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Chest Diseases / Göğüs Hastalıkları

The Effect of COPD Presence, Quality of Life and Nutritional Status on Short-Term Survival in Patients with Non-Small Cell Lung Cancer

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ABSTRACT

Objectives: The aim of this study is to evaluate the association of survival with nutritional status, comorbidity and life quality of patients with locally advanced and advanced non-small cell lung cancer (NSCLC) coexisting with chronic obstructive pulmonary disease (COPD).

Patients and methods: This study was performed with 64 patients (6 female, 58 male) diagnosed with locally advanced and advanced NSCLC from March to August 2015. Demographic features of the patients were evaluated with Mini Nutritional Test (MNT), Charlson Comorbidity Index (CCI), Fat Free Mass Index (FFMI), Nutritional risk screening (NRS 2002), European Organization for Research and Treatment of Cancer (EORTC), Quality of Life (QOL) Group (EORTC-QLQ-C30). The association of those scales' results with survival was analyzed.

Results: Of the patients, 34.4% (n=22) had the diagnosis of COPD. A significant relationship between the presence of COPD and survival was not detected. According to NRS 2002, 33% of the patients were under the risk of nutritional deficiency. According to MNT, 18.8% of the patients showed the presence of malnutrition. According to CCI, the patients were in low, moderate and high-risk groups respectively 57.8%, 37.5% and 4.7%. FFMI averages of the survivors and ex ones were 19.74 kg/m^2 and 18.10 kg/m^2, respectively. After 6 month-follow up, 25% of the patients died. In the univariate analyses, MNT (p=0.000), NRS 2002 (p=0.000) and FFMI (p=0.012) were associated with survival. According to the EORTC-QLQ-C30 scale, performance status, functional scale, physical, occupational, social function values and symptom scores were associated with survival.

Conclusion: In the study, when nutritional status was evaluated with FFMI and life quality scales, the result was detected to be associated with survival. On the other hand, whether or not the patient was diagnosed with COPD, histological type of cancer, stage of the disease, metastasis sites and CCI were not detected to be associated with survival.

Keywords: Non-small cell lung cancer, chronic obstructive pulmonary disease, survival

Küçük Hücre Dışı Akciğer Kanseri Olan Hastalarda KOAH Varlığı, Hayat Kalitesi ve Beslenme Durumunun Kısa Dönem Sağkalım Üzerinde Etkisi

ÖZET

Amaç: Bu çalışmanın amacı, lokal ileri ve ileri evre küçük hücre dışı akciğer kanseri (KHDAK) ve kronik obstrüktif akciğer hastalığı (KOAH) olan hastalarda beslenme durumu, komorbidite ve yaşam kalitesinin sağkalım ile ilişkisini değerlendirmektir.

Hastalar ve yöntem: Bu çalışma Mart-Ağustos 2015 tarihleri arasında KHDAK tanısı alan lokal ileri ve ileri evre olan 64 hasta (6 kadın, 58 erkek) ile yapıldı. Hastalara ait demografik özellikler, Mini Nutrisyonel Test (MNT), Charlson komorbidite indeksi (CCI), Fat Free mass indeks (FFMI), Nutritional risk screening (NRS 2002), European Organization for Research and Treatment of Cancer (EORTC), Quality of Life (QOL) Group (EORTC QLQ-C30) yaşam kalitesi ölçeği değerlendirildi. Bu ölçeklere ait sonuçların sağkalım ile ilişkisi analiz edildi.

Bulgular: Hastaların %34,4'ünde (n=22) KOAH tanısı mevcuttu. KOAH varlığı ile sağkalım arasında anlamlı ilişki saptanmadı (p>0,05). NRS 2002'ye göre hastaların %67'si nutrisyonel açıdan normal, %33'ü beslenme yetersizliği riski altındaydı. MNT'ye göre hastaların %29,7'sinde malnutrisyon riski ve %18,8'inde ise malnutrisyon mevcuttu. CCI'ye göre hastaların %57,8'i düşük, %37,5'i orta ve %4,7'si yüksek risk grubundaydı. Hastaların FFMI ortalaması 19,33 kg/m^2 idi (sağ kalanlar;19,74 kg/m^2, ex;18,10 kg/m^2). Altı aylık takip sonrasında hastaların %25'i kaybedildi. Tek değişkenli analizlerde MNT (p=0,000*), NRS 2002 (p=0,000*) ve FFMI (p=0,012) sağkalım ile ilişkiliydi. EORTC-QLQ-C30 ölçeğine göre genel sağlık durum, fonksiyonel ölçek, fiziksel fonksiyon, uğraş fonksiyonu, sosyal fonksiyon değerleri ve semptom skorları sağkalım ile ilişkili idi.

