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Original Article

Evaluation of Carbonmonoxide, Diffusion Capacity, Respiratory Muscle Strength Values, and Pulmonary Volume in Smoking Men over 40 Years Old

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Abstract

OBJECTIVE: To determine the effects of tobacco use on the lungs before respiratory symptoms or basic functional disorders occur.

MATERIAL AND METHODS: Forty-six active smokers between June 2018 and June 2019 who did not have any respiratory complaints, had no lung or chronic disease affecting the respiratory system, and consumed at least 20 packs/year were prospectively evaluated. In addition, a control group consisting of 50 non-smokers was formed. After confirming that spirometry and chest radiographs were normal, volunteers were taken to measure carboxymetry, plethysmography, respiratory muscle strength, and diffusion capacity, respectively. The changes in the lungs caused by smoking were analyzed with the data obtained from the measurements.

RESULTS: Carbon monoxide values measured by carboxymetry were higher in smokers than non-smokers. Plethysmography tests showed that TLC, TLC%, FRC, FRC%, and RV values were statistically higher in smokers. No significant difference was found between FVC%, FEV1%, PEF, PEF%, MEF75, MEF75%, MEF50, MEF50%, MEF25, MEF25%, sRaw (eff), sRaw (eff%), Raw (eff), Raw (eff%), Raw (tot), Raw (tot%), IC, IC%, ERV, ERV%, RV% values and FEV1/FVC, FEV3/FVC, IC/TLC, and RV/TLC ratios. MIP, MIP%, MEP, MEP% values which measured respiratory muscle strength were similar in smokers and non-smokers. DLCO%, DLCO/VA, DLCO/VA%, DLCOc%, DLCOc/VA, and DLCOc/VA% were found to be lower in the smoker subjects. DLCO and DLCOc values were similar in both groups.

CONCLUSION: Smoking causes the accumulation of toxic gas in the lungs, contributes to the development of hyperinflation and disrupts gas exchange. In our study, there was no evidence that airway resistance developed or respiratory muscles were affected.

KEYWORDS: Carboxymetry, plethysmography, respiratory muscle strength, diffusion capacity, smoking
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INTRODUCTION

Despite itswell-known negative effects on human health and all restrictions on its consumption, smoking remains the leading "legal poison" in the modern world. Over a billion people worldwide consume cigarettes. Although 84% of smokers are males, the proportion of women in developed countries is higher than in developing and underdeveloped countries. Although the prevalence of smoking in developed countries tends to decrease, it is still increasing in other places and thus continues to feed the smoking industry. Moreover, the fact that most underdeveloped countries do not even have a non-smoking policy raises concerns.[1]

Although the damages of smoking to human health are scientifically indisputable, the necessity of informing and constantly stimulating society is just as important. Cigarettes contain 70 carcinogenic substances and more than 7000 chemical compounds, and smoking causes more than 6 million lives each year. Passive smoking alone is estimated to cost 884 000 lives in 2016. Ischemic heart diseases, cerebrovascular diseases, chronic obstructive pulmonary disease (COPD), respiratory infections, cancers, and tuberculosis are the main causes of mortality. Many morbidities are also related to smoking. It should be emphasized that smoking is a preventable cause of many mortality and morbidity.[1]

Many people continue to smoke for years, unaware of the harm created by smoking on their bodies. As chest radiographs and pulmonary function tests are normal, they maintain their smoking behavior because they thought of not adversely affected by smoking. In most of the studies in the literature, subjects were either not adequately examined for respiratory symptoms or randomized for abnormalities of spirometry and radiology. We aimed to find the answer to the question "Can we predict the harmful effects of smoking on the lungs in people whose routine examinations seem normal?" We aimed to study people who are 40 years old and older who have normal spirometry values and chest radiographs, who do not have respiratory symptoms such as cough, sputum, shortness of breath, chest pain, hemoptysis, and whether they have a change in lung volume, diffusion capacity, and respiratory muscle strength.

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MATERIAL AND METHODS

The study lasted between June 2018 and June 2019 with the approval of the Clinical Research Ethics Committee dated June 6, 2018 and numbered 2018/240. A total of 96 healthy volunteers, including 46 smokers and 50 controls, were included in the study. Volunteers were selected through hospital staff and relatives of patients. Informed consent forms were read and signed before volunteers participated in the study.

