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Exercise capacity, muscle strength, dyspnea, physical activity, and quality of life in preoperative patients with lung cancer

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Background/aim: To detect the extent to which physical impairments are observed in patients with lung cancer awaiting lung surgery, exercise capacity, muscle strength, physical activity, dyspnea, and quality of life (QOL) were objectively compared between the patients and healthy individuals in current study.

Materials and methods: Patients with lung cancer (n = 26) and healthy individuals (n = 21) were included. Exercise capacity, respiratory (maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP)) and quadriceps femoris muscle strength, physical activity, dyspnea and QOL were evaluated using 6-min walk test (6-MWT), a mouth pressure device, a hand-held dynamometer, a metabolic holter device, Modified Medical Research Council dyspnea scale and European Organization for Research and Treatment of Cancer QOL Questionnaire C30 version 3.0, respectively.

Results: The 6-MWT distance (mean difference: 78.97 m), percentages of predicted MIP and MEP values, physical activity parameters (energy expenditures, physical activity duration, average metabolic equivalent and number of steps) and QOL subscales scores (functional, social function and global health status) were significantly lower in the patients than healthy individuals ($p < 0.05$). Dyspnea perception and other QOL subscales scores (symptom and fatigue) were significantly higher in patients than healthy individuals ($p < 0.05$). No significant difference was prevalent in quadriceps femoris muscle strength ($p > 0.05$). Sixteen (66.7%) patients were sedentary.

Conclusion: Severe reductions in exercise capacity, respiratory muscle strength, and physical activity level, poorer QOL and evident dyspnea exist in preoperative patients with lung cancer. Therefore, patients should be included in early protective rehabilitation program including aerobic exercise, respiratory muscle training and physical activity counseling before lung surgery.

Key words: Lung neoplasms, walk test, dyspnea, muscle strength, exercise, quality of life

1. Introduction

Patients with lung cancer suffer from many pathophysiological changes due to characteristics of lung cancer and cytotoxic treatments including chemotherapy and radiotherapy. These changes commonly occur in respiratory mechanics and gas exchange mechanism, all of which result in pulmonary function impairments. Moreover, excessive weight loss, anemia, protein catabolism, muscle wasting, skeletal muscle atrophy, inhibition of muscle regeneration, reduced oxidative capacity, and exercise intolerance are observed in patients in course of time [1,2]. Progressive declines in exercise capacity and muscle weakness are also commonly observed in patients with lung cancer [2]. At the diagnosis stage, 40% of the patients meet physical activity guidelines requirements, and the patients are less physically active than healthy individuals. This measurement did not include any outcome regarding energy expenditure, detailed amount and type of physical activity [2]. Based on the limited studies, weakness in respiratory muscles before surgery has been stated; however, there is no detailed knowledge about predicted values representing patients' characteristics to reveal differences [3,4]. Furthermore, these patients experience fatigue and dyspnea, which increase disease burden and afflict quality of life (QOL) [5–7].

On the other hand, the detailed impairment levels related with respiratory muscle strength and physical activity have not yet been investigated along with satisfactory and objective findings in preoperative patients

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with lung cancer in comparison with healthy individuals. Therefore, to reveal impairments in these patients before surgery is of importance in terms of being helpful in both determining the early protective rehabilitation program content and reducing the disease burden and other possible factors. Aim of the current study was to investigate differences in exercise capacity, respiratory and peripheral muscle strength, physical activity level, dyspnea and QOL between preoperative patients with lung cancer and healthy individuals.

2. Materials and methods

2.1. Study design

This is a cross-sectional study that was performed at cardiopulmonary rehabilitation unit of Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey. All patients were referred from Gazi University, Faculty of Medicine, Department of Thoracic Surgery to the cardiopulmonary rehabilitation unit. The Local Ethics Committee of Gazi University approved this study (2019 - 250). Informed consents were taken from each participant. This study followed up the principles of Declaration of Helsinki.

2.2. Participants

The patients with lung cancer who were decided to undergo lung surgery by thoracic surgeons were referred to the physiotherapists. The patients were included based on some inclusion criteria that were being a candidate for lung surgery due to lung cancer diagnosis, between 18 and 80 years, clinically stable, able to walk and receiving optimal medical therapy. The patients were excluded from the study due to the following reasons: having health problems such as cooperation, orthopedical or neurological diseases that limited the walking ability and physical activity, having comorbidities such as unstable diabetes mellitus, heart failure, atrial fibrillation and/or hypertension, acute infections or having myocardial infarction before study at least six months. Healthy individuals were recruited from relatives of the researchers and staff. These healthy individuals were involved if they were between 18 and 80 years and willing to participate in the study. Though, they were excluded from this study because of having any chronic diseases. The patients were matched with healthy individuals according to statistical similarity of both age and sex.

