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RESEARCH ARTICLE

FACTORS THAT MAY AFFECT FEV1 CHANGE OF COPD PATIENTS IN ONE-YEAR PERIOD

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ABSTRACT

Objective: One of the hallmarks of COPD is the rate of FEV1 decline. There are many factors that may affect pulmonary parameters in a COPD patient. It was aimed to investigate the factors affecting FEV1 changes.
Methods: COPD outpatients who attended our pulmonology clinic were included. Spirometric values and inhaler device usage performance at that time and 12 months ago were compared.
Results: Mean FEV1 values of 204 COPD patients decreased from 1.56±0.51 lt (53.4%) to 1.51±0.50 lt (53.2%). There was a statistically significant relationship between FEV1 change (decline / not) and gender, active smoking, regular inhaler device usage, exacerbation, hospitalization history in last year, presence of comorbidities and inhaler device adherence. FEV1 decline had positive correlation with the number of exacerbations in last year (r=0.432, p<0.001), and negative correlation with inhaler device usage score (r=-0.512, p<0.001). Multivariate regression analysis demonstrated that smoking status, number of exacerbations (per year) and inhaler therapy adherence were the factors that affect FEV1 decline in COPD patients (p=0.007, 0.001 ve 0.003, respectively).
Conclusion: Smoking is the major parameter that affects FEV1 value in COPD. Inhaler adherence may directly affect FEV1 change. Smoking cessation, preventing COPD exacerbations and increasing inhaler therapy adherence may decrease FEV1 declines of COPD patients in one-year period.
Key Words: FEV1 decline; COPD; smoking, inhaler machine compliance

ÖZET

KOAH Hastalarında Bir Yıllık Süreçte FEV1'deki Değişimleri Etkileyen Faktörler
Amaç: KOAH seyrini değerlendirmede birinci saniyedeki zorlu ekspiratuar hacim (FEV1) en önemli parametrelerden birisidir. KOAH hastalarında pek çok faktör solunum parametrelerini etkileyebilir. Yıllık FEV1 değişikliğine etki eden faktörlerin incelenmesi amaçlandı.
Yöntem : 2015-2016 arasında polikliniğe başvuran KOAH hastalarının dahil edildiği bu kesitsel çalışmada hastaların 12 ay önce aynı merkezdeki ve yeni spirometreleri karşılaştırıldı. Hastalara inhaler cihaz kullanım becerisini değerlendiren bir test uygulandı.
Bulgular: Çalışmaya dahil edilen 204 KOAH hastasının ortalama FEV1 değerlerinin 1.56±0.51 lt'den (%53.4) 1.51±0.50 lt'ye (%53.2) gerilediği gözlendi. Son 1 yılda KOAH alevlenme ve yatış öyküsünün olup olmaması, inhaler tedavi uyumu, cinsiyet ve sigara içme durumu ile yıllık FEV1'de düşüş olup olmamasıarasında anlamlı ilişki bulundu. FEV1 düşüşünün (ml olarak), alevlenme sayısı ile pozitif (r=0.432, p<0.001), inhaler cihaz performans skoru ile negatif (r= -0.512, p<0.001) korelasyonu mevcuttu. Çok değişkenli regresyon analizinde yaş, aktif sigara içme durumu, alevlenme sayısı ve tedavi uyumunun, KOAH'da yıllık FEV1 düşüşünü etkileyen faktörler olduğu tespit edildi (sırasıyla p=0.007, 0.001 ve 0.003).
Tartışma:KOAH hastalarında sigara içimi FEV1 değişimini etkileyen faktörlerin başında gelmektedir. Sigaranın bırakılması, alevlenmelerin önlenmesi ve inhaler cihaz tedavi uyumunun artırılması ile, yıllık FEV1 düşüşlerinde azalma sağlanabilir.
Anahtar Kelimeler: FEV1 değişikliği; KOAH; sigara içimi; inhaler cihaz uyumu

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently one of the most important causes of death worldwide. The number of deaths due to COPD is increasing while mortality due to the other comorbidities decline [1].

Airflow obstruction, which is measured by using spirometric parameters, is a major characteristic of COPD. Spirometric criteria, including forced expiratory volume in one second (FEV1), have been used for diagnosis and severity assessment of COPD. FEV1, the most widely used spirometric parameter, has been accepted as a strong predictor of mortality in COPD [2].

The rate of FEV1 decline has been used to reflect disease progression for COPD [3]. It has also been accepted as a key marker for a target for therapeutic trials. FEV1, which is a good predictor of exercise tolerance, also correlates with survival and quality of life [4].The normal rate of FEV1 decline is approximately 30 ml/year in healthy people [5]. The decline has been known to be about 60 mL/year in COPD patients [3].