Sonuç: Çalışmamızda nutrisyonel durum FFMI ve yaşam kalitesi ölçekleri ile değerlendirildiğinde sağkalım ile ilişkili saptandı. Buna karşın hastada, KOAH tanısı olup olmaması, kanserin histolojik tipi, hastalığın evresi, metastaz bölgeleri ve komorbidite indeksi sağkalım ile ilişkili saptanmadı.

Anahtar sözcükler: Küçük hücre dışı akciğer kanseri, kronik obstrüktif akciğer hastalığı, sağkalım

Lung cancer accounts for 18% of cancer-related deaths in women and men in the world (1). Lung cancer is the most common type of cancer in our country, the first in men and the 5th in women (2). Smoking is the most important known risk factor for this disease. Other risk factors are passive smoking, air pollution, radon gases, radiation, occupational contact, asbestos fibers, pulmonary diseases such as comorbid chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis, nutrition and genetic-environment interaction (3).

79.2 % of the cases with lung cancer are non-small cell lung cases (NSCLC) (2). Despite all the modern therapy models, the control of the disease in advanced NSCLC patients is very difficult (4). Factors associated with the tumor and the individual affect the length of life more than the therapy. Classic prognostic factors in lung cancer are identified as the stage, performance status, weight loss and gender (5). Advanced stage, Eastern Cooperative Oncology Group performance-status score 3 or 4, weight loss of more than 5% and male gender were found to be associated with poor prognosis. Age is not among the classic prognostic factors (6). Whereas age is not an independent factor affecting survival, Charlson Comorbidity Index (CCI) ≥1 was found to be associated with increased mortality (7). In patients with advanced stage NSCLC, skin and liver metastasis and the presence of more than 4 metastasis are negative prognostic factors. However, brain, bone and liver metastasis were seen not to be efficient in the length of life (8, 9). Knowing the prognostic factors in this group of patients with low survival rates helps in determining the treatment option and separating the patients into subgroups (10). Lung cancer is 3-4 times more common in COPD patients than that in smokers and is an important cause of mortality in these patients (8). Increasing lung cancer risk in COPD patients has been reported to be associated with increased systemic inflammation and oxidative stress (9). Proinflammatory cytokines are thought to stimulate tumor angiogenesis and facilitate cell growth and metastasis (11). The aim of this study is to evaluate the effects of COPD, other comorbidities and sarcopenia on survival and life quality in locally advanced and advanced stage NSNLC cases.

METHODS

By taking June 2015 dated and 889 numbered approval of Kecioren Research and Training Hospital ethical committee, this study was performed with 64 patients diagnosed with NSCLC from March to August 2015 and whose treatment and follow up was done in Ankara Pulmonary Diseases and Thoracic Surgery Research and Training Hospital. Newly diagnosed locally advanced stage NSCLC were included in the study. In the study, age, gender, histopathological type and stage of lung cancer, metastasis sites, diagnosis and stage of COPD, mini-nutritional test (MNT), CCI, fat free mass index (FFMI), nutritional risk screening (NRS 2002), European Organization for Research and Treatment of Cancer (EORTC), Quality of Life (QOL) Group (EORTC-QLQ-C30) quality of life scale were evaluated. Diagnosis and staging of COPD were performed based on the GOLD 2014 guide. Survival duration was determined from the date of diagnosis to the end of the study or the time until death. Six-month survival data were obtained by detecting patients who died in the first 6 months after diagnosis. Forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) were measured at baseline using a spirometer (Spirolab III-MIR, Italy).

CCI

CCI is a high reliable scale in the elderly and patients with 1-year mortality (12). Scoring is done after the evaluation of comorbid factors. The scores of patients were between 0 (with no comorbidity) and 31 (with most comorbidity). In addition, analysis patients were evaluated in four groups according to their scores, which shows 0 low risk (Charlson-0), 1-2 moderate risk (Charlson-1), 3-4 high risk (Charlson-2) and 5 and above very high risk (Charlson-3).

NRS 2002

Patients are evaluated in terms of nutritional deficiency and disease severity. NRS 2002 consists of two stages: beginning and end scan (13). In patients who give a yes answer to any question in the initial screening, the last scan is started. None (0), mild (1), moderate (2) and severe (3). Patients with a total score of ≥ 3 are considered to be at risk of nutrition. NRS 2002 Initial and Final Screening are presented in Table 1 and 2.