2.3. Clinical characteristics

Charlson comorbidity index was used to score chronic diseases accompanying primary disease, which shows that mortality risk gradually increases as the total score increases. Pulmonary risk assessment was performed to determine the risk of developing postoperative complications before surgery of which scores of 0 or 1 indicates a low pulmonary risk, and a score of ≥ 2 indicates a high pulmonary risk. Dynamic lung volumes were measured using a spirometry (Cosmed, Class II/Internally Powered Equipment, Italy).

2.4. Exercise capacity

Six-minute walk test (6-MWT) was performed to evaluate exercise capacity according to the guidelines [8,9]. Heart rate (PE3000 Polar Electro, Finland), blood pressures, oxygen saturation (SpO_2), breathing frequency, dyspnea, and fatigue perceptions (Modified Borg scale) were immediately recorded before and after tests. For the statistical analysis, differences between post and pretest values (Δ) were calculated.

2.5. Muscle strength

Respiratory muscle weakness was detected using volitional measurements of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) via a portable mouth pressure device (Micro Medical MicroRPM, England, UK) based on guidelines. All individuals completed both maximal inspiration against close airway for MIP at residual volume and maximal expiration for MEP at total lung capacity. The highest values for MIP and MEP were recorded for analysis [10]. Reference values were used for interpreting MIP and MEP measurements [11].

To evaluate quadriceps femoris muscle strength, a hand-held dynamometer (JTECH Power Track Commander, Baltimore, USA) was used. All individuals were tested by experienced physiotherapists in sitting position with hips and knees flexed at 90°, hands resting in lap and feet in the air. The measurements were repeated from nondominant side at least three times. The best value in Newton (N) was recorded for analysis. Percentage of predicted value was calculated using reference values [12].

2.6. Physical activity level

A metabolic holter device (SenseWear Armband Model MF-SW, BodyMedia, Inc. Pittsburgh PA 15222, USA) was used to obtain knowledge about total daily energy expenditure (J / d), active energy expenditure (> 3 metabolic equivalents (METs)) (J / d), moderate and severe physical activity duration (energy expended for physical activity requiring > 3 METs) (min / d), number of steps (steps / d), average metabolic equivalent (METs / d), lying down (min / d) and sleeping duration (min / d) [13]. The device was worn in the middle of nondominant muscle body of triceps for two consecutive weekdays [13]. Physical activity levels and intensity were classified according to number of steps and METs [14,15].

2.7. Dyspnea

To evaluate the respiratory disability related with dyspnea, the Modified Medical Research Council (MMRC) dyspnea scale was used. Dyspnea levels are categorized between 0 (dyspnea only with strenuous exercise) and 4 (too breathless to leave the house or when dressing/undressing) [16].

2.8. Quality of life

The European Organization for Research and Treatment of Cancer QOL Questionnaire C30 version 3.0 (EORTC QLQ-C30) was used. This is a self-administered questionnaire which consists of five functional subscales along with a social functioning subscale, three symptom subscales with also a fatigue subscale, a global health status subscale, and several single items. All item scores are converted to values from 0 to 100. Higher values show higher healthy levels in functional and social functioning subscales, a higher QOL level in global health status subscale, and increased presence of symptoms in both symptom and fatigue subscales [17].

2.9. Statistical analyses

Sample size analysis prior to study (G*Power 3.0.10 system, Franz Faul, Universität Kiel, Germany) was performed to detect 6-MWT difference between two independent means/groups for an α value of 0.05, effect size of 1.30, 95% power, and at least 17 participants for each group were calculated [18]. Windows-based SPSS 15.0 statistical analysis program was used (SPSS Inc., USA). To detect normally distribution, variables were examined via visual (histograms, probability plots) and analytical methods (Shapiro-Wilk's test). Variables were descriptively stated as mean ± standard deviation (× ± SD), mean difference between groups, 95% confidence interval (95%CI), median (minimum-maximum (min-max)), U value, frequency (n) and percentage (%). Student *t* test, Mann-Whitney U test and Chi-square test were respectively used to compare normally distributed, undistributed, and nominal variables between the patients and healthy individuals. Level of significance was set to $p \leq 0.05$.

3. Results

Twenty-six patients with lung cancer and 21 healthy individuals were compared as shown in Figure. Demographic characteristics were similar in groups except smoking exposure ($p > 0.05$, Table 1) and pulmonary function test values were lower in the patients compared with healthy individuals ($p < 0.05$). Clinical characteristics of the patients were given in Table 2.