There are many factors for accelerated decline of FEV1 in COPD patients. Smoking is one of the most important factors that affects FEV1 value. Annual FEV1 decline has been found to increase progressively in smokers [6]. Increased airway hyperresponsiveness was another factor which can accelerate the decline in FEV1 [7]. COPD exacerbations also seemed to have an effect on the rate of decline in FEV1 [8]. Predominant emphysema phenotype was showed to have an association with high rates of FEV1 decline [8].

The low-treatment adherence may cause many problems in COPD patients, varying from an increase in pulmonary symptoms to mortality. However, the association between inhaler treatment adherence and changes in FEV1 has been rarely mentioned. We aimed to investigate the factors affecting FEV1 changes of COPD patients in one-year period, including inhaler therapy adherence.

METHOD

COPD outpatients with the spirometric results confirming the post-bronchodilator FEV1/FVC ratio less than 70% for COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [9] who attended Pulmonology clinics of our centers between 2015 and 2016 were included in the study. The patients with incomplete data about previous pulmonary function tests (which had been performed 12 months ago in hospital) were excluded. Another exclusion criteria was a COPD exacerbation story (recorded in hospital data) in one month before patient visits.Written informed consent was obtained from all of the patients. The study was also approved by local ethics committee of Çanakkale 18 Mart University.

Age, gender, sociodemographic variables and characteristics about smoking (smoking status and amount) were recorded. Spirometric values of the patients which had been performed one year ago were collected from hospital database. All patients underwent a standard post-bronchodilator spirometry (spirolab III S/N A23-053, Rome-Italy); FEV1, forced vital capacity (FVC) and FEV1/FVC were recorded. Participants performed a minimum of three forced blows and best values were taken for interpretation.

Patients were classified into groups (A, B, C, or D) based on their spirometric values, exacerbation and hospitalization history in last year, and symptomatic assessment according to combined classification of GOLD 2011 [9]. The definition of a COPD exacerbation is accepted as an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication, which generally includes an acute change in one or more of the cardinal symptoms as increasing dyspnea, cough in frequency and severity and sputum production in volume and/or changes character (9). The rate of hospitalizations and acute exacerbations in previous year for each patient was obtained from hospital database.

A demonstrative test evaluating inhaler device usage and Morisky scale were performed by the authors in the study. All patients demonstrated how they had used their inhaler devices. The inhaler usage performance was standartized according to “National Guide of Turkish Thoracic Society for Asthma” [10] (appendix 1). The time, dosage and frequency of inhaler devices performed in one day were also learnt and recorded. Scoring system for evaluating inhalation therapy success was created with the help of some previous reports about this subject [11]. According to this scoring system, every step in table 1 equals to 1 points.

Self-reported inhaler medication adherence was determined by using the Morisky Medication Adherence Scale-4 (MMAS-4) [12]. It includes four questions and scores according to the answers which may show treatment adherence of patients (appendix 2). This instrument has been validated for use in Turkey [13].

Statistical analyses were performed with SPSS version 13.0®. The mean was used to present the results according to the data distribution.

Mann-Whitney U test was used for comparison of two groups for non-parametric evaluation. The Pearson correlation was used to investigate the relationship between the variables. The chi-square test or Fisher's exact test was used to compare proportions of a categorical outcomes. Linear regression analysis was done to identify independent determinants of the inhaler therapy adherence. In all tests, p values of <0.05 were considered statistically significant.

RESULTS

Two-hundered and four COPD patients (age: 64.8±7.8, gender: 174 male, 30 female) were included in the study (after exclusion of 16 patients with an exacerbation story in one month before the last patient visit). There were 126 participants as smokers (61.8%) and 78 as ex-smokers (38.2%).

The mean number of exacerbations was 0.80±0.61 per year. There were 42.2% of stage A, 12.7%of stage B, 23.5% of stage C and 21.6%of stage D COPD patients. The mean of Morisky score was 2.24±1.66. The mean inhaler device performing score was 6.78±2.33. The most common mistakes during inhaler device performance were; hold breath for 5-10 seconds after inhalation (67.6%) and exhalation away from mouthpiece after inhalation (63.7%).

Mean FEV1 values of patients decreased from 1.56±0.51 lt (53.4%) to 1.51±0.50 lt (53.2%). Smokers had a FEV1 decline from 1.61±0.61 lt to 1.49±0.41 lt, when mean FEV1 value of ex-smokers had a decrease from 1.55±0.50 lt to 1.54±0.48 lt (figure 1).

