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Evaluation of airway responsiveness and pulmonary function test results among obese and non-obese patients with obstructive sleep apnea syndrome

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Abstract. – OBJECTIVE: In this research, we aimed to elucidate the effect of obstructive sleep apnea syndrome (OSAS) and obesity on pulmonary volumes and bronchial hyperreactivity, and particularly the effect of supine position on pulmonary volume and functions.

PATIENTS AND METHODS: This was a prospective, cross-sectional study with a total of 96 patients (age range, 20-65 years). Based on the body mass index (BMI) and Apnea-Hypopnea Index (AHI) scores, the patients were divided into four groups: Group 1: AHI≥15/h, BMI≥30 kg/m² (n=24), Group 2: AHI≥15/h, BMI<30 kg/m² (n=24), Group 3: AHI<15/h, BMI≥30 kg/m² (n=24), and Group 4: AHI<15/h, BMI<30 kg/m² (n=24). All patients first had static and dynamic pulmonary function tests and carbon monoxide diffusion tests (TLco and Kco) in the sitting and supine positions. A bronchial provocation test with methacholine was applied to all patients in the sitting position one day later. Analysis of variance (ANOVA) and multivariate linear regression was used in the statistical analysis.

RESULTS: Airway responsiveness was observed in 4 of the patients included in the study, and there was no statistically significant difference between the groups. A statistically significant decrease was observed in forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), total lung capacity (TLC) and functional residual capacity (FRC), especially in Group 1 in sitting position compared to Group 4 (p=0.001, p=0.001, p=0.025, p=0.043, and p=0.001, respectively). Changes in pulmonary functions in the transition from sitting to a supine position did not show any significant difference in the study groups (p<0.05). We observed no difference in the diffusion capacity in the sitting and supine positions among the groups (p<0.05).

CONCLUSIONS: The severity of AHI and BMI particularly affect the lower airway, but changes in the position did not show any significant difference in the study groups.

Key Words:
Obesity, Obstructive sleep apnea syndrome, Pulmonary function test, Airway responsiveness, Bronchial hyperreactivity.

Introduction

Obesity is a serious health issue, not only in Turkey but also over the globe, with a gradually increasing prevalence[1]. In obesity, chest wall compliance is reduced due to increased adipose tissue on the abdominal and chest wall, and the diaphragm movements are restricted due to increased intraabdominal visceral adipose tissue, leading to reduced expiratory residual volume (ERV) and functional residual capacity (FRC), total lung capacity (TLC), and reduced residual volume (RV). This presents with restrictive-type pulmonary dysfunction in the pulmonary function tests (PFTs)[2]. It has been reported[3] that obstruction can occur in the bronchi due to the effects of peribronchial adipose tissues and systemic inflammation develops with the mediators released from the visceral adipose tissues, which leads to airway responsiveness (bronchial hyperreactivity). Several studies[4] have shown that obese patients with advanced age are often treated with the misdiagnosis of asthma based on the presence of bronchial hyperreactivity.

Obstructive sleep apnea syndrome (OSAS) is a condition characterized by a recurrent complete or partial obstruction of the upper airway, which is accompanied by desaturation episodes and recurrent arousals during sleep[5]. Experiencing snoring, wa-

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king up as choked, witnessing apnea, and daytime fatigue and sleepiness lead to the fact that OSAS patients might be inadvertently diagnosed with asthma due to the nocturnal dyspnea and the feeling of choking[6]. The prevalence of OSAS in the overall population has been reported[7,8] to be 2 to 4%, and more than half (58.5%) of these patients also suffer from obesity. Obesity narrows the upper airway with increased adipose tissue around the neck and pharynx and reduces vital capacity, specifically due to central obesity. Additionally, it also reduces the downward dilating force over the pharynx, resulting in increased pharyngeal ability to close[9,10]. The effect of obesity on the lower airway and lung volumes in OSAS patients has been investigated[11]. These studies[6,12,13] also report controversial findings on increased or decreased bronchial hyperreactivity with continuous positive airway pressure (CPAP) therapy. It is known[14] that obesity has an obstructive effect on the upper airway in obstructive sleep apnea. Previous studies[15-17] evaluated OSAS together with chronic obstructive pulmonary disease (COPD) and showed obstructive airway disease. It has been reported[18] that obese OSAS patients have reduced ERV and forced expiratory volume (FEV) as well as reduced lung compliance and increased airway resistance. Several studies[19] reported small-airway diseases.

