completed the planned treatment schedule (Figure 1). Among the 439 patients treated with systemic chemotherapy, 368 patients (83.8%) received platinum-containing doublet agents. None of the patients were treated with targeted therapy or immunotherapy during the first-line treatment period. The median total RT dose was 60.0 Gy (range: 41.4–66.0 Gy) and the median number of fractions was 30 (range: 12–33). The most frequently used RT technique was 3-dimensional conformal RT (3DCRT).

Two hundred eighty-eight patients (58.4%) showed disease progression at a median time period of 9.3 months after completion of the initial treatment, and 186 of these patients (64.6%) received another round of treatment (Figure 2). At the first progression, most patients (111, 91.7%) received chemotherapy, whereas only 7 patients (5.8%) were treated with tyrosine kinase inhibitors (TKIs), and 3 patients (2.5%) received immunotherapeutic agents. Irradiation was mostly provided to the metastatic sites [56 patients (49.6%) for brain metastasis, 24 patients (21.2%) for bone metastasis, and 3 patients (2.6%) for liver metastasis], and 30 patients (26.6%) were irradiated for local or locoregional recurrence. The median fraction and total RT doses were 3 Gy (range: 1.8-24.0 Gy) and 30 Gy (range: 16-60 Gy), respectively. The SBRT technique was used in 25 patients (22.2%).

The second disease progression was observed in 30 patients at a median of 4.2 months (range: 0.8–11.4 months) after completing treatment for the first progression. Of these patients, 20 (66.7%) received systemic therapy, namely chemotherapy (19 patients, 95.0%) or immunotherapy (1 patient, 5%). None of the patients were treated with RT after secondary progression.

Treatment Outcomes

The median follow-up time periods for the entire cohort and those who survived were 20.2 months