Table 1. NRS 2002 Initial Screening

1. Is BMI <20.5?	YES	NO
2. Has the patient lost weight the last 3 months?	YES	NO
3. Has the patient had a reduced dietary intake in the last week?	YES	NO
4. Is the patient severely ill? (e.g. in intensive therapy)	YES	NO

Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed.
No: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.

Table 2. NRS 2002 Final Screening			
Impaired nutritional status		Severity of disease (≈ increase in requirements)	
0	Normal nutritional status	0	Normal nutritional requirements
1	Wt loss >5% in 3 mths or food intake below 50–75% of normal requirement in preceding wee	1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. Chronic hemodialysis, diabetes, oncology
2	Wt loss >5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or food intake 25–60% of normal requirement in preceding week	2	Major abdominal surgery* Stroke* Severe pneumonia, hematologic malignancy
3	Wt loss >5% in 1 mth (<15% in 3 mths) or BMI <18.5 + impaired general condition or food intake 0-25% of normal requirement in preceding week in preceding week.	3	Head injury* Bone marrow transplantation* Intensive care patients (APACHE-10).
Score ≥3: the patient is nutritionally at-risk and a nutritional care plan is initiated score <3: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

EORTC-QLQ-C30

EORTC-QLQ-C30 3.0 version is a 30-item survey which measures the disease-specific quality of life in cancer patients. The questionnaire administered by the patients themselves includes 30 items associated with 5 functional scales (physical, role, cognitive, emotional and social), 3 symptom scales (fatigue, pain, nausea), general health scale and symptoms in cancer patients (dyspnea, loss of appetite, sleep disorders, constipation and diarrhea, etc.) (14). Each parameter has a score between 0 and 100. Whereas high scores on the functional scale indicate good health status, high scores on the symptom scale indicate the excess of symptoms. On the general health scale, a high score indicates a high quality of life.

MNT

MNT includes anthropometric evaluation (body mass index (BMI), mid-arm circumference, thigh circumference, weight loss in the last three months), general evaluation, personal assessment (a psychological or medical problem in the last three months), diet and appetite evaluation (15). Patients are evaluated out of 30. Those with a score of 12 or above for the first six questions are considered to be normal in terms of nutrition. Total score> 23.5 is considered to be normal, 17-23 malnutrition risk, <17 malnutrition.

FFMI

FFMI measurement gives information about muscle breakdown. FFMI threshold values are accepted as; <16 kg/m^2 for men and <15kg/m^2 for women (16).

Statistical Analysis

The data obtained in this study were analysed with SPSS 22.0 package program. Descriptive statistics were used for frequency and percentage distributions of variables. Mann-Whitney U test was used for two-group comparisons. Kaplan-Meier method was used in life analyses for patients. P-value <0.05 was considered to be significant.

RESULTS

Demographic characteristics of the patients included in the study are given in Table 3. 71.9% of the patients were ex-smokers, 15.6% were still smoking and 12.5% had never smoked. 51.6% of the patients evaluated with MNT were healthy in terms of nutrition, 29.7% had malnutrition risk and 18.8% had malnutrition. According to the CCI used in the evaluation of comorbidity, 57.8% of the patients were in the low risk group, 37.5% in the medium risk group, and 4.7% in the high-risk group. There were no patients in the very high-risk group. According to NRS 2002 used for malnutrition, 67% of the patients were normal and 33% were at risk. According to the 6-month survival data of the patients, 25% of the lost cases died during this period. Of the dead patients, 43.8% had COPD diagnosis. The follow-up period was short, though. There was no significant relationship between the presence of COPD and mean survival periods (p>0.05). Despite not being statistically significant, the mean survival time was lower in the patients with COPD diagnosis. When the association of age, smoking status, pathology, TNM classification and metastasis sites with 6-month survival were examined; 6.3% (n = 1) of the dead were female and 93.8% (n = 15) were male. There was no significant difference between genders in terms of mean survival time (p>0.05). Although it was not statistically significant, the mean survival time was lower in women. Histopathological distribution in the dead patients was 56.3% (n = 9) adenocarcinoma and 31.3% squamous cell carcinoma (n = 5). There was no significant difference between histopathological types in terms of mean survival time (p>0.05). 81.3% (n = 13) of the patients who died were advanced stage, 18.8% (n = 3) were local advanced stage and there was no significant difference between the groups in terms of mean survival (p>0.05). There was no significant difference between the metastasis sites in terms of mean survival (p>0.05). Although it was not statistically significant, patients with metastasis in bones and multiple regions had a lower survival time (Table 3).