A study[20] investigating the effect of a supine position on pulmonary functions reported a slight difference in the FRC values of obese individuals between the sitting and supine positions, compared to non-obese individuals. Another study[21] also reported that FRC increased to a certain degree when OSAS patients turned to the lateral position from the supine position. The study also reported no significant difference in pulmonary function parameters between the sitting and supine positions.

The literature contains a limited number of studies examining the effect of the coexistence of obesity and OSAS on lung volumes and lower airways[11]. Therefore, in this study, we aimed to elucidate the effect of OSAS and obesity on pulmonary volumes and bronchial hyperreactivity, particularly the effect of a supine position on pulmonary volume and functions.

Patients and Methods

Study Population and Planning

This was a prospective, cross-sectional study with a total of 96 patients (32 females, 64 males; mean age: 46.65±10.33 years; range, 20 to 65 years) who applied to the chest diseases clinic with at least 2 of 3 major symptoms of obstructive sleep apnea syndrome such as snoring, apnea with a witness, daytime sleepiness.

Each patient had a complete overnight diagnostic polysomnography (PSG) in the lab. The electrodes for electroencephalography (EEG) were placed using the international 10-20 technique. PSG includes measurements of electrocardiographic rhythm and blood oxygen saturation in addition to electroencephalography, electrooculography, electromyography, airflow, and respiratory muscle effort with the purpose of monitoring sleep. Apneas and hypopneas were detected using the nasal-cannula pressure transducer system, oronasal temperature thermistor, and thoracoabdominal plethysmograph. A transcutaneous finger pulse oximeter was employed to gauge oxygen saturation. The standard method was used to record and score the night's sleep. Split-night studies were not performed[5].

All overnight polysomnographic examinations of patients were conducted using the 55-channel Alice-5 (version 2013, Phillips Respironics, USA) polysomnography device, using diagnostic criteria from the American Academy of Sleep Medicine (AASM) 2007 criteria[5]. OSAS classification and grading were made based on the AASM's International Classification of Sleep Disorders (ICSD-2).

Sleep stages were scored according to the standard criteria of Rechtschaffen and Kales[5]. Apneas are defined as complete cessation of airflow lasting >10 seconds, and hypopneas are defined as a reduction in oronasal airflow >50% lasting >10 seconds. The apnea-hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of sleep.

The height, weight, body mass index (BMI), neck circumference (NC), polysomnographic findings (apnea-hypopnea index – AHI), minimum saturation value (apneic period), and the Epworth Sleepiness Scale (ESS) scores were recorded.

Based on the BMI and AHI scores, the patients were divided into four groups. Group 1: obese patients with moderate to severe OSAS (AHI≥15/h, BMI≥30 kg/m^2; n=24), Group 2 non-obese patients with moderate to severe OSAS (AHI≥15/h, BMI<30 kg/m^2; n=24), Group 3: obese patients with normal or mild OSAS (AHI<15/h, BMI≥30 kg/m^2; n=24), and Group 4: non-obese patients with normal or mild OSAS (AHI<15/h, BMI<30 kg/m^2; n=24).