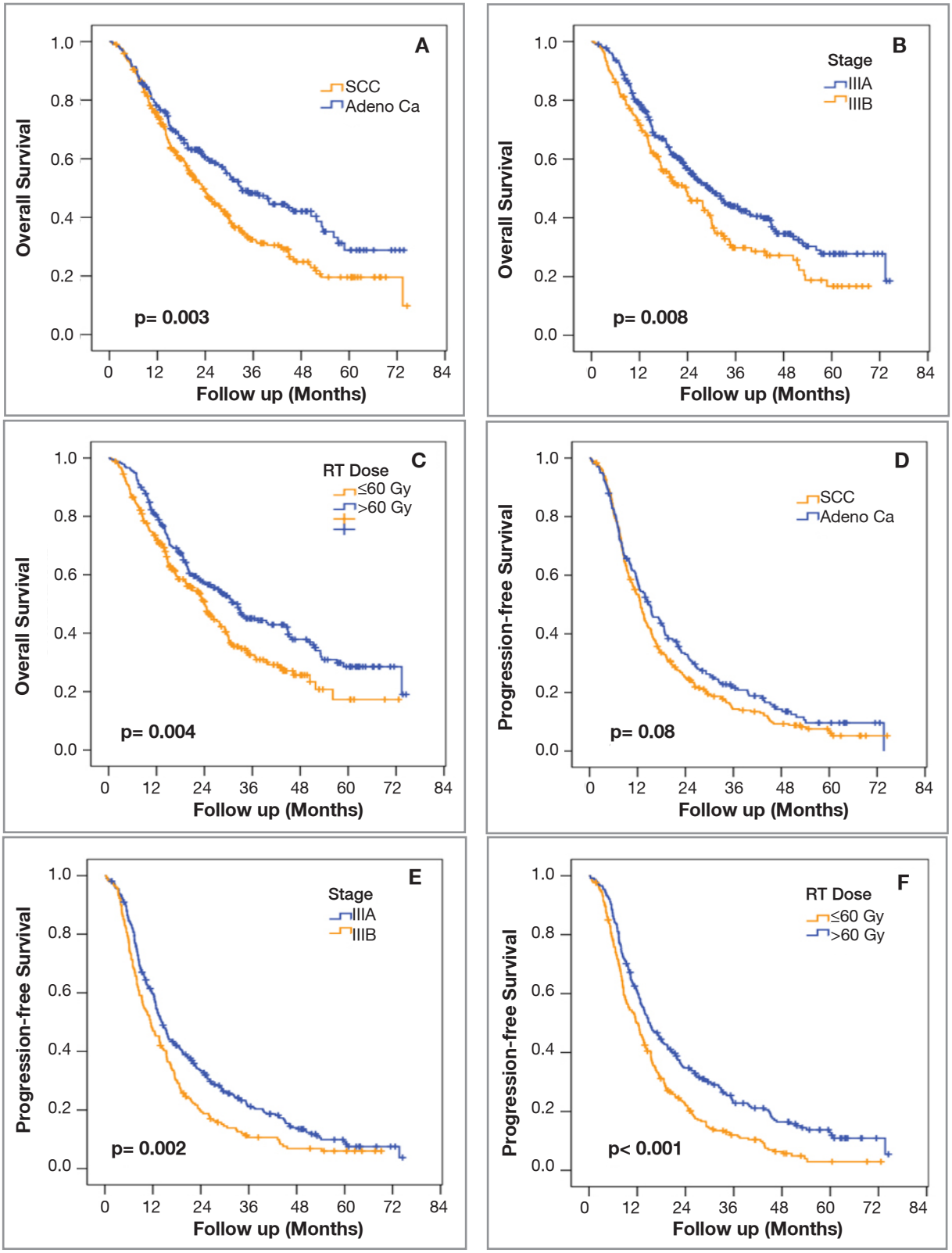

Figure 4. Kaplan-Meier estimates of OS in patients with squamous cell carcinoma (SCC) and adenocarcinoma **(A)**, in stages IIIA and IIIB of the disease **(B)**, and who received radiation doses of ≤ 60 Gy and > 60 Gy **(C)**, and PFS in patients with SCC and adenocarcinoma **(D)**, in stages IIIA and IIIB of the disease **(E)**, and who received radiation doses of ≤60 Gy and > 60 Gy **(F)**

Table 2. Univariate analysis of prognostic factors for overall survival (OS) and progression-free survival (PFS)

Variable	Number	Median OS (months) (95% CI)	p	Median PFS (months) (95% CI)	p
Age, years					
< 65	260	33.1 (27.0–39.3)	< 0.001	15.2 (12.5–17.9)	0.001
≥ 65	232	20.0 (16.2–23.8)		12.3 (10.5–14.1)	
Gender					
Male	435	24.8 (21.4–28.3)	0.005	12.8 (11.6–13.9)	0.04
Female	57	43.6 (26.5–60.8)		17.0 (8.9–25.1)	
Smoking status					
Never	33	39.9 (19.0–60.8)	0.15	15.4 (12.4–18.4)	0.05
Current	181	30.6 (25.4–35.8)		12.5 (10.9–14.1)	
Past	278	23.7 (19.4–28.0)		15.2 (2.1–28.2)	
ECOG PS					
0	203	31.3 (23.1–39.5)	0.01	15.5 (11.9–14.8)	0.04
1	246	27.4 (20.7–34.1)		13.6 (12.0–15.1)	
≥ 2	43	23.1 (18.2–28.0)		12.7 (10.8–14.7)	
Treatment period					
2013–2015	331	24.6 (20.0–29.2)	0.06	12.7 (11.2–14.2)	0.27
2016–2017	161	34.7 (24.2–41.7)		15.2 (13.4–16.9)	
Histology					
SCC	293	23.5 (19.8–27.1)	0.003	12.8 (11.4–14.1)	0.08
Adenocarcionoma	199	32.9 (25.2–40.7)		14.7 (11.4–18.1)	
Tumor size					
< 5 cm	238	30.3 (25.5–35.0)	0.06	14.7 (12.3–17.1)	0.16
≥ 5 cm	254	23.5 (18.5–28.4)		12.4 (10.1–14.6)	
Stage					
IIIA	311	29.5 (24.7–34.3)	0.008	14.2 (12.6–15.8)	0.002
IIIB	181	23.6 (17.6–29.6)		11.4 (8.7–14.1)	
Treatment					
CCRT	393	28.0 (24.1–31.9)	0.32	14.2 (12.0–14.7)	0.36
Seq CT + RT	46	25.0 (15.1–34.9)		13.3 (11.8–16.6)	
RT alone	53	23.1 (16.7–29.5)		11.8 (8.8–14.8)	
RT technique					
3DCRT	282	35.9 (19.5–28.9)	0.07	12.8 (11.3–14.3)	0.37
IMRT/VMAT	210	30.1 (24.8–35.3)		13.9 (11.6–16.2)	
RT dose					
≤ 60 Gy	254	24.0 (20.6–27.5)	0.004	12.2 (10.1–14.3)	< 0.001
> 60 Gy	238	31.3 (24.9–37.6)		15.2 (12.6–17.8)	