As shown in Table 3-6, 6-MWT distance, MIP%, MEP%, physical activity parameters, functional subscale, social function subscale, and global health status subscale scores were significantly lower; MMRC dyspnea, symptom subscale, and fatigue subscale scores were significantly higher in the patients compared with healthy individuals ($p < 0.05$).

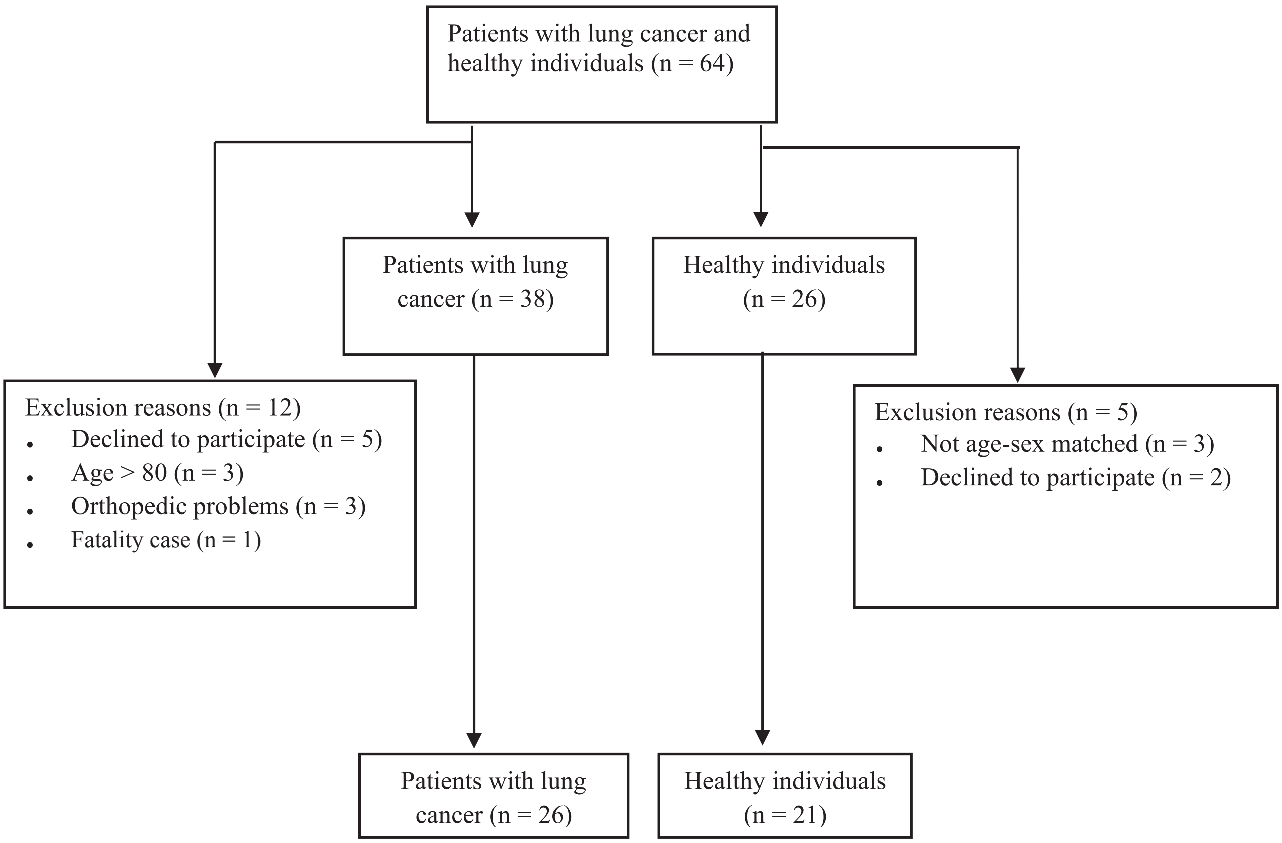

Figure. The follow diagram of patients with lung cancer and healthy individuals in the current study.

Table 1. Demographic characteristics and pulmonary functions in patients with lung cancer and healthy individuals.

