

Evaluation of fatigue-related kinesiophobia and associated factors in individuals with lung cancer with and without respiratory comorbidity

Emine Ozsari¹, Alp Ozel², Eylem Tutun Yumin², Suat Konuk¹

¹Department of Chest Diseases, Bolu Abant Izzet Baysal University, Faculty of Medicine, Bolu, Türkiye

²Department of Physiotherapy and Rehabilitation, Bolu Abant Izzet Baysal University, Faculty of Health Sciences, Bolu, Türkiye

ABSTRACT

Aim: To investigate fatigue-related kinesiophobia and associated factors in individuals with lung cancer.

Methods: A total of 52 individuals were included in the study and the individuals were divided into two groups, each consisting of 26 individuals. Charlson comorbidity index, Brief Fatigue Inventory, modified Medical Research Council dyspnea scale, Tampa Kinesiophobia Scale-Fatigue are applied as data collection tools.

Results: The individuals in the study had similar demographic characteristics. There was no difference between the groups in the study in terms of fatigue-related kinesiophobia. There was a difference between the pain and performance status of the individuals in the study in activities of daily living ($p<0.05$).

Conclusion: At the end of this study, it was observed that individuals with lung cancer with respiratory comorbidity had worse pain, fatigue and performance values in activities of daily living, while kinesiophobia values related to fatigue were similar.

Key words: Lung cancer, kinesiophobia, fatigue, comorbid.

✉ Alp Ozel, Department of Physiotherapy and Rehabilitation, Bolu Abant Izzet Baysal University, Faculty of Health Sciences, Bolu, Türkiye.

E mail: ptalpozel@gmail.com

Received: 2022-03-21 / Revisions: 2022-05-02

Accepted: 2022-05-19 / Published: 2022-07-01

Introduction

Lung cancer is the most common cause of cancer-related deaths in the world and is a cancer with a high mortality rate, causing approximately 1.6 million deaths each year [1]. According to the World Health Organization

(WHO) 2014 report, 19.4% of cancer deaths occur due to lung cancer [2]. Because lung cancer is more common in older ages and is directly related to smoking, comorbidities associated with advanced age and smoking are more common in individuals with lung cancer [3]. Exclusion of patients with comorbidities from studies generally prevents obtaining healthy information about the estimation of the frequency of comorbidity and its prognostic importance in individuals with lung cancer. Shortness of breath is a common symptom, especially in individuals with advanced lung

cancer [4]. However, respiratory symptoms can occur in all stages of lung cancer. When dyspnea occurs in individuals with lung cancer, their daily activity level is restricted and their functional capacity gradually decline [5].

When shortness of breath is acute and severe, it causes emotional stress [6]. In some cases, the stress reaches the level of fear of death. As a result, individuals avoid any activity that will increase their symptoms [7]. Another symptom frequently seen in individuals with lung cancer is fatigue [8]. In a previous study; It has been reported that fatigue is defined by patients with terms such as “weakness, exhaustion, feeling of heaviness, getting tired quickly, slowing down and burnout”, and by physicians with terms such as “loss of energy, weakness, loss of strength” [9]. Fatigue not only reduces the individual's sense of well-being, but also negatively affects his/her daily performance, activities, professional life, relationships with family and friends, and adherence to treatment. When the literature is examined, there are few studies investigating the reason for avoiding physical activity in patients with lung cancer.

Kinesiophobia, or fear of movement, is defined as avoiding physical movements as a result of painful situations [10]. Similarly, individuals with lung disease avoid physical activities or adapt their physical activity levels. This avoidance model is great importance in individuals with lung cancer, as in many chronic diseases. It has been reported that kinesiophobia is associated with dyspnea level, fatigue and comorbidities in individuals with COPD [11]. In case of worsening of symptoms or emergence of symptoms, patients may limit their activities and participation in daily life. As a result, patients experience emotional problems and may result in a decrease in health-related quality of life [12]. The aim of this study is to investigate fatigue-related kinesiophobia

in individuals with lung cancer with and without respiratory comorbidity

Materials and methods

A controlled, cross-sectional study design was used in this study. In this study, the Tampa Kinesiophobia-Fatigue Scale, which evaluates fatigue-related kinesiophobia, was used as the primary variable. The research was conducted in strict accordance with the principles of the Helsinki Declaration. Before starting the study, approval was obtained from the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University with the number 2021/219. To determine the sample size, a priori power analysis was performed in the G power version 3.1.9.4 program. In the power analysis, it was determined that at least 26 individuals in each group and a total of 52 individuals should be included in the study in order to reach a significance level of 0.05, an effect size of 0.8, and 80% power.

