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Title: Pulmonary function changes in COPD patients according to smoking status

Short title: PF changes in COPD according to smoking

Authors: Aşkın Gülşen

Instutions: Interdisciplinary Allergy Outpatient Clinic, Department of Pneumology, University of Lübeck, Germany

Address for correspondence: Aşkın Gülşen, Interdisciplinary Allergy Outpatient Clinic, Department of Pneumology, University of Lübeck, Germany

E-mail: askingulsen@hotmail.com

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ABSTRACT:

OBJECTIVE: The aim of our study was to examine respiratory functions according to smoking cessation status in patients across all stages of COPD who are currently smoking.

MATERIAL AND METHODS: This retrospective case–control study was carried out. A total of 148 patients were enrolled, and divided into two groups (quitters, n=68, and non-quitters, n=80). Pulmonary function parameters, COPD assessment test score, Fagerström Nicotine Addiction Questionnaire score, smoking history and status were obtained from the electronic hospital data system. Patients' admission and 12-month data were recorded.

RESULTS: In non-quitters, the mean FEV_1 values decreased from 2.32 ± 1.14 to 2.24 ± 1.12 (P < 0.001). Particularly in Stage-0, at early high risk group of COPD, the reduction in FEV_1 was 90 mL, while the reduction was 70, 60, 40, and 40 mL in Stages-I, -II, -III, and -IV, respectively. In quitters, the mean FEV_1 levels increased from 2.10 ± 1.19 to 2.19 ± 1.20 (P < 0.001). For COPD patients overall, an average increase of 80–110 mL in FEV_1 was observed. At the end of 12 months' follow-up, 17 (27.5%) of the non-quitters showed deterioration, and five (7.3%) of the quitters showed improvement in COPD stage.

CONCLUSION: FEV_1 decline is accellerated in COPD patients who continue to smoke, and this decline was not prevented by inhaler treatments. The GOLD Stage-0 group, which is not included in the current guidelines, needs to be redefined, and this group is the most important in terms of prevention of the disease.

KEYWORDS: Smoker, quitter, non-quitter, COPD, pulmonary function

Pulmonary function changes in COPD patients according to smoking status

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive and exacerbating, yet preventable, and partially treatable disease, characterized by chronic airflow limitation [1]. The most common cause of the condition is cigarette smoking. However, air pollution, exposure to environmental or occupational dusts and gases, and the consequent chronic systemic inflammation, also plays a role in the development of the disease [1,2]. It is estimated that, in 2030, it will be the third leading cause of death worldwide [3].

For most patients, the first step in treatment is considered to be smoking cessation. Unfortunately, this is not achieved by many patients; patients are generally reluctant to quit smoking, especially in the early stages of COPD, while their clinical symptoms are mild. In a study conducted in 2016, younger patients and socioeconomically disadvantaged persons tended to be less likely to quit smoking in the early stages of COPD [4]. These patient groups tend to continue to smoke even after starting inhaler treatment. A landmark study showed that, in patients with mild COPD at the age of 35-60 years, an aggressive smoking cessation program significantly reduced age-related decline in forced expiration volume in 1 s (FEV_1) [5]. These patients were administered an inhaled anticholinergic bronchodilator, resulting in a relatively small improvement in FEV_1 after discontinuation of the drug. [5]. Following re-analysis of the drug's effects on lung function, a small improvement of 47 ml in FEV_1 was reported in the first year after smoking cessation [6]. The average annual decline in FEV_1 was 31 mL/year in sustained quitters, and 62 mL/year in continuing smokers. During the 5-year period of the study, the mean reduction in FEV_1 was 77 mL in quitters, compared with 296 mL in continuing smokers [6]. These findings are important for 5-year follow-up, but include only a subset of COPD patients.

Furthermore, "healthy looking" individuals and patients who quit smoking have positive gains in terms of future health. This was illustrated by Dhariwal et al. [7], who found an increase in FEV_1 of 184 mL (7.2%) and 81 mL (3.3%) in the first 6 and 12 weeks, respectively, after the cessation of smoking in COPD patients. In addition, both COPD patients and those with normal initial respiratory function who quit smoking showed a significant improvement in the values of the transfer factor of the lung for carbon monoxide from the 6-week to the 1-year follow-up.

Improvement in respiratory function and FEV_1 is to be expected in patients who quit smoking. Nevertheless, the gain in patients with COPD who are receiving inhaler therapy and who are active smokers is uncertain. In our clinical practice, some COPD patients clearly state whether they consider that they are able to quit smoking. It is therefore debatable whether inhaler treatment is beneficial in patients who continue to smoke cigarettes.

The aim of our study was to examine respiratory functions according to smoking cessation status in patients across all stages of COPD who are currently smoking.