	Patients with lung cancer (n = 26)	Healthy individuals (n = 21)		
Characteristics	× ± SD / Median (min – max)	× ± SD / Median (min – max)	Mean difference (95%CI) / U	p
Age (years)	61.85 ± 4.98	59.57 ± 5.75	2.27 (–0.88 to 5.43)	0.153
Sex (n / %)				
Female	4 / 15.4%	7 / 33.3%		0.148
Male	22 / 84.6%	14 / 66.7%		
Height (cm)	166.96 ± 7.5	168.86 ± 8.66	–1.89 (–6.64 to 2.85)	0.425
Body weight (kg)	75 (47–115)	77 (66–103)	234.5	0.409
BMI (kg / m^2)	27.13 ± 3.97	27.67 ± 3.16	–0.54 (–2.69 to 1.61)	0.615
BMI classification (n / %)				
Cachexia	1 / 3.9%	0		
Normal	7 / 26.9%	7 / 33.3%		0.452
Overweight	13 / 50%	7 / 33.3%		
Obese	5 / 19.2%	7 / 33.3%		
Pulmonary function test				
FEV_1 (L)	2.13 ± 0.57	2.71 ± 0.66	–0.58 (–0.94 to –0.22)	**0.002***
FEV_1 (%)	75.88 ± 18.01	93.71 ± 16.85	–17.83 (–28.17 to –7.48)	**0.001***
FVC (L)	2.91 ± 0.74	3.5 ± 0.85	–0.58 (–1.05 to –0.11)	**0.016***
FVC (%)	83.81 ± 19.11	97.05 ± 15.75	–13.24 (–23.7 to –2.78)	**0.014***
FEV_1 / FVC (%)	72.3 ± 9.29	79.43 ± 8.92	–7.13 (–12.52 to –1.73)	**0.011***
PEF (L)	6.02 ± 1.8	7.04 ± 2.2	–1.02 (–2.19 to 0.15)	0.087
PEF (%)	79.96 ± 20.89	94.9 ± 23.51	–14.94 (–27.99 to –1.89)	**0.026***
$FEF_{25-75\%}$ (L)	1.44 (0.55–4.47)	2.45 (0.98– 5.03)	114	**0.001#**
$FEF_{25-75\%}$ (%)	49.92 ± 22.71	78.81 ± 29.9	–28.89 (–44.34 to –13.43)	**< 0.001***
History of smoking (n / %)				
Smoker	5 / 19.2%	5 / 23.8%		
Ex-smoker	16 / 61.6%	8 / 38.1%		0.239
Nonsmoker	5 / 19.2%	8 / 38.1%		
Smoking (pack × year)	40 (1–82.5)	7.5 (2–32)	22	**< 0.001#**

*BMI: body mass index, FEV_1: forced expiratory volume in the first second, FVC: forced vital capacity, FEV_1/FVC: forced expiratory volume in the first second/forced vital capacity, PEF: peak expiratory flow, $FEF_{25-75\%}$: forced expiratory flow from 25% to 75%, cm: centimeter, kg: kilogram, m: meter, L: liter, n: frequency, %: percentage, CI: confidence interval and U: U value.
**Descriptive analyses were presented using (× ± SD), median (min – max) and (n / %) for normally distributed, nonnormally distributed and categorical variables, respectively.
***Student's t-test *p < 0.05, Mann–Whitney U test #p < 0.05 and Chi square test ¥p < 0.05.

The 6-MWT distance was less than 80% of predicted values in 14 (53.8%) patients and 1 (4.8%) healthy individual. Inspiratory and expiratory muscle weakness existed respectively in 5 (19.2%) and 11 (42.3%) patients; 2 (10%) and 4 (20%) healthy individuals. Quadriceps femoris muscle strength was less than 80% of predicted values in 11 (42.3%) patients and 8 (38.1%) healthy individuals. Dyspnea in daily living activities was present in 10 (38.5%) patients and 1 (4.8%) healthy individual.

4. Discussion

Our comprehensive results firstly provided compelling evidence that there was a sharp distinction in terms of dynamic lung volumes, exercise capacity (difference: 78.97

Table 2. Clinical characteristics of patients with lung cancer.

	Patients with lung cancer (n = 26)
Characteristics	× ± SD
Diagnoses (n / %)	
Adenocarcinoma	11 / 42.3%
Squamous cell carcinoma	11 / 42.3%
Large cell carcinoma	1 / 3.9%
Other	3 / 11.5%
Pathological stage of lung cancer (n / %)	
IA	7 / 26.9%
IB	2 / 7.7%
IIA	1 / 3.8%
IIB	4 / 15.4%
IIIA	6 / 23.1%
IV	6 / 23.1%
Tumor size (cm)	2.45 ± 1.37
Charlson Comorbidity Index score (0 - 37)	2.73 ± 1
Very light (0) (n / %)	1 / 3.8%
Light (1– 2) (n / %)	10 / 38.5%
Heavy (3– 4) (n / %)	14 / 53.9%
Very heavy (≥ 5) (n / %)	1 / 3.8%
Pulmonary risk score (0 - 8)	2.04 ± 1.11
Low pulmonary risk (n / %)	10 / 38.5%
High pulmonary risk (n / %)	16 / 61.5%
Induction therapy (n / %)	
No treatment	18 / 69.2%
Chemotherapy	6 / 23.1%
Radiotherapy	0 / 0%
Chemo-radiotherapy	2 / 7.7%
Surgery type (n / %)	
Video-assisted thoracoscopic surgery	7 / 26.9%
Thoracotomy	19 / 73.1%
Pulmonary disease (n / %)	7 / 26.9%
Disease duration (month)	7.35 ± 7.57