Patients: Individuals diagnosed with lung cancer who were hospitalized in Bolu Abant İzzet Baysal University Medical Faculty Chest Diseases Service, volunteered to participate in the study and met the inclusion criteria were included in the study. Inclusion criteria were consisted to be diagnosed with lung cancer at least 4 weeks ago, currently receiving cancer treatment, being at least literate, being over 18 years old, not taking opioids and corticosteroids. Exclusion criteria were severe hearing impairment, ECOG status of 3 and above, life expectancy of less than 6 months, and needing continuous oxygen support. All patients included in the study were outpatients. Therefore, they were not receiving systemic corticosteroid therapy, which is used in hospitalization and/or attacks. In addition, patients who would affect the pain threshold or

who received chemotherapy treatments were also excluded from the study.

The individuals included in the study were divided into 2 groups as with respiratory comorbidities (n=26) and without respiratory comorbidities (n=26). Sociodemographic and disease-related information (duration of disease, employment status, smoking and alcohol habits, lung cancer stage, histological type of lung cancer, weight loss history and physical performance status) of the individuals participating in the study were recorded. The Charlson Comorbidity Index was used to assess comorbidity, the Brief Fatigue Scale to assess fatigue, the modified Medical Research Council Dyspnea Scale to assess shortness of breath, and the Tampa Kinesiophobia-Fatigue Scale to assess fatigue-related kinesiophobia.

Assessment methods

Charlson Comorbidity Index (CKI): CKI is an index that evaluates many potential comorbidity variables and is widely used in many disease groups. This index consists of 19 different items. The total score is obtained by summing the scores of the individuals for their comorbid diseases. In addition, the score obtained by the individuals is added to 1 point for every 10 years old [13].

Brief Fatigue Inventory (BFI): It is a standardized test used to assess fatigue in individuals with cancer. The Turkish validity of the scale was done by Çınar et al [14]. The scale evaluates the level of fatigue in the last 24 hours and its reflection on activities in daily life (general activity, mood, walking ability, work life, relationships with other people, and joy of life). A score between 0 and 10 is given for each of the 9 questions under 4 sections. A high score indicates that the patient is overtired.

Modified Medical Research Council Dyspnea Scale (MRCS): This scale evaluates

individuals' shortness of breath and activity limitation. The scale includes 5 statements about individuals' shortness of breath and divides the level of dyspnea into a 0-4 point category [15].

Tampa Kinesiophobia Scale-Fatigue (TKS-F): The Tampa Kinesiophobia Scale (TKS) was developed to measure the fear of movement and/or re-injury. The Turkish validity and reliability of this questionnaire was conducted by Yılmaz et al. [16] TKS-F, which was created by replacing the expression "pain" with the expression "fatigue" in TKS, was modified by Silver et al. for patients with chronic fatigue syndrome [17]. The scale consists of 17 questions and each item is scored on a 1-4 likert scale. The lowest score of 17 and the highest 68 points can be obtained from TKS-F, and >37 is defined as high degree of fatigue-related kinesiophobia. A high score indicates that individuals have more fatigue-related kinesiophobia.

Visual Analogue Scale (VAS): Numerical scales facilitate the definition of pain intensity, facilitate scoring and recording. The individual marks his or her own pain on a 10 cm long straight line with no pain at one end and the most severe pain at the other. It is stated that this measurement is more sensitive and reliable than other one-dimensional scales [18].

Eastern Cooperative Oncology Group (ECOG) performance scale: In the ECOG Performance Scale, the functional capacity of the individual is scored between 0 and 4. 0 The patient has no complaints; 1 The patient has a complaint, but it does not affect his daily life; 2 The patient has a complaint, but spends less than half the day resting; 3 The patient has a complaint, but spends more time resting half the day; 4 The patient has a complaint, he spends the whole day resting. End-stage cancer patients get 4 points [19].