Lung Volumes and Pulmonary Function Assessments

The PFTs and diffusion test were applied to all patients in the sitting and supine position, while the bronchial provocation test was applied to eligible patients in the sitting position one day later. All patients first had static and dynamic PFTs (Geratherm, Diffustik Model Spirometry and Co Diffusion Test System, Germany, 2014) in the sitting and supine positions. Each test was repeated three times, and the highest PFT measurement was considered the test measurement. Then, using the single breath testing method, carbon monoxide (CO) diffusion test and pulmonary volume measurement (Geratherm, Diffustik Model Spirometry and Co Diffusion Test System, Germany, 2014) were performed. Before the test, hemoglobin measurement was done, and the diffusing capacity of the lung for carbon monoxide (TLco) and carbon monoxide transfer coefficient (Kco) values were calculated. The test was also repeated in the sitting and supine positions. In the sitting position, the patient was instructed to sit at a straight angle on a chair, while the supine position referred to lying on the stretcher with **a 30°** elevated head and chest. Finally, a bronchial provocation test with methacholine was administered to the study population without severe airway obstruction one day after the PFT and TLco tests. Between the groups, the pulmonary function parameters forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC, Peak expiratory flow (PEF), Peak inspiratory flow (PIF), mid-expiratory flow (MEF_{75}), MEF_{50}, and MEF_{25} were measured using dynamic PFT, and total lung capacity (TLC), RV, FRC, TLco, and Kco were measured using the CO diffusion test. Bronchial hyperreactivity was measured using a five-breath dosimetry protocol with automatic dosimetry by taking the baseline PFT values and then in eight measurements by starting from methacholine (acetylmethacholine chloride 98% dry powder) 0.0625 mg/mL and increasing the dose by two-fold, until it reached a maximum dose of 16 mg/mL. The provocative concentration causing a 20% fall in FEV_1 was considered as the PC_{20} value.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all participants. The study has been approved by Izmir Katip Celebi University Faculty of Medicine Clinical Research Ethics Committee with protocol number 31102013;156.

Statistical Analysis

Statistical analysis was performed using the SPSS version 22 (Released 2013. SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA). The descriptive data were expressed in mean and standard deviation. The categorical data were presented in percentages. Between-group comparisons for continuous variables were made using two-way Analysis of variance (ANOVA) followed by post-hoc analyses. Tukey and Games-Howell tests were used based on the variances' equivalence. The Chi-square test was used to compare categorical (discrete/uncountable) variables between groups. Age and gender-adjusted multivariate linear regression were used to assess the relationship between AHI, BMI, smoking, and pulmonary function parameters. A p-value<0.05 was considered as the statistically significant.

Results

A total of 96 patients (32 females, 64 males; mean age: 46.65±10.33 years; range, 20 to 65 years) participated in the study. The mean age and sex distribution among the groups were significantly different. Group 2 included a significantly lower number of female patients ($p<0.05$), and Group 3 involved a significantly higher number of female patients ($p<0.05$) compared to other groups. Descriptive data and the number of patients are shown in Table I.

The bronchial provocation test revealed bronchial hyperreactivity in four patients. There was bronchial hyperreactivity in two patients (one patient with 1 μg provocation dose; the other with 4 μg provocation dose) in Group 1, whereas the provocation dose was 1 μg in one patient in Group 2 and 8 μg in one patient in Group 3. Bronchial hyperreactivity was not identified in Group 4 (Table I). There was no significant difference in the Chi-square test results among the groups ($p=0.555$).

The results of the standard PFT in the sitting position are presented in Table II. Peak expiratory flow (PEF) was significantly lower in Group 1 compared to Groups 2 and 4 in the upper airway assessment (Table II). In the present study, mean PIF values did not significantly differ between groups. Mean PEF values were significantly lower in Group 1 compared to Groups 2 and 4. The FVC

Table I. Demographic characteristics of patients.

	Group 1 (n=24) AHI ≥15/h, BMI ≥30 kg/m²	Group 2 (n=24) AHI ≥15/h, BMI <30 kg/m²	Group 3 (n=24) AHI <15/h, BMI ≥30 kg/m²	Group 4 (n=24) AHI <15/h, BMI <30 kg/m²	*p*-value
Age (years)	49.38±9.22	51.83±8.03[a]	42.96±10.44	42.42±10.66	**0.001**
Female, n (%)	10 (41.7%)	2 (8.3%)[b]	13 (54.2%)[c]	7 (29.2%)	**0.006**
AHI (/h)	57.08±30.42	41.52±19.42	3.08±2.81	2.67±2.37	**<0.001**
Min SpO_2 (%)	71.54±14.99	79.29±8.47	89.00±3.24	90.29±3.97	**<0.001**
BMI (kg/m²)	39.26±5.80	28.20±2.28	33.55±3.70	26.37±2.26	**<0.001**
Neck circumference (cm)	43.58±4.12	40.38±4.03	39.55±3.03	38.14±3.19	**<0.001**
Waist circumference (cm)	115.88±10.49	103.38±8.33	105.73±9.16	95.00±9.73	**<0.001**
Hip circumference (cm)	121.13±11.20	105.95±5.78	116.05±5.12	105.45±5.15	**<0.001**
Epworth sleepiness score	8.96±5.88	8.63±5.82	5.83±5.06	5.71±4.78	0.063
Smoking >10, n	11	12	6	7	0.202
Bronchial hyperactivity, n	2	1	1	0	0.555