(range: 0.4-74.5 months) and 31.0 months (range: 2.7 - 74.5 months), respectively. The median OS and PFS times were 27.0 months (95% CI: 23.8-30.2 months) and 13.4 months (95% CI: 12.0 - 14.8 months), respectively (Figure 3). At last visit, 196 patients (40.4%) were alive (131 [27.2%] with disease), and 293 patients (59.6%) had died. Of these deaths, 275 (55.9%) were due to NSCLC, and 18 (3.7%), to other causes. Disease progression was observed in 288 patients (58.4%). Of these patients, 104 (21.1%) and 78 (15.8%) had local and locoregional recurrences, respectively. Distant metastasis was seen in 109 patients (22.2%).

Table 3. Multivariate analysis of prognostic factors for OS and PFS

Variables	Risk factors	HR (95%CI)	p
	Overall survival		
Age	1.04 (1.03-1.06)	< 0.001	
Gender	Male vs. female	1.81 (1.21-2.72)	0.004
ECOG PS	0-1 vs. ≥ 2	0.72 (0.56-0.84)	0.03
Treatment period	2013-2015 vs. 2016-2017	1.44 (1.07-1.92)	0.02
Tumor size	≥ 5 cm vs. < 5 cm	1.24 (0.99-1.57)	0.07
Histopathology	SCC vs. adenocarcinoma	1.17 (0.92-1.50)	0.21
Stage	IIIA vs. IIIB	0.79 (0.62–0.98)	0.04
RT technique	3DCRT vs. IMRT/VMAT	1.34 (1.05-1.71)	0.02
RT dose	≤ 60 Gy vs. > 60 Gy	1.46 (1.14-1.85)	0.002
	Progression-free survival		
Age	1.02 (1.01–1.03)	< 0.001	
Gender	Male vs. female	1.29 (0.93-1.80)	0.13
ECOG PS	0-1 vs. ≥ 2	0.79 (0.63-0.96)	0.03
Histopathology	SCC vs. adenocarcinoma	1.08 (0.88-1.33)	0.44
Smoking	Yes vs. no	1.19 (0.96-1.46)	0.11
Stage	IIIA vs. IIIB	0.81 (0.66-0.97)	0.04
RT dose	≤ 60 Gy vs. > 60 Gy	1.48 (1.22-1.80)	< 0.001

Prognostic Factors for OS and PFS

In the univariate analysis, age, gender, histopathology, AJCC stage, and RT doses (Figure 4A–C) were significant prognostic factors for OS (Table 2). Treatment period, tumor size, and RT techniques showed close to the levels of significance for OS. For PFS, patients' age, gender, AJCC stage, and RT dose were found to be significant in the univariate analysis, whereas smoking habits and histopathology had borderline significance (Figure 4D–F).

Older age, male gender, treatment period between 2013 and 2015, stage IIIB disease, 3DCRT technique, and RT dose ≤ 60 Gy were independent predictors for poor OS in the multivariate analysis (Table 3). Age, tumor stage, and RT dose were significant prognostic factors for PFS in the multivariate analysis.