Karnofsky: In the scale, the patient's symptoms, ability to perform daily activities, independence status and need for medical care are questioned. While 100 points indicate normal health, functions deteriorate gradually with ten-point decreases, and 0 points corresponds to death. Individuals are divided into 3 parts according to the evaluation result: Individuals in category A (80-100%) can continue their normal activities and work; Individuals in category B (50-70%) can take care of themselves with assistance, but cannot work; Individuals in category C (0-40%) cannot take care of themselves and the disease progresses rapidly towards death [20].

Statistical analysis: The descriptive values, numbers and % frequencies of the obtained data are shown in tables as mean and standard deviation. The Kolmogorov test was used to determine whether the numerical features showed a normal distribution or not. The t-test was used to compare two groups in terms of normally distributed numerical characteristics, and the Mann Whitney U test was used for group comparisons in terms of non-normally distributed characteristics. The statistical significance level was accepted as $p < 0.05$ and the SPSS (ver. 20) program was used in the calculations.

Results

A total of 52 individuals were included in the study between 13.9.2021 and 07.01.2022. Of all individuals, 2 (3.8%) were female and 50 (96.2%) were male. The mean age and BMI of the group with respiratory comorbidity were 66.85 ± 12.17 years and 26.48 ± 1.03 kg/m², and the mean age and BMI of the group without respiratory comorbidity were 67.81 ± 7.69 years and 24.86 ± 0.81 kg/m², respectively. Smoking exposure of the group with respiratory comorbidity was 47.08 ± 4.05 pack years; in the

group without respiratory comorbidity, it was 53.19 ± 5.13 pack years. The individuals included in the study had similar demographic characteristics ($p > 0.05$, Table 1).

Lung cancer characteristics and stages of individuals included in the study are shown in Table 2.

When the two groups were compared according to the TKS-F, pain, modified CCI, MMRC, ECOG and Karnofsky scores of the individuals included in the study; There was a statistically significant difference between the two groups in parameters of pain ($p = 0.003$), ECOG ($p = 0.033$) and Karnofsky ($p = 0.005$) parameters (Table 3).

When the two groups were compared according to the BFI results of the cases included in the study; there was a statistically significant difference in all sub-parameters of BFI ($p < 0.05$, Table 4).

Discussion

At the end of this study, it was observed that individuals with lung cancer with respiratory comorbidity had worse pain, fatigue and performance values in activities of daily living, while kinesiophobia values related to fatigue were similar. Fatigue is one of the complex, multifaceted, and important problems that increase health expenditures experienced by individuals with cancer [21]. With the occurrence of fatigue, symptoms such as pain, sleep problems, concentration problems, and decrease in functional capacity are frequently seen [22-25]. The fact that the fatigue of individuals with cancer increases during and after treatment may adversely affect the physical functions, daily living activities and quality of life of the patients [26,27]. Cancer related fatigue is one of the most frequently reported and activity limiting problems. Approximately 70% of individuals with cancer

Table 1. Sociodemographic information of groups with and without respiratory comorbidity.

Parameters	Group with respiratory comorbidity (n=26)		Group without respiratory comorbidity (n=26)		P
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	
Age (year)	66,85±12,17	45 - 92	67,81±7,69	57 – 85	0,735 (t=-0,340)
Height (cm)	170,19±8,76	150 - 188	168,96±8,90	150 – 185	0,618 (t=0,502)
Weight (kg)	76,35±2,72	50 - 105	70,73±2,19	52 – 88	0,115 (t=1,606)
BMI (kg/m ²)	26,48±1,03	17,72 – 37,65	24,86±0,81	18,42 – 32,47	0,223 (t=1,235)
Smoking exposure (pack years)	47,08±4,05	15 - 100	53,19±5,13	30 – 120	0,635 (z=-0,474)
		n (%)		n (%)	
Smoking status					
Active smoker		11 (42,3)		10 (38,5)	
Quit smoking		14 (53,8)		16 (61,5)	
Total		25 (96,2)		26 (100)	
Working status					
Full or part time		6 (23,1)		9 (34,6)	
Quitting work due to illness		3 (11,5)		5 (19,2)	
Retired		15 (57,7)		11 (42,3)	
Other		2 (7,7)		1 (3,8)	
Total		26 (100)		26 (100)	
Weight loss					
No weight loss		10 (38,5)		13 (50)	
<%5		7 (26,9)		4 (15,4)	
>%5		6 (23,1)		6 (23,1)	
Unknown		3 (11,5)		3 (11,5)	
Total		26 (100)		26 (100)	
Non-respiratory chronic diseases					
Coronary artery disease		5 (19,2)		2 (7,6)	
Congestive heart failure		4 (15,3)			
Peptic ulcer disease		1 (3,8)			
Diabetes mellitus		2 (7,6)		2 (7,6)	
Solid tumor		1 (3,8)		1 (3,8)	
Peripheral vascular disease		1 (3,8)		2 (7,6)	
Liver disease		1 (3,8)			