Table 3. The relationship between 6 months survival and smoking status, sex, pathological diagnosis, TNM classification, area of metastasis

		Survived		Exitus		Total		p
		n	%	n	%	n	%	
Sex	Male	43	89.6	15	93.8	58	90.6	0.700
	Female	5	10.4	1	6.3	6	9.4	
	Total	48	100.0	16	100.0	64	100.0	
Smoking status	Never smoked	7	14.6	1	6.7	8	12.7	0.848
	Quit	33	68.8	12	80.0	45	71.4	
	Active smoking	8	16.7	2	13.3	10	15.9	
	Total	48	100.0	15	100.0	63	100.0	
Pathological diagnosis	Adenocarsinoma	25	52.1	9	56.3	34	53.1	0.985
	Squamous	19	39.6	5	31.3	24	37.5	
	NOS	4	8.3	1	6.3	5	7.8	
	Sarcomatoid	0	0.0	1	6.3	1	1.6	
	Total	48	100.0	16	100.0	64	100.0	
TNM classification (7th edition)	Stage 3B	11	22.9	3	18.8	14	21.9	0.729
	Stage 4	37	77.1	13	81.3	50	78.1	
	Total	48	100.0	16	100.0	64	100.0	
Areas of metastasis	Lung	8	16.7	1	6.3	9	14.1	0.818
	Bone	6	12.5	4	25.0	10	15.6	
	Multi organ	12	25.0	6	37.5	18	28.1	
	LAP	3	6.3	1	6.3	4	6.3	
	Adrenal	3	6.3	1	6.3	4	6.3	
	Liver	2	4.2	0	0.0	2	3.1	
	Pleural fluid	2	4.2	0	0.0	2	3.1	
	Other	1	2.1	0	0.0	1	1.6	
	Total	48	100.0	16	100.0	64	100.0	

The nutritional status of the patients was evaluated with NRS 2002 and MNT and its relationship with 6-month survival was evaluated. In 18.8% of the patients, MNT was <17 (malnutrition), and the mean survival time was significantly lower than those with a test score of 17-23.5 and> 23.5 ($p<0.05$). In the 34.4 % of the patients, NRS was 2002>=3 (nutritional deficiency), the mean survival time of these patients was significantly lower compared to those <3 ($p<0.05$).

Relationship of 6-month survival was evaluated with CCI by which comorbidity was evaluated. There was no significant difference between CCI and survival time ($p>0.05$) (Table 4).

Table 4. The relationship between 6 months survival and CCI, MNT ve NRS 2002 test results.

		Survived		Exitus		Total		p
		n	%	n	%	n	%	
MNT	<17 malnutrition	2	4.2	10	62.5	12	18.8	<0.0001
	>23.5 normal	31	64.6	2	12.5	33	51.6	
	17-23 risk of malnutrition	15	31.3	4	25.0	19	29.7	
	Total	48	100.0	16	100.0	64	100.0	
CCI	Mild	29	60.4	7	43.8	36	56.3	0.103
	Moderate	16	33.3	9	56.3	25	39.1	
	Severe	3	6.3	0	0.0	3	4.7	
	Total	48	100.0	16	100.0	64	100.0	
NRS 2002	<3	37	77.1	5	31.3	42	65.6	<0.0001
	>=3	11	22.9	11	68.8	22	34.4	
	Total	48	100.0	16	100.0	64	100.0	

The mean FFMI of the study population was 19.33 kg/m2 (survivors; 19.74 kg/m2, ex ones; 18.10 kg/m2). FFMI values were significantly lower in dead patients ($p<0.05$).

According to EORTC-QLQ-C30, general health status values, functional scale scores, physical function values, occupational function values, social function values were significantly lower in ex-patients ($p<0.05$). Symptom scores, fatigue values, pain, shortness of breath and insomnia scores, loss of appetite scores were significantly higher in ex-patients ($p<0.05$) (Table 5, Table 6 and Table 7, respectively).

DISCUSSION

The association between lung cancer and COPD has been suggested in several epidemiological, pharmacological and observational studies. For the first time, Skillrud et al. have suggested an independent relationship between COPD and lung cancer (17). The relationship between COPD and lung cancer can provide significant improvement in the prevention and clinical treatment of both diseases. Based on this idea, we aimed in our study to determine the relationship between the combined assessment results of the patient's groups newly diagnosed with NSCLC local advanced and advanced stage with or without COPD diagnosis and survival. 25% of our patients died within 6 months of the diagnosis. According to the literature, while the 5-year survival rate is 15% in all lung cancer patients, the 5-year survival rate in stage 3B in NSCLC is 5-20%, the median duration varies between 9-20 months.