Approximately forty percentage of patients had a FEV1 decline at the spirometric evaluation after one year. Over one-year period, 7.8% of COPD patients had a decline in FEV1 over than 40 ml per year, 16.7% had a decrease between 21 and 40 ml per year, 22.5% had a decline of 1 to 20 ml per year. There was an increase in 26.5% of participants from 1 to 20 ml per year, 13.7% had an increase between 21 and 40 ml per year and 12.8% with an increase over than 40 ml per year in FEV1 values in one-year period (figure 2).

There was a statistically significant relationship between the FEV1 change (decline or not) and gender, active smoking, regular inhaler device usage, exacerbation, hospitalization history in last year and presence of comorbidities (table 1).

There was no significant difference about FEV1 decline between COPD A-B groups and C-D groups (p=0.351). However, FEV1 decline was statistically significant in B-D groups when compared with A-C groups (p=0.002). In the comparison of two stages of COPD, group B and D, there was statistically significant higher rate of FEV1 decline in group B COPD patients (p=0.036).

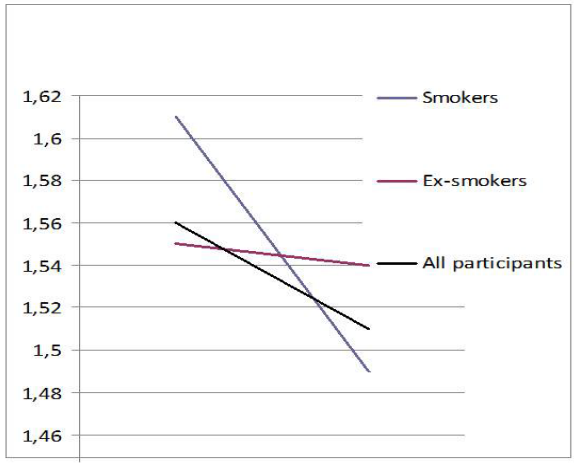

Figure 1: FEV1 changes after one year (as liter)

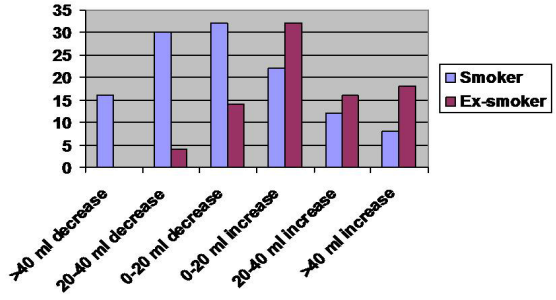

Figure 2: The distribution of rates of FEV1 change in one-year period over a one-year period in COPD patients (as liter)

Twenty-eight patients had taken the diagnosis of COPD last year and were assessed by spirometry after one-year treatment. There was no FEV1 change between new patients and the rest after one year (p=0.139).

There was a positive correlation between FEV1 decline and the number of exacerbations in last year (r=0.432, p<0.001), and negative correlation between FEV1 decline and inhaler device usage score (r=-0.512, p<0.001). There was no correlation between FEV1 decline and age, body mass index (kg/m2) and the amount of smoking (pack-year) (p=0.151, 0.679 and 0.436 respectively).

A relationship was indicated between the status of FEV1 decline and inhaler adherence score (p<0.001). The inhaler devices performance score between FEV1 decline and not were found statistically significant in active smokers (p<0.001). Patients with FEV1 decline had a inhaler performance score with the mean of 5.09±2.75 and Morisky: 3.26±1.23; participants without FEV1 decline had 7.66±1.41 as inhaler score and 1.19±0.41 as Morisky score.

Parameters	Decline in FEV_1 (n)	No Decline in FEV_1 (n)	p value
Men (n)	64	110	0.015*
Women (n)	18	12	
Smoker (n)	62	64	0.002*
Ex-smoker (n)	20	56	
Using inhaler device regularly (n)	44	100	<0.001*
Using inhaler device irregularly (n)	38	22	
Presence of comorbidity (n)	44	46	0.018*
No comorbidity (n)	38	76	
Hospitalization in last year (n)	22	14	0.005*
No hospitalization in last year (n)	60	108	
Exacerbation in last year (n)	46	46	0.007*
No exacerbation in last year (n)	36	76	

Table 1: The comparisons of patients groups with and without FEV1 decline

We observed no significant difference of FEV1 decline according to the type of inhaler devices used by the patients (metered dose inhaler: p=0.075, dry powder inhaler: p=0.232, turbuhaler: p=0.307, discus: p=0.389).

Multivariate regression analysis demonstrated that smoking status, number of exacerbations (per year) and inhaler therapy adherence were the independent factors that affected FEV1 decline of COPD patients in one-year period (p=0.007, 0.001 ve 0.003, respectively), in the contrary of age, gender, presence of comorbidities and socioeconomical status (table 2).