* $p < 0.05$ statistically significant difference; SD: Standard deviation; min-max: Minimum, maximum values; t: t test in independent groups; z: Mann Whitney U test; BMI: Body mass index.

Table 2. Lung cancer characteristics and stages of groups with and without respiratory comorbidity.

Parameters	Group with respiratory comorbidity, n (%)	Group without respiratory comorbidity, n (%)
SCLC		
Pread	10 (38,5)	6 (23,1)
Restricted	-	1 (3,8)
Unknown	16 (61,5)	19 (73,1)
Total	26 (100,0)	26 (100,0)
NSCLC		
Stage 1	-	2 (7,7)
Stage 2	2 (7,7)	2 (7,7)
Stage 3	2 (7,7)	2 (7,7)
Stage 4	6 (23,1)	8 (30,7)
Unknown	16 (61,5)	12 (46,2)
Total	26 (100,0)	26 (100,0)
Histological Type		
Adenocarcinoma	-	1 (3,8)
Squamous cell	13 (50,0)	18 (69,3)
Large cell	1 (3,8)	-
Small cell	11 (42,4)	7 (26,9)
Others	1 (3,8)	-
Total	26 (100,0)	26 (100,0)

SCLC: Small-Cell Lung Cancer; NSCLC: Non-Small Cell Lung Cancer.

Table 3. Comparison of pain, modified CCI, MMRC, ECOG and Karnofsky parameters of groups with and without respiratory comorbidity.

Parameters	Group with respiratory comorbidity (n=26)		Group without respiratory comorbidity (n=26)		P
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	
TKS-F (17-68)	48,76±1,76	27 - 61	46,15±1,74	31 - 61	0,35 (z=-0,935)
Pain (0-10)	3,69±0,57	0 - 8	1,54±0,52	0 - 7	0,003* (z=-3,005)
Modified CCI	2,88±0,36	0 - 6	3,73±0,275	1 - 8	0,084 (z=-1,727)
MMRC (0-4)	1,12±0,16	0 - 4	1±0,147	0 - 2	0,791 (z=-0,265)
ECOG (0-6)	1,85±0,18	0 - 3	1,31±0,17	0 - 3	0,033* (z=-2,135)
Karnofsky (0-100)	78,85±2,43	40-100	87,31±1,52	70 - 100	0,005* (z=-2,836)
		n (%)		n (%)	
TKS-F					
Yes		22 (84,6)		20 (76,9)	
No		4 (15,4)		6 (23,1)	
MMRC					
0		4 (15,4)		7 (26,9)	
1		17 (65,4)		12 (46,2)	
2		4 (15,4)		7 (26,9)	
3		-		-	
4		1 (3,8)		-	
Total		26 (100,0)		26 (100,0)	
ECOG					
0		2 (7,7)		4 (15,4)	
1		7 (26,9)		13 (50)	
2		10 (38,5)		6 (23,1)	
3		7 (26,9)		3 (11,5)	
Total		26 (100,0)		26 (100,0)	
Karnofsky					
0		-		-	
10		-		-	
20		-		-	
30		-		-	
40		1 (3,8)		-	
50		-		-	
60		2 (7,7)		-	
70		4 (15,4)		2 (7,7)	
80		11 (42,3)		6 (23,1)	
90		7 (26,9)		15 (57,7)	
100		1 (3,8)		3 (11,5)	
Total		26 (100,0)		26 (100,0)	

*p<0.05 statistically significant difference; SD: Standard deviation; Min-max: Minimum, maximum values; z: Mann Whitney U test; TKS-F: Tampa Kinesiophobia Scale-Fatigue; CCI: Charlson Comorbidity Index; MMRC: Modified Medical Council Dyspnea Scale; ECOG: Eastern Cooperative Oncology Group.