Data are expressed in mean±SD. A $p<0.05$ was considered significant (bold). Two-way analysis of variance with post-hoc tests was used. AHI: apnea-hypopnea index, BMI: Body Mass Index. [a]Mean values of Group 2 were significantly older than Group 3 and 4. [b]Mean values of Group 2 were significantly lower than Groups 1, 3, 4. [c]Mean values of Group 3 were significantly higher than Groups 1, 2, and 4.

and FEV_1 values and % of predicted values were found to be significantly lower in Group 1 compared to the other groups (Table II).

Total lung capacity as measured in the sitting position was lower in Group 1, compared to Group 4 (p=0.028). There was a significant difference in the FRC values between Group 1 and Group 4 (p=0.04). Similarly, there was a significant difference in the FRC values between Group 3 and Group 4 (p=0.03) (Table II). Based on the lung volume measured in the supine position, TLC, RV, and FRC were found to be significantly lower in Group 1 compared to the other groups (Table III).

According to the potential changes in lung volume and capacity, while shifting from a sitting position to a supine position, no statistically significant difference was observed among the groups (difference in mL, %, % difference of predicted values or rate of change) (Table IV). In addition, when the patients were examined based on obesity alone, the FRC change was 272±721 mL in obese patients (BMI≥30 kg/m²) compared to 574±865 mL in non-obese patients. As a result, obesity was considered to affect FRC, although the difference was not statistically significant (p=0.064).

The correlation analysis showed that TLC was associated with AHI and smoking, whereas no correlation was found between TLC and BMI. The regression analysis, however, revealed the duration of smoking and AHI as the significant factors for TLC. In addition, FRC was found to be correlated with AHI and BMI, while smoking was not correlated. The regression analysis revealed that the only significant factor for FRC was BMI. Based on the age- and sex-adjusted values, the correlation analysis revealed a moderate correlation between AHI and FVCPred %, FEV_1Pred %, TLCPred %, RVPred %, FRCPred %, and KcoPred %. Similarly, a correlation was found between the aforementioned pulmonary function parameters and BMI (Table V).

Discussion

Published studies[14,22-24] investigating the effects of OSAS on pulmonary function parameters have been conducted primarily with inspiratory and expiratory loop assessments in flow-volume curves, which is an indicator of upper airway obstruction. Katz et al[14] showed that a flattened or indented inspiratory loop in the flow-volume curve and a more than two-fold increase in the PEF-PIF ratio might be diagnostic for OSAS[14]. On the other hand, Hoffstein et al[25] found no difference in these assessments among the groups with and without OSAS. In our case, PIF values were

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similar across groups, but PEF values were significantly higher in Groups 2 and 4 compared to Group 1. The AHI score was higher in patients with restricted inspiratory flow (p=0.022). On the other hand, restricted inspiratory flow may not be associated with BMI, which is an indicator of obesity (p=0.350).

The PFTs have also been performed in patients with an overlap syndrome in whom OSAS is accompanied by COPD and asthma, which involve the lower airway[16,17,26,27]. A high rate of airway disease of the obstructive pattern was observed in OSAS patients[16,17,28]. However, the present study did not identify obstructive airway disease (FEV_1/FVC <70%), as those with a known airway disease were excluded from the study. Additionally, no statistical difference was found in the FEV_1/FVC values among the groups (p=0.852).

Hao et al[24] found a significant statistical difference in diffusion function parameters and the number of pulmonary ventilation among the non-OSAHS group, the mild-to-moderate OSA group, and the severe OSA group. However, only airway resistance parameters increased with the severity of OSA, and they were also positively correlated with the apnea-hypopnea index. The

Table II. Pulmonary function and diffusion test results in sitting position.