Table 5. The relationship between 6 months survival and FFMI, EORTC-QLQ-C30 (General health status and functional score)										
		Result						Mann-Whitney U testi		
		n	Mean	Median	Min	Max	SS	Mean rank	U	p
FFMI	Survived	48	19.74	19.87	15.80	26.20	2.49	35.86	222.5	0.012
	Exitus	16	18.10	17.69	14.87	24.12	2.14	22.41		
	Total	64	19.33	19.29	14.87	26.20	2.50			
Global health status / Quality of life	Survived	48	66	67	0	100	24	37.75	132	<0.0001
	Exitus	16	35	37	0	67	22	16.75		
	Total	64	58	50	0	100	27			
Functional scales	Survived	48	82	87	36	100	16	36.93	171.5	0.001*
	Exitus	16	58	52	23	98	25	19.22		
	Total	64	76	84	23	100	21			
Physical functioning (PF)	Survived	48	72	80	0	100	28	36.92	172	0.001
	Exitus	16	38	37	0	100	34	19.25		
	Total	64	64	74	0	100	33			
Role functioning	Survived	48	82	100	0	100	28	36.56	189	0.001*
Emotional functioning	Survived	48	82	84	17	100	20	33.41	340.5	0.488
	Exitus	16	76	84	34	100	25	29.78		
	Total	64	81	84	17	100	21			
Cognitive functioning	Survived	48	89	100	34	100	17	33.71	326	0.314
	Exitus	16	87	84	50	100	15	28.88		
	Total	64	89	100	34	100	16			
Social functioning	Survived	48	88	100	0	100	23	35.75	228	0.006*

Tablo 6. The relationship between 6 months survival and EORTC-QLQ-C30 (Symptom scales /items)										
		Result						Mann-Whitney U testi		
		n	Mean	Median	Min	Max	SS	Mean rank	U	p
Symptom scales / items	Survived	48	21.10	15.38	0.00	71.79	17.26	28.05	170.5	0.001*
	Exitus	16	39.42	41.02	0.00	64.10	17.39	45.84		
	Total	64	25.68	21.79	0.00	71.79	18.93			
Fatigue	Survived	48	33.45	33.33	0.00	77.77	24.71	28.15	175	0.001*
	Exitus	16	60.41	66.66	0.00	100.00	27.21	45.56		
	Total	64	40.19	33.33	0.00	100.00	27.75			
Nausea and vomiting	Survived	48	10	0	0	67	18	31.14	318.5	0.241
	Exitus	16	22	0	0	100	30	36.59		
	Total	64	13	0	0	100	22			
Pain	Survived	48	21	17	0	100	24	29.16	223.5	0.011*
	Exitus	16	43	33	0	100	30	42.53		
	Total	64	27	17	0	100	27			
Dyspnea	Survived	48	33	33	0	100	34	29.75	252	0.033*
	Exitus	16	54	67	0	100	32	40.75		
	Total	64	39	33	0	100	34			
Insomnia	Survived	48	22	0	0	100	31	29.22	226.5	0.008*
	Exitus	16	42	33	0	67	26	42.34		
	Total	64	27	17	0	100	31			

Tablo 7. The relationship between 6 months survival and EORTC-QLQ-C30 (Symptom scales/items)

		Result						Mann-Whitney U testi		
		n	Mean	Median	Min	Max	SS	Mean rank	U	p
Loss of appetite	Survived	48	20	0	0	100	29	28.33	184	0.001*
	Exitus	16	56	50	0	100	40	45.00		
	Total	64	29	17	0	100	35			
Constipation	Survived	48	15	0	0	100	24	31.71	346	0.492
	Exitus	16	23	0	0	100	34	34.88		
	Total	64	17	0	0	100	27			
Diarrhea	Survived	48	6	0	0	67	15	31.88	354	0.492
	Exitus	16	8	0	0	33	15	34.38		
	Total	64	7	0	0	67	15			
Financial difficulties	Survived	48	15.97	0.00	0.00	100.00	26.62	33.33	344	0.441
	Exitus	16	14.58	0.00	0.00	100.00	32.13	30.00		
	Total	64	15.62	0.00	0.00	100.00	27.84			