The volunteers were selected from men over 40 years and older. The anamnesis of the volunteers was taken before the study. No symptoms such as shortness of breath, cough, sputum, hemoptysis, chest pain; pulmonary, cardiac, rheumatologic, neurological, hematological, endocrinological, etc., without chronic diseases; body mass index is below 30; has not previously had pneumonia and/or tuberculosis; subjects without asbestos or biomass exposure were included in the study.

Postero-anterior chest radiographs of the volunteers were taken, and spirometric measurements were performed. MasterScreen™ PFT (CareFusion, Hoechberg, Germany) was used for spirometry measurement. For each volunteer, a new mouthpiece was attached to the device, the volunteers were told to sit upright, and their noses were closed with pegs. Deep inspiration was performed after at least 3 resting tidal respirations followed by forced expiratory maneuver. In this way, 3 maneuvers were performed, and the best results were recorded. The results obtained by radiological lung images and spirometry were reviewed and interpreted by 2 chest disease doctors.

Volunteers with anomalies on chest radiographs and/or spirometry (based on the GOLD Spirometry 2010 Guidelines; FEV1/FVC < 70, FEV1 < 80%, FVC < 80%, current-volume loop anomalies) were excluded from the study by performing procedures such as reversibility test, thorax computed tomography, etc., for further investigations.

Volunteers with normal history, radiological images, and spirometric measurements were divided into 2 separate study groups. The groups were composed of 2 arms: smoker and non-smoker. The smoker group consisted of people with active smoking for at least 20 packs/year; those who had previously smoked and quit were not included in the study.

Volunteers should be rested for half an hour before the test, at least 2 hours of fasting, should not consume at least 4 hours of alcohol, avoid thick and constrictive clothing, if necessary provide urine mixes, smoking volunteers should not smoke for at least 24 hours.

Volunteers were measured for carboxymetry, plethysmography, respiratory muscle strength and diffusion capacity, respectively. Respiratory tests were performed with 2 respiratory laboratory technicians in the respiratory test laboratory in our outpatient clinic.

PiCOTM Smokerlyzer® (Bedfont Scientific Ltd, Kent, UK) was used for carboxymetry measurement. The nose latch was inserted and after the mouthpiece was placed in the device, the volunteers were asked to perform a deep inspiration maneuver in the room air and then hold their breath for 15 seconds. Then, the mouthpiece was firmly grasped and a slow expiratory maneuver was performed for 15 seconds. The carbon monoxide (CO) values obtained were recorded in ppm.

Volunteers were then taken to the MasterScreen™ Body Plethysmography (CareFusion, Hoechberg, Germany) booth for plethysmography measurement. After fitting the nose latch and closing the cabin door, the interior temperature was allowed to stabilize for 30 seconds. The mouthpiece was breathing 4-5 times and then the shutter was closed at the end of normal expiration. Deeply expiratory and then deep inspiratory maneuver was performed against closed shutter. The method was applied 3 times and the mean of the data was accepted as test values.

MasterScreen™ Body Plethysmography (CareFusion, Hoechberg, Germany) cabinet was used for Maximal inspiratory pressure (MIP) and Maximal expiratory pressure (MEP) measurements. After the plethysmography measurement, the volunteers were taken to rest and the nose latch was re-inserted and then taken back into the cabin. In order to adapt to the device, breathing at the resting tidal volume was observed first. Deep expiratory and then deep inspiratory maneuvers were performed for MIP measurement against the shutter shut down suddenly. After confirming that the blowing was achieved for at least 1.5 seconds, the most negative value taken for 1 second was accepted. Volunteers were administered the test 5 times with 1 minute interval and the most negative value was accepted as the test value and recorded in kilopascals (kPa). For the MEP measurement, a deeply closed inspiratory maneuver was then performed against the shutter, which was similarly closed. After confirming that the blowing was achieved for at least 1.5 seconds, the most positive value