*cm: centimeter, n: frequency, %: percentage.
**Descriptive analyses were presented using (× ± SD) and (n / %) for normally distributed and categorical variables, respectively.

m), respiratory muscle strength, physical activity level, dyspnea and QOL between patients with lung cancer and healthy counterparts. Quadriceps femoris muscle strength was interestingly preserved in patients. This study also revealed the presence and prevalence of impairments regarding decreased exercise capacity, inspiratory muscle weakness, expiratory muscle weakness, increase in dyspnea perception, and sedentary lifestyle in patients with lung cancer awaiting surgery.

Six-MWT distance values of our patients were considerably less than values of healthy counterparts. Brocki et al. [19] showed that preoperative 6-MWT distance values (506 m, 100%) are in normal ranges in patients who scheduled for lung resection of lung cancer [19]. Whereas 6-MWT distance value of these patients is lower than our result, predictive value is higher than ours. Study of Brocki et al. [19] also presented that 15 (19%) patients had no malignancy, and the others were newly diagnosed with lung cancer [19] which may have caused relatively high predictive value for 6-MWT distance of these patients compared to ours [19]. Disease durations of our patients were about seven months. On the other hand, after 6-month following diagnosis, progressive reduction in 6-MWT distance (mean difference: 77.9 m, from 84% of the predicted distance at the diagnosis stage to 69% by 6-month) has been also shown in preoperative patients with lung cancer following anticancer treatments [2]. In fact, 30.4% of these patients had chronic obstructive pulmonary disease [2]. Consistent with this result, our study demonstrated that 6-MWT distance was comparatively reduced (78.97 m) in preoperative patients with lung cancer (26.9% had pulmonary disease) whose disease duration was about 7-month. It is also worth noting that there were no control groups in both studies [2,19]. Morano et al. [20] investigated effects of rehabilitation programs before lung surgery and presented low 6-MWT distance (425 to 339 m) values in both research groups [20]. Both our patients and healthy individuals had higher 6-MWT distance values compared to results of Morano et al.'s [20] study that have neither a healthy group nor additional knowledge about predictive value, disease duration or induction therapy status of the patients. Another newly published study related effects of pulmonary rehabilitation for inoperable patients with lung cancer found that pre-rehabilitation 6-MWT distance of patients (434.52 m) was 83.16% of predicted values [21]. These inoperable patients have walked lower distance than our patients; however, the percentage of walked distance was higher than ours. This may arise from using different reference values [22]. Moreover, our patients suffered from increased heart rate, breathing frequency, and general fatigue along with decreased SpO_2 before 6-MWT compared with healthy counterparts. Decreased SpO_2 and increased dyspnea perception were also evident in our patients after 6-MWT. Unlike other studies, changes in these physiological outcomes have been revealed in current study. Given all results related with 6-MWT and

Table 3. Comparison of exercise capacity in patients with lung cancer and healthy individuals.