DISCUSSION

This retrospective national observational study of patients with unresectable stage III NSCLC provides real-world data about treatment patterns at the time of the initial diagnosis and during the first and second progression periods. We found that most patients were treated with concurrent CRT at the time of the initial diagnosis, which is consistent with the clinical guidelines for unresectable stage III NSCLC. Although nearly two-thirds of the patients received treatment during the first and second progression periods, the treatment choice varied widely due to the lack of a consensus for treatment strategies during the progression. Our study demonstrated an unmet need for consolidative treatment, with a median PFS of 13.4 months and a median OS of 27.0 months, especially for patients with high-risk features including older age, stage IIIB disease, poor PS and lower RT doses.

Definitive RT is a standard approach for patients with locally advanced NSCLC, but progress in the past two decades has broadened the therapeutic landscape to include chemotherapy and even surgery as viable strategies.[14,15] A one-size-fits-all strategy is not suitable for all patients, and trial data are often limited by the heterogeneity in patient populations and the disease entity itself. Few studies have examined real-world data.[10,16,17] A Surveillance, Epidemiology, and End Results–Medicare

database study analyzed 2,958 patients aged 65 years or older with stage IIIA NSCLC.17 The most common treatment choices were RT in combination with chemotherapy (36%), RT alone, and surgery (24%), and 534 patients (18%) did not receive any treatment. Treatment of elderly patients with stage IIIA NSCLC depended on patient and tumor characteristics as well as regional income level. In a Dutch population-based study, comparing treatment patterns in patients aged 65 years and older with stage III NSCLC, Driessen et al.16 found that CRT was more often provided to patients aged 65-74 years than to those aged ≥ 75 years. In another study with 478 inoperable stage III NSCLC patients, Ryan et al.[10] found that most patients were treated with concurrent CRT, whereas only 10.0% received chemotherapy alone. The utilization of RT and chemotherapy at diagnosis in stage III NSCLC ranged from 84% to 92% and 88%, respectively.[18,19] As in the case of previous database studies and guidelines, the most frequent treatment modality in our patient cohort was concurrent CRT. Age is one of the major determinants of treatment compliance, as was demonstrated in previous studies.[10,16] In the current study, nearly half of the patients were 65 years or older, and 17.6% of the patients aged ≥ 65 years did not finish the entire treatment as planned, while the compliance rate in patients aged < 65 years was 9.4%, and the difference was statistically significant (p= 0.003). Furthermore, older patients presented a higher frequency of treatment with RT alone than their younger counterparts (15.5% vs. 7.3%; p= 0.002). Due to the intensified treatment and compliance rates, age was one of the independent predictors of OS and PFS in this study.

Despite curative intent, prior research has found that the median OS in patients with stage III NSCLC treated with CRT ranges from 15 to 29 months.[7,20] A few studies have analyzed population-based treatment outcomes for stage III NSCLC patients.1[1,13,16] Vinod et al.[11] evaluated 2,153 patients with stage III NSCLC treated with surgery, RT, and chemotherapy. The median OS was 11 months, because the majority of these patients were treated with palliative intent. The predictive factors for survival were gender, age, ECOG PS, stage, and diagnosis year. In another population-based study, Ryan et al.[13] evaluated 478 stage III NSCLC patients treated mostly with CRT, while 8.4% of the patients did not receive anti-cancer therapy. The reported median OS and PFS were 19.5 months and 10.0 months, respectively, and the authors found that stage, ECOG PS, and treatment RT were significant prognostic factors for OS, whereas ECOG PS was the only predictor of PFS. In this study, we found that age, ECOG PS, stage, and RT dose were independent predictors for both OS and PFS, and additional predictive factors for OS were gender, treatment period, and RT technique. Our study differs from previous works in several ways.[11,13] First, in this study, all the patients received anti-cancer therapy, particularly CRT, and none underwent surgery. Our study period encompassed the patient population treated between 2013 and 2017, a later period compared to those in previous studies. Lastly, the median age (64 years) was lower than that in Vinod et al.'s[11] (69 years) and Ryan et al.'s[13] (67 years) research. As a consequence of these differences, our median OS and PFS were higher than those in previous population studies evaluating outcomes in patients with stage III NSCLC. However, the application of new systemic therapeutic agents has led to improvements in the median OS and median PFS to 47 months and 17 months, respectively, clearly indicating the room for improvement in the treatment of these patients.[21-23]