Sitting Position	Group 1 (n=24) AHI ≥15/h, BMI ≥30 kg/m²	Group 2 (n=24) AHI ≥15/h, BMI <30 kg/m²	Group 3 (n=24) AHI <15/h, BMI ≥30 kg/m²	Group 4 (n=24) AHI <15/h, BMI <30 kg/m²	*p*-value
FVC (mL)	3,229±935[a]	3,962±940	3,720±1,336	4,469±1,249	**0.001**
% Pred FVC	89±15[a]	97±13	97±12	105±15	**0.005**
FEV_1 (mL)	2,748±790[a]	3,399±804	3,129±1,141	3,822±1,102	**0.001**
% Pred FEV_1	93±17[a]	103±13	101±12	108±16	**0.006**
FEV_1/FVC %	86±8	86±6	87±5	86±6	0.852
MEF_{75} (L/s)	5.526±1.829[a]	6.905±1.854	6.458±2.164	6.985±2.266	**0.057**
% Pred MEF_{75}	83±24	94±19	94±19	95±20	0.154
MEF_{50} (L/s)	4.103±1.617	4.770±1.634	4.559±1.686	5.067±1.837	0.263
% Pred MEF_{50}	95±33	105±30	101±26	105±27	0.641
MEF_{25} (L/s)	1.576±0.658	1.810±0.775	1.727±0.834	2.157±0.815	0.087
% Pred MEF_{25}	93±36	99±39	95±31	105±28	0.709
PEF (L/s)	5.797±1.856[a,c]	7.485±2.014	6.932±2.372	7.499±2.361	**0.025**
% Pred PEF	77±22	90±19	89±19	88±17	0.087
PIF (L/s)	4.471±1.188	4.939±1.748	5.246±1.322	5.101±2.219	0.416
TLco (Hb) (mmol/kPa/min)	7.427±1,981	8.284±1.822	8.412±1.999	8.981±2.586	0.092
% Pred TLco (Hb)	84±22	87±16	90±13	89±19	0.681
Kco (Hb) (mmol/kPa/min/L)	1.624±0.339	1.600±0.469	1.620±0.237	1.557±0.257	0.893
%Pred Kco (Hb)	104±19	109±36	99±14	99±17	0.366
TLC (mL)	4,845±1,065[a]	5,580±1,229	5,488±1,133	5,905±1,669	**0.043**
% Pred TLC	85±12	87±16	94±12	93±19	0.107
RV(mL)	1,708±494	1,873±338	1,730±371	1,838±468	0.458
% Pred RV	90±22	89±12	98±20	97±19	0.213
FRC (mL)	2,261±821[a]	2,710±814	2,231±680[b]	3,104±1,016	**0.001**
% Pred FRC	76±22[a]	82±22	75±20[b]	96±25	**0.004**

Data are expressed in mean±SD. A p<0.05 was considered significant (bold). Two-way analysis of variance with post-hoc tests was used. AHI: apnea-hypopnea index BMI: Body Mass Index, FVC: forced vital capacity, FEV1: forced expiratory volume in 1st second, MEF: maximal expiratory flow, FRC: functional residual capacity, TLco: mean transfer factor of carbon dioxide, Kco%: carbon monoxide transfer coefficient, PEF: peak expiratory flow, PIF: peak inspiratory flow, RV: expiratory residual volume, TLC: total lung capacity, VC: vital capacity. [a]Mean values of Group 1 were significantly lower than Group 4. [b]Mean values of Group 3 were significantly lower than Group 4. [c]Mean values of Group 1 were significantly lower than Group 2.

Table III. Pulmonary function and diffusion test results in the supine position.