Table 4. Brief Fatigue Scale characteristics of the subjects included in the study.

Parameters	Group with respiratory comorbidity (n=26)		Group without respiratory comorbidity (n=26)		p
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	
Fatigue Severity					
Fatigue now	4,35±0,53	0 - 9	1,31±0,40	0 - 7	0,001* (z=-4,215)
Fatigue usual	5,23±0,56	0 - 9	2,04±0,48	0 - 8	0,001* (z=-3,749)
Fatigue worst	6,31±0,63	0 - 10	2,96±0,67	0 - 10	0,002* (z=-3,110)
Fatigue Interference					
General activity	4,92±0,50	0 - 10	2,35±0,54	0 - 8	0,002* (z=-3,144)
Mood	5,08±0,54	0 - 9	2,62±0,56	0 - 10	0,003* (z=-2,974)
Walking	5,46±0,51	0 - 9	2,58±0,52	0 - 9	0,001* (z=-3,405)
Work	5,81±0,51	0 - 10	2,58±0,56	0 - 10	0,001* (z=-3,746)
Relations	5,19±0,58	0 - 9	2,46±0,54	0 - 10	0,002* (z=-3,051)
Enjoyment	5,08±0,51	0 - 8	2,04±0,56	0 - 10	0,001* (z=-3,575)
Summation Scores					
BFI severity	5,29±0,55	0 - 10	2,1±0,50	0 - 10	0,001* (z=-3,779)
BFI interference	5,26±0,45	0 - 10	2,44±0,51	0 - 10	0,001* (z=-3,516)
BFI total	5,27±0,45	0 - 10	2,32±0,49	0 - 10	0,001* (z=-3,736)

*p<0.05 statistically significant difference; SD: Standard deviation; min-max: Minimum, maximum values; z: Mann Whitney U test; BFI: Brief Fatigue Inventory.

report that they feel fatigue during cancer treatment [1]. Polanski et al. study on individuals with a diagnosis of lung cancer; reported that the level of fatigue negatively affects the daily life activities and quality of life of individuals [28]. Blaney et al. reported that patients with lung cancer are increasingly inactive in relation to fatigue and prefer social isolation [29]. It is very important for health professionals to evaluate individuals at the right time and with the right methods and direct them to appropriate rehabilitation programs in order to avoid such vicious circles that negatively affect each other. The comorbidities of individuals with cancer in advanced ages directly affect the results of cancer treatment [30]. In particular, it becomes difficult for the individual with respiratory comorbidity to perform daily life activities alone and to participate in activities outside the home [31,32]. This situation increases the patient's dependence on others and causes physical, social and psychological problems [33,34].

The prevalence of fatigue is greater than 50% in those with advanced disease; it has been reported that it is over 30% in newly diagnosed cancer cases [2]. In our study, patients with lung cancer with respiratory comorbidity had higher fatigue levels. Although the physiological mechanisms are complex, low hemoglobin levels have been postulated to be associated with severe fatigue [3]. Lung cancer and its treatment have significant adverse effects on the patient's respiratory function, weight, muscle strength, cognitive functions, symptoms such as pain and loss of appetite [4].

In patients with chronic pain, kinesiophobia is defined as the fear of a specific movement or physical activity that is presumed to cause re-injury [5]. TKS-F, on the other hand, evaluates fatigue-related kinesiophobia [6]. In our study, 22 individuals (84.6%) in the group with

respiratory comorbidity had fatigue-related kinesiophobia. In the group without respiratory comorbidity, this value was 20 individuals (76.9%). Wang et al. reported that 45.7% of individuals had varying degrees of kinesiophobia, and 18.5% had moderate to severe kinesiophobia [3]. Dabek et al. found high levels of kinesiophobia in more than 70% of individuals in their study [7]. In the literature, it has also been shown that the degree of kinesiophobia is related to education [8]. Individuals with lower levels of education are more likely to show fear of movement. The result of our study is compatible with the literature in this respect. Due to the increased level of fear, stopping or limiting physical activity may lead to a decrease in the quality of life [9]. Individuals experiencing severe fatigue may be reluctant to give up treatment or take adequate doses of various forms of therapy.