The majority of recurrences in stage III NSCLC after concurrent CRT occurred at distant sites, likely due to the higher incidence of initial micrometastases.[6,24] Therefore, new therapeutic advances are needed to improve survival for these patients. Checkpoint inhibitors, including PD-1 (pembrolizumab and nivolumab) and PD-L1 (atezolizumab and durvalumab) inhibitors, have been evaluated for use in advanced NSCLC. These inhibitors are approved in lines of treatment with favorable safety profiles compared those of chemotherapy, often with durable responses.[21,22,25,26] Crizotinib, the first-in-class ALK inhibitor, was established as the standard of care, but rapid development of second- and third-generation ALK-TKIs have changed treatment paradigms.[23,27] These studies addressed the importance of consolidation therapies after concurrent CRT, and in the near future, they should become the new standard of care for patients with stage III unresectable NSCLC. Therefore, a na-

tional database describing the treatment patterns of stage III NSCLC patients is essential to design treatment protocols consistent with new treatment strategies. However, due to the time period of this study, only a few patients were treated with immunotherapy or TKIs during the progression period rather than consolidative therapy after concurrent CRT. The checkpoint inhibitors pembrolizumab and nivolumab were approved as a second-line treatment in patients with metastatic NSCLC in the second half of 2015. However, these new systemic agents are not approved by the Turkish social security system, and only a few patients can afford these new drugs.

Patients with oligometastasis or oligoprogression present characteristics different from those with diffuse metastases. Oligometastatic patients are unlikely to experience rapid progression, consistent with cells of low malignant potential.[28] Systemic therapies alone may not be optimal for certain cases, such as oligometastatic lung cancer, where long-term control can be expected. Recent retrospective data suggest that lung metastases from many primary sites may benefit from various combinations of stereotactic ablation and systemic treatments that can be personalized based on disease progression and the number of metastases.[29] Our study differs from previous research in that we include the details of the RT technique. One of the most important findings of this study is that higher doses of radiation are predictive for improved disease control and longer survival, similar to the results demonstrated in previous works.[30,31]

Nonetheless, several limitations must be considered when interpreting our findings. First, the period covered by this study largely preceded the approval of new therapeutic options, including TKIs and immunotherapy. These new options may influence future treatment patterns and survival outcomes. Second, this study included data from patients treated in radiation oncology departments. Therefore, our findings may not be generalized to all stage III NSCLC patients who underwent surgery or did not receive any treatment. Despite these limitations, this work is important, because it is the first national database study demonstrating treatment patterns and outcomes for patients with stage III NSCLC in Turkey.

CONCLUSIONS

This multi-center observational retrospective study showed that the majority of patients with unresectable stage III NSCLC were treated with concurrent CRT at the time of the initial diagnosis, which was consistent with the current guidelines. All the patients received treatment at the time of the initial diagnosis, and 84.6% of the patients completed all treatment schedules. Although most patients were treated in accordance with current guidelines, nearly 58% of the patients, who received concurrent CRT as the first treatment, experienced disease progression, and one-third of these patients remained untreated during the progression intervals. Given the resulting median OS of 27.0 months and the median PFS of 13.4 months, our findings demonstrated the unmet treatment needs for patients with unresectable stage III NSCLC and high-risk features, such as older age, poor PS, stage IIIB disease, poor PS and lower irradiation dose, in the context of improving treatment outcomes. Further research is warranted to evaluate the effectiveness of new adjuvant systemic therapies on the evolution of real-world treatment patterns and clinical outcomes.

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