DISCUSSION

Our results revealed a significant relationship between the presence of FEV1 decline and active smoking in COPD patients. Current smoking had been showed as the most important risk factor associated with the rate of FEV1 decline [8]. Our study confirmed this relationship with odds ratio of 31.9. Smoking impacts lung development and limits the lung function, which may accelerate the FEV1 decline of COPD patients in one-year period [14]. The reduction in FEV1 decline of a smoker may become approximately equal to the one who never smokes in years after smoking cessation [15].

Parameters	OR	(95% CI)		p value
		Lower	Upper	
Age (continous)	0.828	0.688	0.995	0.055
Gender(m/f)	0.832	0.020	1.555	0.923
Socioeconomical status	2.002	0.423	3.924	0.404
Number of exacerbations (per year) (continous)	6.450	2.081	19.991	0.001*
Smoking status (smoker/ex-smoker)	31.884	2.587	392.909	0.007*
Presence of comorbidities	2.012	0.408	9.921	0.390
Morisky score (continous)	2.446	1.354	4.486	0.003*

OR: odds ratio; CI: confidence interval.

Table 2: Results of multiple linear regression analysis for the decline of FEV1

COPD exacerbations seemed to play a role in FEV1 decline in our study. Not only the presence, but also the number of exacerbations was found to be related with FEV1 decline according to our results. Previous studies revealed a relationship between frequent exacerbations and more FEV1 decline in lung functions [16]. However, this effect was found smaller compared with the effect of smoking [8]. It was reported that there was an increased rate of FEV1 decline in COPD patients with more frequent exacerbations compared with infrequent exacerbators [8], COPD exacerbations which constitute a health burden in COPD, may cause a lack of disease stability and a rapid decline of FEV1.

Our results demonstrated no relationship between FEV1 decline and age. It is still unclear if age is a factor influencing FEV1 decline among COPD patients. Fletcher-Peto et al. showed that the rate of FEV1 decline accelarates with age [17]. On the contrast, some studies reported that rapid decliners were younger COPD patients [18]. Older COPD patients may have a longer history of smoking, which may cause a worse lung function and a less FEV1 decline in one-year period.

There was a higher rate of FEV1 decline in group B COPD patients in our study. This group of patients seem to have FEV1 higher than 50%, like stage 1 and 2 according to old COPD classification. Tantucci et al. reported that the more accelarated FEV1 decline was in GOLD stage 2 [6]. The rate of FEV1 decline had been found inversely related with GOLD stage [6]. COPD patients in early stages have a higher lung capacity, which means they have more to lose than those in advanced stages of COPD.

The findings on gender differences in effects

of smoking on pulmonary functions remain controversial in literature. There are some studies revealed an increased rate of FEV1 decline in men to be greater than in women [19]. Xu et al found greater rates of FEV1 decline among female smokers in their study [20]. Our study demonstrated a similar result, with higher rates of FEV1 decline in female COPD patients. The observed gender differences about FEV1 decline may be related to the frequency of smoking. There were much more active smoker female patients (when compared with men) according to our results, which supports this theory.

It is not usual to see COPD patients with increasing FEV1 levels in one year period. However, our results revealed nearly 60% of COPD patients without FEV1 decline. Vestbo et al. demonstrated a FEV1 increase varying between 8% and 31% in their study [8]. Ex-smokers are most likely to improve their FEV1 levels [19]. Our study revealed that nearly a half of our patient population with FEV1 improvement were active smokers. This is an unexpected result, which does not exist in the literature. These patients (with FEV1 improvement) had a higher inhaler therapy adherence than other active smokers with FEV1 decline. TORCH study indicated that regular COPD treatment may help a lower FEV1 decline [5]. Adherence to medication in COPD is an issue optimizing clinical outcomes [20]. This is the first studywhich expresses the relationship between improvement in FEV1 and adherence to COPD medication.

There are some limitations in the study. First of all, we did not use a complicated spirometry tool for measuring lung volumes. A body plethysmography which may measure residual volume, functional residual capacity and total lung capacity will reach more detailed and highly accurate results. Since there were only 30 women in the study, it is hard to compare men and women about FEV1 change. Besides, there can be other parameters that may affect FEV1 change in one-year period, such as clinical phenotype (like emphysema), biomarkers specific for COPD and airway hyperreactiveness; our study did not examine these factors. One-year period and two times of lung function assessments per patient in a year may not be adequate enough to consider lung volumes of patients, so it is more reasonable to evaluate FEV1 decline in one-year period by a prospective study with frequent times of spirometric evaluations in a longer period.

Conclusion

Smoking is the major factor that affects FEV1 value in COPD. Medication adherence is an important process that may prevent FEV1 decline in COPD patients with active smoking. Smoking cessation, preventing COPD exacerbations and increasing inhaler therapy adherence may decrease FEV1 declines in COPD patients in one-year period.

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