MAIN POINTS

- Lung diseases caused by smoking can be revealed through spirometric and radiological studies. Especially spirometry is the gold standard method in obstructive pulmonary diseases. Many of the studies have focused on spirometric anomalies caused by smoking. Based on this information, the absence of respiratory complaints and no pathological findings in spirometry or chest X-ray may suggest an opinion that the lungs are not affected.
- In contrast to other studies in the literature, our study was conducted on healthy people, excluding who developed spirometric anomaly and investigated anomalies in advanced respiratory tests. In this way, we aimed to demonstrate the effects of smoking on the lungs objectively.
- The results of our study reveal disorders such as diffusion disorders and hyperinflation in the lungs that cannot be detected in the spirometry and do not present clinical symptoms yet. Due to conflicting information in the literature regarding other findings, there is need another studies with larger patient groups. In addition, prospective studies are needed to determine the relationship between the information obtained and the diseases that may develop in the future.

Table 1. Results Obtained by Carboxymetry

	Smokers		Non-smokers		
	Mean ± SD	**Min–max**	**Mean ± SD**	**Min–max**	***P***
ppm	14.78 ± 7.56	4.00-39.00	1.80 ± 2.08	1.00-12.00	**<.0001**

taken for 1 second was accepted. Volunteers were administered the test 5 times with 1 minute interval and the most positive value was recorded as kPa by accepting the test value.

MasterScreen ™ PFT (CareFusion, Hoechberg, Germany) was used for diffusion capacity measurement. A gas mixture containing CO 0.3%, methane (CH_4) 0.3%, cyanogen (C_2N_2) 0.3% was used. Single breath test was performed. The subjects were deeply inspired by maneuvering the gas mixture by resting tidal maneuvers and providing gas distribution for less than 4 seconds. They were told to hold their breath for 8-12 seconds. Immediately afterwards, a deep expiratory maneuver was performed in less than 3 seconds and measurements were taken by the device. The test was performed a second time after 4 minutes and the best values were recorded as the test value.

During the study, the application, maintenance and calibrations of pulmonary function test devices were performed on the basis of the American Thoracic Society and European Respiratory Society (ATS/ERS) Tasko Force Standardisation of Lung Function Testing (2005) and Single-Breath Carbon Monoxide Uptake in the Lung (2017).[2,3]

Statıstıcal Method

Sample size was calculated via G*Power: Statical Power Analysis programme. Data were summarized using mean, standard deviation, minimum and maximum values. After the compliance of the data to the normal distribution was evaluated using the Shapiro–Wilk test, the difference between the groups was analyzed by independent *t*-test or Mann–Whitney *U*-test. Age, body mass index and hemoglobin covariant were taken and the effect on the results was eliminated. Statistical significance was accepted as $P < .05$. Statistical analyzes were performed using STATISTICA 13.5.0 (TIBCO Software, USA).

RESULTS

All 46 volunteers and 50 non-smokers included in the study were male. The study was continued for 12 months. The mean age of the volunteers was 47.9 ± 5.97. The mean body mass index was found to be 25.92 ± 2.41 kg/m^2. The effects of the results were eliminated by taking age and body mass index as covariant. Average smoking consumption in the smoking group was calculated as 27.86 ± 7.24 pack/years.

In smokers, ppm values reflecting CO levels in lungs and measured by carboxymeter were found to be significantly higher than non-smokers ($P < .0001$) (Table 1).

Spirometric values were not statistically different between smokers and non-smokers. Expected FVC%, FEV1% values and FEV1/FVC ratios indicating restriction and obstruction, as well as other parameters indicating small airways, were also not significantly different in terms of liters and expected percentage values (Table 2).

Plethysmography tests revealed some signs of hyperinflation in the smoker group. TLC, TLC%, FRC, FRC%, and RV values reflecting hyperinflation were significantly higher in smokers.