The increase in comorbid conditions is associated with adverse health outcomes in lung cancer cases. Currently, there is no gold standard method for assessing comorbidities in individuals with lung cancer. In this study, modified CCI, which is widely used in various studies, including lung cancer, was used. Currently, the prognostic predictors of NSCLC are performance status, male gender, age 60 and over, non-squamous histology, and weight loss [10]. Since cancer metastasis is very common in these cases, the CCI score is usually >6 . In our study, there was no difference between the groups in terms of modified CCI score. Laor et al. reported the modified CMI mean score as 1.87 for elderly patients (75-84 years) and 2.65 for older patients (≥ 85 years) [11]. In our study, while the modified CMI score was 2.88 ± 0.36 in the group with respiratory comorbidity, this value was 3.73 ± 0.275 in the group without respiratory comorbidity. Considering the average age of the individuals in our study, the

modified CCI score was consistent with the literature. Pain; It is an unpleasant sensation arising from any part of the body, with or without a pathological cause [35]. Individuals with lung cancer complain of intense pain and experience intense anxiety due to pain [36]. This situation can cause social, emotional, physical and mental depression in individuals [37,38]. Stephenson et al. investigated the effects of foot reflexology on anxiety and pain in individuals with breast and lung cancer [39]. As a result of their study, they reported that foot reflexology intervention showed a significant reduction in anxiety in patients with breast and lung cancer and a significant reduction in pain in individuals. In our study, the pain levels of the groups were evaluated with the VAS method, and the pain level of individuals with respiratory comorbidity was 3.69 ± 0.57 , while the pain scores of individuals without respiratory comorbidity were 1.54 ± 0.52 .

Aging is associated with the development of conditions that can affect individuals' ability to tolerate cancer treatment. Some comorbidities preclude optimal treatments [12]. The literature shows that comorbidity and performance status are independent prognostic factors for the outcome of lung cancer cases [40,41].

The ECOG scale and Karnofsky Performance Scale are the two main scoring systems that help predict the ability of lung cancer patients to perform their daily activities and are routinely used to determine performance status. Patients who are able to take care of themselves but cannot perform most of the related activities (ECOG ≥ 2 or Karnofsky Performance Scale $\leq 70\%$) are considered to have poor performance status [42]. The performance status of the individuals in our study was better in the group without respiratory comorbidity. Lilenbaum et al. reported that 2 out of 5 cancer patients have poor performance status [43].

This study has some limitations. The limitation of our study is that we did not collect information about whether the individuals included in the study had orthopedic problems, had a history of surgery, and received oxygen support before diagnosis and laboratory parameters. The other limitations of our study are that social, psychological, educational and economic conditions were not analyzed in our study.

Conclusion

At the end of this study, it was observed that individuals with lung cancer with respiratory comorbidity had worse pain, fatigue and performance values in activities of daily living, while kinesiophobia values related to fatigue were similar. The highest mean fatigue levels were reported in individuals with respiratory comorbidities. Individuals in both groups had fatigue-related kinesiophobia; however, there was no statistically significant difference between the groups. Further research with a larger sample will be required to confirm the presence of fatigue-related kinesiophobia in individuals with lung cancer with respiratory comorbidities.

Funding: *The author(s) received no financial support for the research, authorship, and/or publication of this article.*

Conflict of Interest: *The authors declare that they have no conflict of interest.*

Ethical Statement: *Bolu Abant İzzet Baysal University ethics committee approved the study protocol (Approval ID: 2021/61).*

Open Access Statement

Experimental Biomedical Research is an open access journal and all content is freely available without charge to the user or his/her institution. This journal is licensed under

a [Creative Commons Attribution 4.0 International License](#). Users are allowed to read, download, copy, distribute, print, search, or link to the full texts of the articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author.

Copyright (c) 2021: Author (s).