Supine Position	Group 1 (n=24) AHI ≥15/h, BMI ≥30 kg/m²	Group 2 (n=24) AHI ≥15/h, BMI <30 kg/m²	Group 3 (n=24) AHI <15/h, BMI ≥30 kg/m²	Group 4 (n=24) AHI <15/h, BMI <30 kg/m²	*p*
FVC (mL)	3,167±959[a]	3,660±1,076	3,458±1,262	4,329±1,232	**0.002**
% Pred FVC	88±13[a]	92±15	94±12	102±14	**0.009**
FEV_1 (mL)	2,657±818[a]	3,157±785	3,093±867[b]	3,673±1,141	**0.004**
% Pred FEV_1	89±15[a]	96±14	97±12	103±14	**0.027**
FEV_1/FVC %	85±8	84±7	87±7	85±7	0.722
MEF_{75} (L/s)	5.269±1.922	6.359±1.973	5.511±1.736	6.671±2.555	0.078
% Pred MEF_{75}	79±24	87±22	81±17	90±23	0.255
MEF_{50} (L/s)	3.833±1.593	4.310±1.499	4.384±1.504	4.737±1.807	0.317
% Pred MEF_{50}	89±33	95±26	96±25	99±27	0.718
MEF_{25} (L/s)	1.432±0.652	1.640±0.750	1.789±0.626	1.947±0.860	0.117
% Pred MEF_{25}	84±35	91±34	92±28	95±29	0.711
PEF (L/s)	5.596±2.062	6.661±2.254	5.931±2.055	7.152±2.690	0.108
% Pred PEF	73±20	80±23	76±17	84±20	0.297
TLco (Hb) (mmol/kPa/min)	7.551±1.845	8.210±2.695	8.068±2.860	9.388±2.479	0.070
% Pred TLco (Hb)	85±16	85±23	89±17	88±18	0.289
Kco (Hb) (mmol/kPa/min/L)	1.756±0.311	1.521±0.377	1.726±0.334	1.685±0.297	0.075
% Pred Kco (Hb)	112±18	102±24	106±19	106±17	0.563
TLC (mL)	4,617±1,170[a,c]	5,572±1,012	5,050±938	5,797±1,452	**0.003**
% Pred TLC	80±12[a]	86±10	88±10	91±15	**0.024**
RV (mL)	1,563±459[a]	1,793±568	1,541±328	1,849±378	**0.032**
% Pred RV	80±16[a]	84±19[d]	86±16	98±13	**0.002**
FRC (mL)	1,900±633[a]	2,349±743	2,028±847	2,668±1,249	**0.019**
% Pred FRC	62±16	70±18	67±23	75±16	0.085

Data are expressed in mean±SD. A $p<0.05$ was considered significant (bold). Two-way analysis of variance with post-hoc tests was used. AHI: apnea-hypopnea index BMI: Body Mass Index, FVC: forced vital capacity, FEV_1: forced expiratory volume in 1st second, MEF: maximal expiratory flow, FRC: functional residual capacity, TLco: mean transfer factor of carbon dioxide, Kco%: carbon monoxide transfer coefficient, PEF: peak expiratory flow, PIF: peak inspiratory flow, RV: expiratory residual volume, TLC: total lung capacity, VC: vital capacity Data are expressed in mean±SD. A $p<0.05$ was considered significant (bold). [a]Mean values of Group 1 were significantly lower than Group 4. [b]Mean values of Group 3 were significantly lower than Group 4. [c]Mean values of Group 1 were significantly lower than Group 2. [d]Mean values of Group 2 were significantly lower than Group 4.

study by Zerah-Lancner et al[19] included patient groups with similar BMI values to eliminate the possible effect of obesity. The authors investigated PFT parameters based on the AHI changes (based on the OSAS severity) but did not achieve any significant difference between the groups despite reduced vital capacity (VC), TLC, FRC, and ERV in all groups. However, a significant reduction related to OSAS severity was observed in forced expiratory flow rates (FEF_{25}, FEF_{50}, and FEF_{25-75}) between the groups, and airway resistance was shown to increase in parallel to the severity among OSAS patients. The authors also reported small airway disease in OSAS patients. In another study, Abdeyrim et al[18] did not observe any significant difference in the MEF_{75}, MEF_{50}, and MEF_{25} between the groups with and without OSAS. Similarly, we did not find any significant difference in the MEF_{75}, MEF_{50}, and MEF_{25} among the groups. However, we found significantly reduced FVC and FEV_1 in Group 1.

Furthermore, the present study established that changes in the FVC and FEV_1 values were negatively correlated with AHI, BMI, and smoking duration. In the multivariate regression analysis, the duration of smoking was correlated with BMI, while smoking and AHI scores were correlated with FEV_1 values.

In the literature, there is a limited number of studies[24,27-31] performing single-breath CO diffusion tests to examine lung volumes and diffusion tests in patients with OSAS. Publications[27] reported increased TLco in the diffusion test[29], while some authors reported no significant difference. Similarly, we observed no difference in the TLco and Kco values in the diffusion tests performed in the sitting and supine positions among the groups.