	Patients with lung cancer (n = 26)	Healthy individuals (n = 21)		
	× ± SD / Median (min – max)	× ± SD / Median (min – max)	Mean difference (95%CI) / U	p
Exercise capacity				
6-MWT (m)	529.34 ± 57.59	608.31 ± 61.1	−78.97 (−113.94 to −44.01)	**< 0.001***
6-MWT (%)	79.72 (55.34 – 87.34)	91.39 (77.02 – 105.51)	50	**< 0.001**#
Resting values before 6-MWT				
HR (beats / min)	86.31 ± 13.62	74.33 ± 11.71	11.97 (4.4 to 19.54)	**0.003***
SBP (mmHg)	119.65 ± 12.04	124.14 ± 14.28	−4.49 (−12.22 to 3.24)	0.248
DBP (mmHg)	72.5 (60 – 100)	80 (68 – 90)	237	0.424
SpO_2 (%)	96 (92 – 98)	97 (94 – 98)	177	**0.034**#
Breathing frequency (breaths / min)	24 (16 – 28)	20 (16 – 28)	147.5	**0.004**#
Dyspnea (MBS) (0 - 10)	0 (0 – 0.5)	0	252	0.199
General fatigue (MBS) (0 - 10)	0 (0 – 3)	0	199.5	**0.011**#
QFM fatigue (MBS) (0 - 10)	0 (0 – 3)	0	241.5	0.112
MaxHR (%)	82.16 (53.25 – 98.1)	74.85 (46.43 – 98.21)	186	0.063
Δ HR (beats / min)	42.85 ± 14.44	47.05 ± 18.23	-4.2 (-13.8 to 5.39)	0.383
Δ SBP (mmHg)	22.5 (-20 – 98)	20 (-15 – 60)	229	0.344
Δ DBP (mmHg)	0 (-12 – 22)	0 (-10 – 24)	255.5	0.700
Δ SpO_2 (%)	-1.5 (-16 – 3)	0 (-5 – 3)	169.5	**0.025**#
Δ Breathing frequency (breaths / min)	4 (0 – 16)	4 (0 – 16)	255	0.685
Δ Dyspnea (MBS) (0 – 10)	0.75 (0 – 4)	0 (0 – 2)	166.5	**0.010**#
Δ General fatigue (MBS) (0 – 10)	0 (-1 – 4)	0 (0 – 3)	252.5	0.603
Δ QFM fatigue (MBS) (0 – 10)	0 (-0.5 – 5)	0 (0 – 2)	263.5	0.784

*6-MWT: 6-minute walk test, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, SpO_2: oxygen saturation, QFM: quadriceps femoris muscle, maxHR: maximal heart rate, Δ: difference between post and pretest values, m: meter, %: percentage, min: minute, mmHg: millimeter of mercury, MBS: modified Borg scale, CI: confidence interval and U: U value.
**Descriptive analyses were presented using (× ± SD) and median (min – max) for normally and nonnormally distributed variables, respectively.
***Student's t-test *p < 0.05 and Mann–Whitney U test #p < 0.05.

being a mortality predictor of decreased 6-MWT distance, exercise capacity should be evaluated as soon as possible following diagnosis. Then an appropriate aerobic exercise training program should be initiated immediately.

Respiratory muscle weakness composes higher risk for postoperative pulmonary complications in patients undergoing thoracic surgery [23]. Predicted values of respiratory muscle strength were decreased in our patients (mean difference for MIP: −19.74% and MEP: −14.65 %) compared to healthy individuals; however, MIP and MEP mean values were in normal ranges. These results should be concluded as; patients' respiratory muscles tend to weaken and should be followed during the course of the time. Inspiratory (19.2%) and expiratory (42.3%) muscle weakness also existed in many of our patients. The study without a healthy control group of Brocki et al. [19] showed that MIP (85 cmH_2O, 104%) and MEP (102 cmH_2O, 106%) values were consistently in normal ranges in newly diagnosed patients with lung cancer [19]. The study of Morano et al. [20] also presented the lower MIP and MEP values in patients, included in both pulmonary rehabilitation and chest physical therapy programs [20]. These values were considerably lower than our results and had no detailed knowledge about predicted values or patients' characteristics to reveal differences. On the other hand, it has been known that patients with lung cancer are physically inactive and do not exercise enough which may contribute to many physical impairments and muscle

Table 4. Comparison of respiratory and peripheral muscles strength and dyspnea in patients with lung cancer and healthy individuals.

	Patients with lung cancer (n = 26)	Healthy individuals (n = 21)		
	× ± SD / Median (min – max)	× ± SD / Median (min – max)	Mean difference (95%CI) / U	p
MIP (cmH_2O)	105.88 ± 22.56	119.3 ± 36.05	–13.41 (–32.19 to 5.36)	0.155
MIP (%)	103.83 ± 24.17	123.57 ± 32.27	–19.74 (–36.49 to –2.98)	**0.022***
MEP (cmH_2O)	156.38 ± 33.08	174.5 ± 48.58	–18.11 (–42.4 to 6.16)	0.140
MEP (%)	81.03 ± 14.74	95.67 ± 19.53	–14.65 (–24.82 to –4.47)	**0.006***
MMRC dyspnea score (0 - 4)	0 (0 – 2)	0 (0 – 1)	179	**0.007#**
QFM strength (N) (ND)	346.46 ± 98.26	333.48 ± 84.93	12.98 (–41.72 to 67.69)	0.635
QFM strength (%) (ND)	86.36 ± 22.15	83.59 ± 20.1	2.77 (–9.79 to 15.33)	0.659

*MIP: maximal inspiratory pressure, MEP: maximal expiratory pressure, MMRC: Modified Medical Research Council, %: percentage, cmH_2O: centimeter of water, ND: nondominant, N: newton, CI: confidence interval and U: U value.
**Descriptive analyses were presented using (× ± SD) and median (min – max) for normally and nonnormally distributed variables, respectively.
***Student's t-test *p < 0.05 and Mann–Whitney U test #p < 0.05.