References

- [1]Lucía A, Earnest C, Pérez M. Cancer-related fatigue: can exercise physiology assist oncologists? *Lancet Oncol.* 2003;4(10):616-25.
- [2]Mystakidou K, Tsilika E, Parpa E, et al. Psychometric properties of the brief fatigue inventory in Greek patients with advanced cancer. *J Pain Symptom Manage.* 2008;36(4):367-73.
- [3]Wang XS, Giralt SA, Mendoza TR, et al. Clinical factors associated with cancer-related fatigue in patients being treated for leukemia and non-Hodgkin's lymphoma. *J Clin Oncol.* 2002;20(5):1319-28.
- [4]Montoya M, Fossella F, Palmer JL, et al. Objective evaluation of physical function in patients with advanced lung cancer: a preliminary report. *J Palliat Med.* 2006;9(2):309-16.
- [5]Lundberg MK, Styf J, Carlsson SG. A psychometric evaluation of the Tampa Scale for Kinesiophobia—from a physiotherapeutic perspective. *Physiother Theory Pract.* 2004;20(2):121-33.
- [6]Nijs J, De Meirleir K, Duquet W. Kinesiophobia in chronic fatigue syndrome: assessment and associations with disability. *Arch Phys Med Rehabil.* 2004;85(10):1586-92.
- [7]Dabek J, Knapik A, Gallert-Kopyto W, et al. Fear of movement (kinesiophobia)—an underestimated problem in Polish patients at various stages of coronary artery disease. *Ann Agric Environ Med.* 2020;27(1):56-60.
- [8]Cai L, Liu Y, Xu H, et al. Incidence and risk factors of kinesiophobia after total knee arthroplasty in Zhengzhou, China: a cross-sectional study. *J Arthroplasty.* 2018;33(9):2858-62.
- [9]Luque-Suarez A, Martinez-Calderon J, Falla D. Role of kinesiophobia on pain, disability and quality of life in people suffering from chronic musculoskeletal pain: a systematic review. *Br J Sports Med.* 2019;53(9):554-59.
- [10]Zhao L, Leung L-H, Wang J, et al. Association between Charlson comorbidity index score and outcome in patients with stage IIIB-IV non-small cell lung cancer. *BMC Pulm Med.* 2017;17(1):1-7.
- [11]Laor A, Tal S, Guller V, et al. The Charlson Comorbidity Index (CCI) as a mortality predictor after surgery in elderly patients. *Am Surg.* 2016;82(1):22-27.
- [12]Ganti AK, Siedlik E, Marr AS, et al. Predictive ability of Charlson comorbidity index on outcomes from lung cancer. *Am J Clin Oncol.* 2011;34(6):593-96.
- [13]Birim Ö, Maat A, Kappetein AP, et al. Validation of the Charlson comorbidity index in patients with operated primary non-small cell lung cancer. *Eur J Cardiothorac Surg.* 2003;23(1):30-34.
- [14]Çinar D, Yava A. Validity and reliability of functional assessment of chronic illness treatment-fatigue scale in Turkish patients with type 2 diabetes. *Endocrinol Diabetes Nutr (Eng Ed).* 2018;65(7):409-17.
- [15]Ruparel M, Quaife SL, Dickson JL, et al. Prevalence, symptom burden, and underdiagnosis of chronic obstructive pulmonary disease in a lung cancer screening cohort. *Ann Am Thorac Soc.* 2020;17(7):869-78.