Table 2. Results Obtained by Spirometry

	Smokers		Non-smokers		
	Mean ± SD	**Min–max**	**Mean ± SD**	**Min–max**	***P***
FVC%	106 ± 13.90	82.00-143.00	102.44 ± 10.99	81.00-133.00	.088
VC-IN%	96.89 ± 14.32	71.00-137.00	93.72 ± 11.19	71.00-117.00	.227
FEV1%	103.71 ± 11.79	83.00-133.00	100.82 ± 10.68	80.00-135.00	.274
FEV1/FVC	79.38 ± 4.78	70.19-92.59	79.71 ± 4.76	70.53-89.10	.799
FEV3/FVC	94.13 ± 2.76	88.47 ± 99.95	94.15 ± 2.98	87.98 ± 99.85	.979
PEF	8.13 ± 1.65	5.49-13.91	8.18 ± 1.38	5.61-11.32	.870
PEF%	91.19 ± 17.11	56.00-146.00	94.88 ± 14.80	64.00-131.00	.261
MEF75	7.67 ± 1.49	5.17-12.14	7.77 ± 1.43	5.44-11.31	.732
MEF75%	98.97 ± 17.95	60.00-146.00	102.96 ± 17.51	72.00-150.00	.274
MEF50	4.89 ± 1.05	2.87-7.71	4.52 ± 1.28	2.73-8.64	.241
MEF50%	101.21 ± 23.62	55.00-178.00	96.62 ± 24.54	56.00-166.00	.353
MEF25	1.48 ± 0.53	0.68-2.99	4.83 ± 24.84	0.68-177.00	.184*
MEF25%	73.30 ± 25.90	32.00-161.00	69.88 ± 22.39	36.00-136.00	.489

*Mann–Whitney *U*-test, other results obtained by independent *t*-test.

Table 3. Results Obtained by Plethysmography

	Smokers		Non-smokers		
	Mean ± SD	**Min–max**	**Mean ± SD**	**Min–max**	***P***
sRaw (eff)	1.13 ± 0.45	0.45-3.03	1.13 ± 0.38	0.57-2.36	.578
sRaw (eff%)	96.84 ± 39.14	38.00-258.00	96.16 ± 32.66	48.00-200.00	.523
Raw (eff)	0.28 ± 0.12	0.09-0.68	0.30 ± 0.09	0.12-0.55	.154*
Raw (eff%)	96.69 ± 42.63	31.00-226.00	101.48 ± 31.46	40.00-184.00	.165*
Raw (tot)	0.34 ± 0.13	0.14-0.77	0.36 ± 0.10	0.14-0.71	.497
Raw (tot%)	114.15 ± 45.71	45.00-257.00	120.92 ± 35.25	45.00-237.00	.500
TLC	6.82 ± 1.07	4.38-10.27	6.22 ± 0.83	4.01-7.98	.001
TLC%	98.04 ± 13.37	69.00-127.00	92.90 ± 9.80	64.00-109.00	.011
IC	3.26 ± 0.62	2.05-5.30	3.02 ± 0.70	1.34-4.60	.146
IC%	95.58 ± 16.39	66.00-139.00	93.76 ± 18.44	44.00-133.00	.610
FRC	3.69 ± 1.29	1.53-9.76	3.19 ± 0.69	1.78-5.38	.009
FRC%	103.45 ± 25.79	45.00-156.00	94.38 ± 19.48	56.00-158.00	.018
ERV	1.67 ± 0.67	0.45-3.68	1.44 ± 0.66	0.53-3.57	.134
ERV%	125.47 ± 51.07	36.00-252.00	113.42 ± 50.49	38.00-261.00	.200
RV	1.88 ± 0.63	0.53-3.23	1.75 ± 0.50	0.22-2.68	.020
RV%	89.15 ± 26.50	27.00-135.00	82.72 ± 21.25	11.00-116.00	.050
IC/TLC	0.48 ± 0.08	0.34-0.70	0.48 ± 0.09	0.28-0.66	.876
RV/TLC	28.86 ± 8.87	12.01-56.00	28.27 ± 6.96	10.14-41.33	.165

*Mann–Whitney *U*-test, other results obtained by independent *t*-test.

No statistically significant difference was found between RV% values, IC/TLC and RV/TLC ratios which reflect hyperinflation. There was no statistically significant difference between sRaw (eff), sRaw (eff)%, Raw (eff), Raw (eff), Raw (tot), Raw (tot%) values reflecting pulmonary resistance. No statistically significant difference was found between IC, IC%, ERV, ERV% values reflecting pulmonary volumes among other parameters measured by plethysmography (Table 3).