Table 5. Comparison of physical activity levels in patients with lung cancer and healthy individuals.

	Patients with lung cancer (n = 26)	Healthy individuals (n = 21)		
	× ± SD / Median (min – max)	× ± SD / Median (min – max)	Mean difference (95%CI) / U	p
Physical activity parameters				
Total energy expenditure (J / d)	8918.29 ± 2684.21	11056.38 ± 1676.5	–2138.09 (–3507.08 to –769.09)	**0.003***
Active energy expenditure (> 3 METs) (J / d)	1068 (71 – 4809)	1955 (353 – 5681)	149	**0.019#**
Physical activity duration (> 3 METs) (min / d)	56.5 (3 – 216)	106 (21 – 299)	148.5	**0.019#**
Average metabolic equivalent (METs / d)	1.2 (0.9 – 1.9)	1.4 (1.2 – 1.8)	152.5	**0.022#**
Sedentary (n / %)	22 / 91.7%	16 / 76.2%		0.225
Light-intensity (n / %)	2 / 8.3%	5 / 23.8%		
Number of steps (steps / d)	3821.5 (152 – 15951)	8828 (2446 – 17307)	121	**0.003#**
Sedentary (n / %)	16 / 66.7%	5 / 23.8%		**0.030¥**
Low active (n / %)	4 / 16.6%	3 / 14.3%		
Somewhat active (n / %)	1 / 4.2%	5 / 23.8%		
Active (n / %)	1 / 4.2%	3 / 14.3%		
Highly active (n / %)	2 / 8.3%	5 / 23.8%		
Lying down (min / d)	506.87 ± 158.05	437.24 ± 128.91	69.64 (-17.88 to 157.15)	0.116
Sleep duration (min / d)	393 (165 – 1440)	368 (171 – 586)	186.5	0.136

*J: joule, d: day, min: minute, MET: metabolic equivalent, n: frequency, %: percentage, CI: confidence interval and U: U value.
**Descriptive analyses were presented using (× ± SD), median (min – max) and (n / %) for normally distributed, nonnormally distributed and categorical variables, respectively.
***Student's t-test *p < 0.05, Mann–Whitney U test #p < 0.05 and Chi square test ¥p < 0.05.

Table 6. Comparison of quality of life in patients with lung cancer and healthy individuals.

	Patients with lung cancer (n = 26)	Healthy individuals (n = 21)		
	Median (min – max)	Median (min – max)	U	p
EORTCQLQ-C30 subscales scores				
Functional subscale (0 - 100%)	90 (55.56 – 100)	97.78 (64.44 – 100)	144	**0.005**#
Social function subscale (0 - 100%)	100 (33.33 – 100)	100 (66.67 – 100)	193	**0.017**#
Symptom subscale (0 - 100%)	7.69 (0 – 41.03)	0 (0 – 20.51)	133	**0.002**#
Fatigue subscale (0 - 100%)	11.11 (0 – 77.78)	0 (0 – 55.56)	190	**0.051**#
Global health status subscale (0 - 100%)	75 (41.67 – 100)	83.33 (58.33 – 100)	180.5	**0.044**#

*EORTCQLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, %: percentage, CI: confidence interval and U: U value.
**Descriptive analyses were presented using median (min – max) for nonnormally distributed variables.
***Mann–Whitney U test #p < 0.05.

weakness [24]. Our study has a superiority in terms of having a control group and detailed predictive values which may be used to predict the risk for postoperative pulmonary complications such as prolonged mechanical ventilation etc. in patients undergoing thoracic surgery due to lung cancer. However, there are both scarce and conflicting results regarding respiratory muscle strength in the literature. Therefore, further investigations are needed.