While the 1-year survival rate in stage IV NSCLC is 30-35%, the median survival time is 8-10 months. Most cases with lung cancer are detected in advanced (stage IV) or locally advanced stage (stage IIIA and IIIB) (18). In the study of the Thoracic Society Pulmonary and Pleural Malignancies Working Group, 83.6% of the patients were seen to be diagnosed with local advanced and advanced stages (19). When the patients were diagnosed in our study, 78.1% of them were stage 4, 21.6% were stage 3B. 56.3% of the patients were adenocarcinoma and 31.3% were squamous cell carcinoma. There was no significant difference in terms of mean survival time. 81.3% of the patients who died were stage 4 and 18.8% were stage 3B. There was no significant difference between the stages in terms of survival time. The low number of patients included in the study and the short follow-up period of the patients may have caused not being able to identify any difference in terms of survival between the stages and histopathological types. In the study, 36% of stage 4 NSCLC patients had multiple metastases and bone metastasis was detected to be the most common one. There was no significant relationship between metastasis sites and mean survival time. Although it was not significant, the mean survival time was lower in patients with bone and multiple metastases. In a study by Luketich et al., skin and liver metastasis and the presence of more than four metastasis were negative prognostic factors in advanced NSCLC patients [20]. Schuchert et al. showed that brain, bone and liver metastasis had no effect on survival time [21]. Çalıkuşu et al. identified that there was not a significant difference between survival time and the number and the sites of metastasis in NSCLC diagnosed patients (22). This discrepancy in the literature may be due to insufficiency in the distribution of patient groups. In the study, 34.4% of the patients had a diagnosis of COPD. In a similar study by Çilli et al., this rate was 23.5% (23). Janssen-Heijnen et al. reported the prevalence of COPD as 22% in their large series of 3864 lung cancer studies (24). In another study by Kurishima et al., they identified the prevalence value as 76% without gender discrimination (25). Differences in the study results may be caused from the differences in smoking rates, differences in exposure to environmental toxins, genetic susceptibility and methodology for the definition of COPD. In our study, 43.8% of the ex-patients had a diagnosis of COPD. There was no significant difference between being diagnosed with COPD or not in terms of survival time. Although it is not significant, mean survival was lower in patients with COPD. Malnutrition is a common problem in advanced patients and it accounts for a risk factor for morbidity and mortality. In a study by Priegnitz et al., it was reported that in 705 patients who were admitted to the respiratory care clinic, 14.3% had nutritional risk and 2.5% had malnutrition according to NRS 2002 (26). In a study of 401 oncologic patients by Planas et al., 33.9% of patients had a risk of malnutrition (NRS 2002 score>3) (27). In our study, 67% of the patients whose nutritional status was evaluated with NRS 2002 were found to be normal and 33% were at risk for malnutrition in accordance with this literature. Mean survival time was significantly lower in patients with NRS 2002> = 3 (34.4%) than those with <3. When patients were evaluated according to FFMI, these values were significantly lower in ex-patients. In recent years, FFMI provides more accurate results in the assessment of muscle destruction

for that reason it is more preferred than BMI. In the literature, NRS 2002 is mostly used to evaluate preoperative nutritional deficiencies in hospitalized patients. In our study, we used the nutritional status of the patients with NRS 2002 without any distinction between outpatients and inpatients. NRS 2002 may be a valuable indicator of prognosis in patients at risk of malnutrition. In the study, of the patients whose nutritional status were evaluated with MNT, 29.7% were detected to be under risk of malnutrition, 18.8% were detected to have malnutrition. In the study of Gioulbasanis et al. on 115 lung cancer patients, it was reported that according to MNT, 51.3% of the patients were under the risk of malnutrition and 25.2% had the diagnosis of malnutrition. Survival, age, number of metastasis were associated with MNT score and leptin among the patients (28). In the study of Gioulbasanis et al. on 171 patients with metastatic lung cancer, the MNT score was important in determining prognosis (29). Being compatible with the literature in our study, mean survival time was significantly lower in those with <17 MNT score (malnutrition) than 17-23.5 (malnutrition risk) and>23.5 (normal). However, the number of patients was not sufficient in order to make a multivariable analysis. In cancer patients, the risks and the benefits of the patients should be measured and how much comorbid diseases may affect survival time and tolerability of treatment should be evaluated (30). It was supported by a study that the presence of comorbid conditions may also affect the patient's tolerance to cancer treatment. In patients over 70 years with advanced stage NSCLC, the ones with CCI ≥2 were detected to quit chemotherapy at an early period at higher rates (31). In the study performed by Canadian International Cancer Institution on 1255 NSCLC patients, the rate of patients with CCI≥1 was 42% in patients over 65 years old and it was 26% in the young group. Also, it was detected that age only itself was not an effective independent factor in survival and comorbidity and CCI score 1 and above had an association with increased mortality (7). Birim et al. displayed that survival time decreased as CCI increased in 205 NSCLC patient group (32). When the 6-month short-term survival of the patients was examined in our study, there was no relationship between CCI and mean survival time.