The diffusion capacity test was found to have lower diffusion capacity in the lungs of smokers. DLCO%, DLCO/VA, DLCO/VA%, DLCOc%, DLCOc/VA, and DLCOc/VA% were significantly lower in smokers. There was no statistically significant difference in DLCO and DLCOc values in both groups (Table 4).

No significant difference was found between the 2 groups in respiratory muscle strength tests. When MIP, MIP%, MEP, MEP% values were compared, no statistically significant difference was found between smokers and non-smokers (Table 5).

According to the tests and analyzes we obtained, ppm, TLC, TLC%, FRC, FRC%, RV values were significantly higher in smokers than non-smokers; DLCO%, DLCO/VA, DLCO/VA%, DLCOc%, DLCOc/VA, and DLCOc/VA% values were found to be statistically lower. FVC%, FEV1%, FEV1/FVC, FEV3/FVC, PEF, PEF%, MEF75, MEF75%, MEF50, MEF50%, MEF25, MEF25%, DLCO, DLCOc, MIP, MIP %, sRaw (eff), sRaw (eff%), Raw (eff), Raw (eff%), Raw (tot), Raw (tot%), IC,

Table 4. Diffusion Capacity Test Results

	Smokers		Non-smokers		
	Mean ± SD	**Min–max**	**Mean ± SD**	**Min–max**	***P***
DLCO	9.28 ± 1.71	4.88-13.72	9.37 ± 1.43	5.61-12.93	.719
DLCO%	89.19 ± 15.89	50.00-119.00	95.50 ± 16.48	58.00-144.00	.048
DLCO/VA	1.51 ± 0.27	0.96-2.62	1.68 ± 0.34	1.14-3.10	.006
DLCO/VA%	100.82 ± 18.16	64.00-173.00	114.16 ± 24.15	81.00-199.00	.007
DLCOc	9.15 ± 1.63	4.97-13.39	9.33 ± 1.41	5.55-12.68	.568
DLCOc%	88.06 ± 15.14	51.00-116.00	95.14 ± 16.83	58.00-151.00	.047
DLCOc/VA	1.49 ± 0.27	0.96-2.66	1.67 ± 0.34	1.14-3.06	.004
DLCOc/VA%	99.54 ± 18.32	61.00-176.00	113.90 ± 24.93	79.00-209.00	.005

Table 5. Respiratory Muscle Strength Test Results

	Smokers		Non-smokers		
	Mean ± SD	**Min–max**	**Mean ± SD**	**Min–max**	***P***
MIP	8.02 ± 2.41	3.24-12.76	7.35 ± 2.39	2.00-12.90	.177
MIP%	86.10 ± 24.66	36.00-136.00	79.68 ± 26.29	25.00-156.00	.220
MEP	9.15 ± 2.94	0.40-16.35	9.85 ± 2.75	2.49-15.31	.226
MEP%	67.08 ± 21.16	3.00-124.00	71.90 ± 20.19	19.00-115.00	.257

IC%, IC/TLC, and RV/TLC values were statistically significant no differences.

DISCUSSION

In our study, we found that CO (ppm) values were significantly higher in smokers than in non-smokers, as in the literature with carboxymetry. Although there are some differences in the parameters indicating hyperinflation, it is seen that the findings of hyperinflation in smokers have been found in the literature and in our study in general. In accordance with the literature and our study, it is seen that diffusion capacity is impaired in smokers. There are conflicting results in studies on plethysmography and respiratory muscle strength.

In their study, Chatrchaiwiwatana et al.[4] compared the carboxymetry values of smokers and non-smokers.[4] Totally 291 smokers and 584 non-smoking volunteers were measured; carboxymetry values in smokers average 11.24 ppm; The average of 2.25 ppm in non-smokers was calculated and this difference was statistically significant. In our study, ppm values were found to be higher in the smoker group.