In general, body plethysmography was recommended to assess lung volumes[30,31]. Since the measurements were made both in the sitting and supine positions in our study, the lung volumes were unable to be evaluated using body plethysmography. Instead, a CO diffusion test was utilized. The TLC was lower in Group 1, compared to Group 4 (p=0.028), while there was a significant difference in the FRC values between Group 1 and Group 4 (p=0.04). Besides, a significant difference in the FRC values was observed between Group 4 and Group 2 (p=0.03). Of note, reduced FRC values in the OSAS group were consistent with previous findings[18,20]. In the correlation analysis, TLC was found to be correlated with AHI and smoking, whereas no correlation was found between TLC and BMI. On the other hand, the regression analysis revealed that smoking duration and AHI scores were significant factors. The FRC was also found to be correlated with AHI and BMI, while smoking was found to be non-significant. In the regression analysis, BMI was found to be the only significant factor for FRC.

The primary aim of the present study was to investigate whether there was a difference in values measured in the sitting position and supine position among the groups. To the best of our knowledge, there is a very limited number of studies[20,27,30,32] conducted with PFTs in the supine position. The study by Kunos et al[32] FEV_1 increased from evening to morning in patients with untreated OSA and the magnitude of this change was directly related to the severity of OSA. The study by Watson and Pride[20] elaborated on the effects of obesity on lung volumes and airway resistance. The authors

Table IV. Pulmonary function test result changes from a sitting position to a supine position.

Sitting position to supine position (Difference in mL, %)	Group 1 (n=24) AHI ≥15/h, BMI ≥30 kg/m²	Group 2 (n=24) AHI ≥15/h, BMI <30 kg/m²	Group 3 (n=24) AHI <15/h, BMI ≥30 kg/m²	Group 4 (n=24) AHI <15/h, BMI <30 kg/m²	*p*-value
FVC (mL)	1,319±862	1,613±1,027	1,650±1,078	1,608±1,035	0.384
% Pred FVC	4±5	5±10	3±8	3±7	0.292
FEV_1 (mL)	57±152[c]	242±146	162±268	150±239	**0.035**
% Pred FEV_1	4±8	10±8	8±10	6±10	0.146
FEV_1/FVC %	0.8±2.6	2.16±3.84	0.17±4.43	0.66±4.73	0.366
TLco (Hb) (mmol/kPa/min)	-0.139±1.469	0.072±1.540	0.304±1.911	-0.305±1.911	0.553
% Pred TLco (Hb)	-0.87±0.18	1.12±1.534	0.69±1.228	-3.20±1.051	0.722
Kco (Hb) (mmol/kPa/min/L)	-0.127±0.210	0.078±0.527	-0.120±0.196	-0.127±0.215	0.071
% Pred Kco (Hb)	-8±14	6±38	-7±12	-7±13	0.074
TLC (mL)	217±530	8±1076	449±629	172±798	0.283
% Pred TLC	4.41±9.36	0.41±14.6	5.87±6.11	3.29±11.79	0.364
RV (mL)	139±399	121±276	195±313	22±340	0.349
% Pred RV	9.79±17.18	4.45±17.91	12.12±19.40	0.58±22.06	0.160
FRC (mL)	354±572	361±1018	210±858	761±624	0.107
% Pred FRC	13.37±19.18	11.12±28.88	7.66±26.81	21.39±19.84	0.258

Data are expressed in mean±SD. A $p<0.05$ was considered significant (bold). Two-way analysis of variance with post-hoc tests was used. AHI: apnea-hypopnea index BMI: Body Mass Index, FVC: forced vital capacity, FEV_1: forced expiratory volume in 1st second, MEF: maximal expiratory flow, FRC: functional residual capacity, TLco: mean transfer factor of carbon dioxide, Kco%: carbon monoxide transfer coefficient, PEF: peak expiratory flow, PIF: peak inspiratory flow, RV: expiratory residual volume, TLC: total lung capacity, VC: vital capacity [c] Mean values of Group 1 were significantly lower than Group 2.

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Table V. Correlation analysis of AHI, BMI, and smoking during pulmonary function and diffusion tests in a sitting position.