There are many quality of life scales evaluating the health-related quality of life in NSCLC patients. Some of them are EORTC-QLQ-C30 and EORTC-QLQ-LC13 peculiar to lung cancer module, lung cancer symptom scale and Functional Assessment of Cancer Therapy-Lung Cancer Quality of Life Instrument. For being more reliable and comprehensive, EORTC-QLQ-C30 is the most commonly used questionnaire in the routine (33). Braun et al. detected that categories of general health and physical function in the EORTC-QLQ-C30 quality of life questionnaire were important prognostic factors for NSCLC patients. They emphasized that physical function, nausea, vomiting, insomnia, and diarrhea categories were important for survival in newly diagnosed patients whereas only physical function was important in previously treated patients (34).

In a study performed on 225 lung cancer patients whose data were obtained from multicentered hospitals, it was detected that change of general well-being in EORTC-QLQ-C30 scale through the time determined survival at a significant level and death risk was decreased as general well-being increased. The risk of death was seen to be decreased as physical, occupational, emotional and cognitive functions improved. It was detected that fatigue, nausea and vomiting, pain, shortness of breath, insomnia, loss of appetite, constipation, changes in financial difficulties over time affected survival significantly. The effect of change of symptoms in the scale was seen to have a similar effect on survival (35). In our study, general health status, functional scale, physical function, occupational function, social function scores were significantly lower in ex-patients. Symptoms, fatigue, pain, shortness of breath and insomnia, loss of appetite scores were significantly higher in ex-patients. There was no significant difference between the groups in terms of other values. As a result, in our study in univariate analysis, it was detected that there was a relationship between nutritional status, FFMI, quality of life and survival.

However, a significant relationship was not detected between the presence or absence of COPD, histological type of cancer, stage of the disease (stage 3B-4), metastasis sites, comorbidity score and short-term survival. Multivariate analysis of survival effects could not be performed due to the insufficient number of patients.

Our study supports that only age, stage and performance status are not determinants of survival in NSCLC patients. Especially comorbid diseases such as COPD and nutritional status have an effect on survival. Prospective studies with longer follow-up periods are needed to evaluate the effects of comorbidities and nutritional status on short and long-term survival and quality of life in patients with lung cancer.

Conflict of interest

The authors state that they have no conflicts of interest in this study.