Loss of skeletal muscle mass and strength is related with the risk of perioperative complications and worse long-term survival rates in patients with lung cancer undergoing lung surgery [25]. Quadriceps femoris muscle strength was preserved in our patients, 30.8% to whom induction therapy were given and disease durations were approximately 7 months. However, 11 (42.3%) patients had weakness in quadriceps femoris muscle in current study. In contradiction to our results, Granger et al. [2] demonstrated that patients newly diagnosed with nonsmall cell lung cancer have impaired quadriceps femoris muscle strength (18.8 versus 23.7 kg) than healthy individuals [2]. The results of Granger et al. [2] presented much decreased results in muscle strength than the present study. The difference reasons may be derived from some characteristics of this study [2] that are the inclusion of patients with only nonsmall cell cancer and older age of the patients (68.5 years) compared to ours. Similar to study of Granger et al. [2], Hummler et al. [18] demonstrated common weakness in upper and lower extremity muscles of patients with advanced stage lung cancer who had no surgery history compared to healthy reference data. Naito et al. [26] also found skeletal muscle depletion (evaluated using lumbar skeletal muscle index and hand grip strength) and physical functional decline in the early phase of chemotherapy in elderly patients with lung cancer. The loss of muscle mass is associated with an increase in protein catabolism. Increased expression of components in the ubiquitin-proteasome proteolytic pathway and decreased protein production cause a decline in muscle and muscle fiber cross-sectional area which is resulted in loss of muscle extensibility and strength [27]. If we also consider the tendency to weaken of muscle strength seen in our patients, both respiratory and peripheral muscles strength, which predict perioperative complications, should be evaluated and strengthened in patients with lung cancer.

Our study results demonstrated that total and active energy expenditures, physical activity duration, average metabolic equivalent and number of steps were substantially decreased in the patients. Moreover, 66.7% of our patients adopted sedentary lifestyle. Consistent with our results, Granger et al. [2] showed that only 40% of patients with newly diagnosed lung cancer meet physical activity guidelines at the diagnosis stage, and the patients are less physically active than healthy individuals [2]. Moreover, Edbrooke et al. [28] demonstrated that number of steps per day is considerably decreased in inoperable patients with newly diagnosed lung cancer [28]. As seen, patients with lung cancer mostly adopt both sedentary lifestyle and walk less in a day from the diagnosis stage. This may cause many deteriorations regarding muscle weakness and exercise intolerance; increase in symptoms such as fatigue and dyspnea and impairment in QOL [24]. Therefore, these patients should be directed to physical activity counseling as soon as possible since all dimensions including energy expenditure and number of steps, type and duration of physical activity are affected in these patients, which has been shown in our comprehensive study.

Based on present study results, both exertional dyspnea and dyspnea in daily living activities (38.5%)

were evident in the patients compared with healthy individuals. The study without a healthy group of Brocki et al. [19] (19% of patients had no malignancy and 81% were diagnosed as lung cancer) consistently showed that mean of dyspnea evaluated using Borg scale was two units in the patients. There is a scarcity regarding investigating the dyspnea in patients with lung cancer in the literature, therefore current study presents valuable contribution to the literature. Because these results show that patients with lung cancer suffer from both exertional dyspnea and dyspnea in daily living activities, which is possible to be improved via inspiratory muscle training, frequently used in rehabilitation clinics, while awaiting surgery.

Both all aspects of QOL were impaired and the symptoms related with lung cancer were increased in patients with lung cancer awaiting lung surgery in current study. In consistent with our results, Hummler et al. [18] demonstrated that poorer QOL exists in patients with advanced stage lung cancer who had no surgery history compared to healthy reference data. Granger et al. [2] also demonstrated that at the diagnosis stage, the patients with lung cancer have worse mood and QOL compared to healthy individuals. After six months, these patients experience worsening symptoms following chemotherapy, radiotherapy and/or surgery [2]. As a result, patients with lung cancer are exposed to a long-lasting QOL impairment after surgery and/or chemotherapy, radiotherapy which should be followed up in these patients.

5. Conclusion

Given that our results firstly showed both sharp reduction in dynamic lung volumes, exercise capacity, respiratory muscle strength, physical activity level, and QOL and increase in dyspnea perception, and the symptoms in preoperative patients with lung cancer, it is of importance to evaluate these patients before surgery. Of importance patients' well-being, patients in the preoperative phase should be involved in rehabilitation programs including aerobic exercise, respiratory muscle training, and physical activity counseling. After surgery, patients should also be followed to observe changes in these outcomes in terms of applying appropriate rehabilitation approaches during whole process.

6. Limitations

The gold standard method for the evaluation of exercise capacity and dyspnea perception is cardiopulmonary exercise testing, but it could not be performed due to technical problems, which should better be used in further studies. Hand-held dynamometer use, to evaluate isometric quadriceps femoris muscle strength, is commonly based on practitioner's muscle strength. Therefore, if possible, using isokinetic system, which is a gold standard technique for isokinetic muscle strength evaluation, should be considered in future studies.

Acknowledgement/disclaimers/conflict of interest

There are no funding and conflicts of interests for any of the authors for this study.

Informed consent

The Local Ethics Committee of Gazi University approved this study (2019 - 250). Informed consents were taken from each participant.

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