- [16] Yılmaz ÖT, Yakut Y, Uygur F, et al. Tampa Kinezyofobi Ölçeği'nin Türkçe versiyonu ve test-tekrar test güvenilirliği. *Fiz Rehabili.* 2011;22(1):44-49.
- [17] Silver A, Haeney M, Vijayadurai P, et al. The role of fear of physical movement and activity in chronic fatigue syndrome. *J Psychosom Res.* 2002;52(6):485-93.
- [18] Hollen P, Gralla R, Kris M, et al. A comparison of visual analogue and numerical rating scale formats for the Lung Cancer Symptom Scale (LCSS): does format affect patient ratings of symptoms and quality of life? *Qual Life Res.* 2005;14(3):837-47.
- [19] Dall'Olio FG, Maggio I, Massucci M, et al. ECOG performance status ≥ 2 as a prognostic factor in patients with advanced non-small cell lung cancer treated with immune checkpoint inhibitors—A systematic review and meta-analysis of real world data. *Lung Cancer.* 2020;145:95-104.
- [20] Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky Performance Status and proposal of a simple algorithmic system for its evaluation. *BMC Med Inform Decis Mak.* 2013;13(1):1-7.
- [21] Horneber M, Fisher I, Dimeo F, et al. Definition and prevalence of cancer-related fatigue. *Dtsch Arztebl Int.* 2012;109(9):161-72.
- [22] Stasi R, Abriani L, Beccaglia P, et al. Cancer-related fatigue: evolving concepts in evaluation and treatment. *Cancer.* 2003;98(9):1786-801.
- [23] Kirkova J, Aktas A, Walsh D, et al. Cancer symptom clusters: clinical and research methodology. *J Palliat Med.* 2011;14(10):1149-66.
- [24] Cooley ME, Short TH, Moriarty HJ. Symptom prevalence, distress, and change over time in adults receiving treatment for lung cancer. *Psycho-Oncology.* 2003;12(7):694-708.
- [25] Fan G, Filipczak L, Chow E. Symptom clusters in cancer patients: a review of the literature. *Curr Oncol.* 2007;14(5):173-79.
- [26] Gupta D, Lis CG, Grutsch JF. The relationship between cancer-related fatigue and patient satisfaction with quality of life in cancer. *J Pain Symptom Manage.* 2007;34(1):40-47.
- [27] Mock V, Pickett M, Ropka ME, et al. Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Pract.* 2001;9(3):119-27.
- [28] Polanski J, Jankowska-Polanska B, Rosinczuk J, et al. Quality of life of patients with lung cancer. *Onco Targets Ther.* 2016;9:1023-28.
- [29] Blaney J, Lowe-Strong A, Rankin J, et al. The cancer rehabilitation journey: barriers to and facilitators of exercise among patients with cancer-related fatigue. *Phys Ther.* 2010;90(8):1135-47.
- [30] Sun V, Burhenn PS, Lai L, et al. The impact of comorbidity on surgical outcomes in older adults with cancer. *Semin Oncol Nurs.* 2017;33(1):80-86.
- [31] Thorpe O, Kumar S, Johnston K. Barriers to and enablers of physical activity in patients with COPD following a hospital admission: a qualitative study. *Int J Chron Obstruct Pulmon Dis.* 2014;21(9):115-28.
- [32] Granger CL, Connolly B, Denehy L, et al. Understanding factors influencing physical activity and exercise in lung cancer: a systematic review. *Support Care Cancer.* 2017;25(3):983-99.
- [33] Bade BC, Thomas DD, Scott JB, et al. Increasing physical activity and exercise in lung cancer: reviewing safety, benefits, and application. *J Thorac Oncol.* 2015;10(6):861-71.

- [34] Berterö C, Vanhanen M, Appelin G. Receiving a diagnosis of inoperable lung cancer: patients' perspectives of how it affects their life situation and quality of life. *Acta Oncol.* 2008;47(5):862-69.
- [35] Świeboda P, Filip R, Prystupa A, et al. Assessment of pain: types, mechanism and treatment. *Ann Agric Environ Med.* 2013;1:2-7.
- [36] Hopkins KG, Hoffman LA, Dabbs ADV, et al. Postthoracotomy pain syndrome following surgery for lung cancer: symptoms and impact on quality of life. *J Adv Pract Oncol.* 2015;6(2):121-32.
- [37] Lo C, Zimmermann C, Rydall A, et al. Longitudinal study of depressive symptoms in patients with metastatic gastrointestinal and lung cancer. *J Clin Oncol.* 2010;28(18):3084-89.
- [38] Kim Y, Duberstein PR, Sörensen S, et al. Levels of depressive symptoms in spouses of people with lung cancer: effects of personality, social support, and caregiving burden. *Psychosomatics.* 2005;46(2):123-30.
- [39] Stephenson N, Weinrich SP, Tavakolil AS. The effects of foot reflexology on anxiety and pain in patients with breast and lung cancer. *Oncol Nurs Forum.* 2000;27(1):67-72.
- [40] Ngeow J, Leong SS, Gao F, et al. Impact of comorbidities on clinical outcomes in non-small cell lung cancer patients who are elderly and/or have poor performance status. *Crit Rev Oncol Hematol.* 2010;76(1):53-60.
- [41] Colinet B, Jacot W, Bertrand D, et al. A new simplified comorbidity score as a prognostic factor in non-small-cell lung cancer patients: description and comparison with the Charlson's index. *Br J Cancer.* 2005;93(10):1098-105.
- [42] Gajra A, Marr AS, Ganti AK. Management of patients with lung cancer and poor performance status. *J Natl Compr Canc Netw.* 2014;12(7):1015-25.
- [43] Lilenbaum RC, Cashy J, Hensing TA, et al. Prevalence of poor performance status in lung cancer patients: implications for research. *J Thorac Oncol.* 2008;3(2):125-29.