Sitting position	AHI		BMI		Smoking	
	p	β	*p*	β	*p*	β
% Pred FVC	**0.001**	**-0.257**	**0.015**	**-0.223**	**0.007**	**-0.256**
% Pred FEV_1	**0.003**	**-0.285**	**0.011**	**-0.236**	**0.010**	**-0.242**
% Pred TLC	**<0.0001**	**-0.367**	0.075	-0.148	**0.038**	**-0.189**
% Pred RV	**0.004**	**-0.268**	0.178	-0.095	0.466	0.009
% Pred PEF	**0.032**	**-0.190**	**0.040**	**-0.180**	**0.023**	**-0.207**
% Pred FRC	**0.006**	**-0.310**	**<0.0001**	**-0.344**	0.383	-0.031
% Pred Kco (Hb)	**0.011**	**+0.233**	0.217	0.081	**0.001**	**-0.334**

Data are expressed as a Beta coefficient. A $p<0.05$ was considered significant (bold). Multivariate linear regression was used in the analysis. AHI: apnea-hypopnea index BMI: Body Mass Index, FVC: forced vital capacity, FEV_1: forced expiratory volume in 1st second, TLC: total lung capacity, RV: expiratory residual volume, PEF: peak expiratory flow, FRC: functional residual capacity, Kco %: carbon monoxide transfer coefficient.

reported reduced FEV_1, TLC, and FRC values and significantly lower FRC values in obese patients in the supine position (the mean reduction was 740 mL in non-obese patients, compared to 70 mL in obese patients). However, the reduction in the TLC, FEV_1, and RV was not found to be significantly different between the groups. In another study, Joosten et al[21] divided patients with similar BMI values into three groups with/without OSAS, positional OSAS, and rapid eye movement REM-dependent OSAS. In the aforementioned study, the changes in the PFT results and airway resistance were examined among the groups. The authors concluded that the reduction in FRC was lower in the positional OSAS group, compared to the control group, and the FRC slightly increased in the lateral position. In the present study, the reduction in the FRC values was 761±624 mL in Group 4, compared to 210±858 mL in Group 3. Also, the FRC was 272±721 mL in BMI≥30 kg/m² patients, compared to 574±865 mL in BMI<30 kg/m² patients. As a result, obesity was considered to affect the FRC, although the difference did not reach statistical significance (p=0.064). Nevertheless, the presence of OSAS did not affect the FRC changes, and BMI and obesity were the main significant factors for FRC.

Limitations

There are some limitations in our study. Firstly, the study has a cross-sectional design, which might limit the assessment of the causal relationship due to the temporality problem. Second, we can not generalize our findings to the community settings as the sample was selected from a tertiary care hospital, and the baseline risk of the participants could be higher than that of the general population. Lastly, the low sample size might have caused type 2 errors in some comparisons. We implemented post-hoc power analysis for TLco (Hb) (mmol/kPa/min) and FEV_1. The differences in mean FEV_1 values presented an effect size=0.39, and we detected the differences at 90.4% power. On the other hand, differences for TLco (Hb) (mmol/kPa/min) provided a medium effect size (0.26) with a power level of 56%, indicating that some of the insignificant differences might be due to low sample size.

Conclusions

In FVC, FEV_1, and PEF values are affected both by AHI and BMI in standard PFTs in a sitting position and these values may decrease as the severity of OSAS and obesity increase. In addition, our study results confirm that smoking affects the PFT results. Briefly, AHI, as an OSAS indicator, and BMI, as an obesity indicator, particularly affect the lower airway and FRC in the pulmonary function test.

Conflict of Interest

The authors declare that they have no conflict of interest.

Data Availability

All data generated or analyzed during this study are included in this published article; the datasets are available from the corresponding author upon reasonable request.

Ethics Approval

Ethical approval for this study was obtained from the Izmir Katip Celebi University Faculty of Medicine Clinical Research Ethics Committee (identification code: number 311013;156, Izmir, Turkey). All procedures conducted in this study adhered to the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent

Written informed consent was obtained from all participants prior to their inclusion in the study. Patients were provided with detailed information regarding the study design and objectives.

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Authors' Contributions

Sibel Ayık: Planning, designing, literature survey, statistical analysis, interpretation of the results, writing, submission. Ayse Dalli: Planning, designing, data collection, literature survey. Melih Kaan Sözmen: Planning, designing, statistical analysis, interpretation of the results, writing, submission. Galip Akhan: Planning, designing, literature survey.

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