Fortis et al.[5] suggested that although spirometric values were normal, obstruction or restriction may be encountered. They based their study in the literature on the presence of air confinement or emphysema on radiological imaging in patients with normal spirometric values and normal spirometric values despite the presence of respiratory symptoms in active/old smokers. When retrospective analysis of spirometry and plethysmography measurements of 1805 patients, spirometry measurements of 708 patients were found to be normal. Of these 708 cases, 74 (10%) had air trapping, 41 (5.8%) had hyperinflation, 88 (12.4%) had air trapping and/or hyperinflation. Restrictive defects were found in 51 (7.2%) cases and abnormal values in lung volumes were found in 138 (19.5%) cases. Lung volume anomalies were found to be older and smoking history. The medical records of the patients were examined 6 months after the respiratory tests and they were diagnosed with asthma, COPD, interstitial lung disease, other obstructive pulmonary diseases, cough and dyspnea. In the statistical breakdowns, TLC% and RV/TLC ratio were found to be significantly higher in smokers ($P < .001$). In our study, those with abnormalities in radiological imaging were not included. Similarly, in our study, TLC% values were significantly higher in smokers but no statistically significant difference was found in RV/TLC ratios.

Gomes et al.[6] observed the effects of smoking in their case–control study.[6] The group of 32 smokers and the control group of 32 non-smokers consisted of subjects with no respiratory symptoms and normal chest radiographs. In the plethysmographic data they compared these groups, there was no statistically significant difference between FVC%, FEV1%, FEF25%, FEF50%, PEF%, TLC%, RV%, RV/TLC ratio, Raw and sGaw values. They found a statistically significant difference between FEV1/FVC, FEF75%, and FEF25-75% ($P = .026$ for FEV1/FVC, $P = .002$ for FEF75%, and $P = .029$ for FEF25-75%). They concluded that smoking predicts pulmonary dysfunction. In addition, COPD was found in 3 people during the test, although they did not include the patients with pulmonary disease before; and those with non-related diseases such as coronary artery disease, cerebrovascular disease and hypertension as a separate subgroup of 12 people. FEV1% and RV/TLC rates were found to be statistically significantly lower when compared with the other subgroup of 20 smokers but without smoking related disease ($P = .039$ for FEV1, $P = .009$ for RV/TLC). In our study, patients with abnormalities in spirometry values or chronic diseases that could affect respiratory parameters were not included. In our study, TLC was found to be higher in smokers; Spirometry values and RV/TLC ratios were not statistically significant. Similarly, no statistically significant difference was observed in airway resistance values.

In their study, Banur et al.[7] wanted to show the changes in smoking in spirometry, plethysmography and diffusion capacity tests in asymptomatic people. Totally, 47 asymptomatic smokers and 55 non-smokers between the ages of 18 and 40 were included in the study. The patients in the study group were formed with similar height, weight and body mass index. The smoking group consumed at least 6 months and 5 of them were older smokers. FEV1/FVC ratio was found to be less than 70 in 68% of smokers and it was found to be statistically lower than non-smoking group ($P < .001$). While there was no statistically significant difference between PEF and MEF75, there was a statistically significant decrease in MEF50 and MEF25 among smokers ($P < .001$). Similarly, DLCO values were significantly lower in smokers (4.65 ± 0.35 vs. 4.95 ± 0.36 $P < .01$). While the value of TLC was 6.10 ± 0.64 liters in smokers, it was found to be 5.44 ± 0.87 in smokers and the rate of increase above the threshold value of 110% in the study was found to be 44.68% against 1.58% and this difference was found to be statistically significant ($P = .04$). While the level of RV was 1.45 ± 0.08 liters in smokers, it was 1.45 ± 0.12 in non-smokers and no statistically significant difference was found. In our study, people who quit smoking or people who smoked under 20 packs/year were not included. Those with FEV1/FVC ratio below 70 were excluded from the study. Similarly,

in our study, TLC values were significantly higher in smokers. In our study, contrary to Banur's study, no statistically significant difference was found between the DLCO values, but the expected DLCO percentages were significantly lower in smokers. As another difference, in our study, RV values were significantly higher in smokers.

Ethics Committee Approval: This study was approved by Ethics committee of Mersin University, (Approval No: 2018/240).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer Review: Externally peer-reviewed.

Author Contributions: Supervision – K.B.A.; Design – K.B.A.; Concept– K.B.A.; Resources – K.B.A., C.Ö.; Materials – K.B.A.; Data Collection and/or Processing – B.T.; Analysis and/or Interpretation – B.T.; Literature Search – K.B.A.; Writing Manuscript – K.B.A., C.Ö.; Critical Review – C.Ö.

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