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REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61(2):69-90.
2. Republic of Turkey. Ministry of Health. Turkey Public Health Institution Turkey Cancer Statistics Report. 2017.
3. Metintaş S. Akciğer Kanseri Epidemiyolojisi. In: Özlü T, Metintaş M, Karadağ M, Kaya A, eds. Solunum Sistemi ve Hastalıkları 1. Baskı. İstanbul Medikal Yayıncılık; 2010:1347-429.
4. Fu XL, Zhu XZ, Shi DR, Xiu ZL, Wang LJ, Zhao S, et al. Study of prognostic predictors for non small cell lung cancer. Lung Cancer 1999; 23:143-52.
5. Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. J Clin Oncol 2007; 25:1824–31.
6. Stanley KE. Prognostic factors for survival in patients with inoperable lung cancer. J Natl Cancer Inst 1980; 65:25–32.
7. Asmis TR, Ding K, Seymour L, Shepherd FA, Leighl NB, Winton TL, et al. Age and comorbidity as independent prognostic factors in the treatment of non small-cell lung cancer: a review of National Cancer Institute of Canada Clinical Trials Group trials. J Clin Oncol 2008; 26: 54-9.
8. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: role of comorbidites. Eur Respir J 2006; 28: 1245-57.
9. Zhang H. Moleculer signaling and genetic pathways of senescence: its role tumorigenesis and aging. J Cell Physiol 2007; 210: 567-74.
10. Wagner H. Rational integration of radiation and chemotheraphy in patients with unresectable stage IIIA or IIIB NSCLC. Result from Lung Cancer Study Group, Eastern Cooperative Oncology Group, and Radiation Theraphy Oncology Group. Chest 1993; 103:35-42.
11. Malhotra D, Thimmulappa R, Navas-Acien A, Sandford A, Elliott M, Singh A, et al. Decline in NRF2-regulated antioxidants in chronic obstructive pulmonary disease lungs due to loss of its positive regulator, DJ-1. Am J Respir Crit Care Med 2008; 178: 592-604.
12. Extermann M, Overcash J, Lyman GH, Parr J, Balducci L. Comorbidity and functional status are independent in older cancer patients. J Clin Oncol 1998; 16:1582-7.
13. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003; 22: 415-21.
14. Cankurtaran ES, Ozalp E, Soygur H, Ozer S, Akbıyık DI, Bottomley A. Understanding the reliability and validity of the EORTC QLQ-C30 in Turkish cancer patients. Eur J Cancer Care 2008;17: 98-104.
15. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition 1999; 15:116-22.
16. Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. Am J Clin Nutr 2005; 82: 53-9.
17. Skillrud DM, Offord KP, Miller RD. Higher risk of lung cancer in chronic obstructive pulmonary disease. A prospective, matched, controlled study. Ann Intern Med 1986; 105:503-7.
18. Spiro SG, Porter JC. Lung cancer-Where are we today? Current advances in staging and nonsurgical treatment. Am J Respir Crit Care Med 2002; 166:1166-96.
19. Goksel T, Akkoclu A; Turkish Thoracic Society, Lung and Pleural Malignancies Study Group. Pattern of lung cancer in Turkey 1994-1998. Respiration 2002; 69:207-10.
20. Luketich JD, Burt ME. Does resection of adrenal metastases from non-small cell lung cancer improve survival? Ann Thorac Surg 1996; 62:1614-6.
21. Schuchert MJ, Luketich JD. Solitary sites of metastatic disease in n on-small cell lung cancer. Curr Treat Options Oncol 2003; 4:65-79.
22. Çalıkuşu Z, Sakallı H, Yılmaz B, Mertsoylu H, Akçalı Z, Özyılkan Ö. Evre I V küçük hücreli dışı akciğer kanserli olgularda prognostik faktörlerin incelenmesi. Acıbadem Üniversitesi Sağlık Bilimleri Derg 2011;2(2):88-91.
23. Çilli A, Özdemir T, Özbulak Ö, Yakışan A, Öğüş C. Akciğer kanserli hastalarda KOAH birlikteliği. Solunum 2003; 5: 20-4.
24. Janssen-Heijnen ML, Schipper RM, Razenberg PP, Crommelin MA, Coebergh JW. Prevalence of co-morbidity in lung cancer patients and its relationship with treatment: a population-based study. Lung Cancer 1998; 21:105-13.
25. Kurishima K, Satoh H, Ishikawa H, Yamashita YT, Homma T, Ohtsuka M, et al. Lung cancer patients with chronic obstructive pulmonary disease. Oncol Rep 2001; 8:63-5.
26. Priegnitz C, Galetke W, Treml M, Randerath WJ. Nutritional risk screening 2002 in clinical pneumology. Pneumologie 2014;68(7):478-82.
27. Planas M, Álvarez-Hernández J, León-Sanz M, Celaya-Pérez S, Araujo K, García de Lorenzo A; PREDyCES® researchers. Prevalence of hospital malnutrition in cancer patients: a sub-analysis of the PREDyCES® study. Support Care Cancer 2015;27: 1049-59.
28. Gioulbasanis I, Georgoulias P, Vlachostergios PJ, Baracos V. Mini Nutritional Assessment (MNA) and biochemical markers of cachexia in metastatic lung cancer patients: Interrelations and associations with prognosis. Lung Cancer 2011; 74:516-20.
29. Gioulbasanis I, Baracos VE, Giannousi Z, Xyrafas A, Martin L, Georgoulias V, et al. Baseline nutritional evaluation in metastatic lung cancer patients: Mini Nutritional Assessment versus weight loss history. Ann Oncol 2011;22(4):835-41.
30. Welch HG, Albertsen PC, Nease RF, Bubolz TA, Wasson JH. Estimating treatment benefits for the elderly: the effect of comppeting risks. Ann Intern Med 1996; 124(6):577-84.
31. Frasci G, Lorusso V, Panza N, Comella P, Nicolella G, Bianco A, et al. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small cell lung cancer. J Clin Oncol 2000; 18:2529-36.
32. Birim O, Maat AP, Kappetein AP, van Meerbeek JP, Damhuis RA, Bogers AJ. Validation of the Charlson comorbidity index in patients with operated primary non-small cell lung cancer. Eur J Cardio Thorac Surg 2003; 23:30-4.
33. Bozcuk H, Dalmis B, Samur M, Ozdogan M, Artac M, Savas B. Quality of life in patients with advanced non-small cell lung cancer. Cancer Nurs 2006; 29:104-10.
34. Braun DP, Gupta D, Staren ED. Quality of life assessment as a predictor of survival in non-small cell lung cancer. BMC Cancer 2011; 11:353.
35. Öz A. Akciğer kanserli hastalarda izlem sürecindeki değişikliklerin yaşam kalitesine etkisinin EORTC-C 30 yaşam kalitesi ölçeği ve izlem sonuçlarıyla değerlendirilmesi. Thesis. 2012.