MATERIAL AND METHODS

Study Design

This retrospective case–control study was carried out between 2013 and 2015 in patients admitted to the chest disease polyclinic for smoking cessation in Izmir, Turkey. Patients' referral and 12-month data were collected from electronic medical records. A total of 162 patients were included in the study. Patients were divided into two groups according to smoking status: quitters (n = 68) and non-quitters (n = 80). The flow of the study is given in Figure 1. This study was performed in accordance with the current Helsinki Declaration and good clinical practice guidelines. The study protocol was approved by the local ethics committee (Nr: 198-60, Date: 29.10.2014).

Inclusion and exclusion criteria

Our inclusion criteria were: (i) patients older than 18 years; (ii) actively smoking at referral; (iii) newly diagnosed or known COPD. Patients who met the following criteria were excluded from the study: (i) presence of restrictive lung disease (interstitial lung disease, sarcoidosis, etc.); (ii) known asthma; (iii) bronchiectasis; (iv) chronic heart failure; (v) other acute diseases causing shortness of breath; (vi) active infection.

Data collection

The data of all patients who applied to our outpatient clinic for smoking cessation assistance were obtained from the electronic hospital data system (Bizmed HBYS, Istanbul, Turkey) and were retrospectively evaluated. The following data were analyzed: (i) epidemiological data (age, sex, smoking history, age at onset of cigarette smoking, body mass index); (ii) clinical manifestations and active complaints; (iii) pulmonary function parameters such as FEV_1, forced vital capacity (FVC), FEV_1/FVC, peak expiratory flow (PEF), and forced expiratory flow between 25% and 75% of vital capacity (FEF_{25-75}) (Spirolab III series, MIR, Rome, Italy); (iv) COPD stage according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018 guidelines [3]; (v) Fagerström Nicotine Addiction Questionnaire (FNAQ) score [8]; (vi) COPD Assessment Test (CAT) score [9]. Patients' admission and 12-month data were recorded. The FNAQ is the most widely used, valid questionnaire for measuring nicotine addiction [8]. The validity and reliability of the Turkish version of the scale has previously been confirmed by Uysal et al. [10]. The questionnaire consists of six questions, each rated individually. The highest score is 10. The CAT consists of eight items that assess patients according to their clinical symptoms (cough, sputum, dyspnea, and chest compressions), exercise capacity, self-confidence, sleep quality, and energy levels [9]. Patients can score between 0 and 40.

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COPD classification and smoking cessation program

The diagnosis of COPD was made according to the GOLD 2018 criteria and pulmonary function parameters [3]. According to this, patients with post-bronchodilator $FEV_1/FVC < 70\%$ were classified as follows: $FEV_1 > 80\%$ Stage-I, 50–80% Stage-II, 30–50% Stage-III, and < 30% Stage-IV. Patients with a chronic cough and sputum production, with a CAT score >10, and a normal pulmonary function test were classified as Stage-0 [11]. While this stage had been included in the first published GOLD guidelines, it was not included in the last few guidelines.

Patients were treated with a long-acting bronchodilator β_2-agonist (LABA) and muscarinic antagonist (LAMA), in accordance with the GOLD guidelines for patients with newly diagnosed COPD GOLD Stages-III and IV. All patients had been enrolled in a smoking cessation program, and had been informed of the diseases caused by cigarette smoking. The smoking cessation treatments, nicotine replacement, and medical treatment had been recommended in accordance with their levels of nicotine dependence. Smoking cessation statuses were analyzed based on data obtained at the end of the 3rd and 12th months.

Statistical analysis

Study data are presented using descriptive statistics (mean ± standard deviation for continuous variables, percentile for categorical variables). The chi-square test was used to compare demographic data and Student's *t*-test was used to compare normally distributed data, while the Mann–Whitney U Test was used to compare non-normally distributed data. Statistical significance was set at $p < 0.05$ for Student's *t*-test, and at $p < 0.01$ for the Mann–Whitney U test. Differences between groups were analyzed by paired *t* test. The cut-off value for smoking cessation on the CAT score was calculated by the receiver operating characteristic (ROC) curve analysis. All statistical analysis was performed using SPSS version 19 (SPSS, Chicago, IL, USA).

RESULTS

Demographic data at baseline

The mean age of the 148 patients (68 women and 80 men) was 48.6 ± 15.1 years (range 20–83 years). The mean age at which patients started smoking was 18.4 ± 3.9 years (range 9–40 years). The cumulative levels of smoking was 24.9 ± 16.4 pack-years. The daily average amount of smoking was 19.2 ± 8.6 cig/day. Of the patients, 4.8% were mild smokers, 29.7% were moderate smokers, and 66.2% were heavy smokers. Pulmonary function tests revealed that the mean FEV1 value was 2.22 ±

1.17 L (67.9 ± 29.1%) and the FEV_1/FVC value was 67.49 ± 12.80%. The distribution of patients according to COPD GOLD stages was 43.9% for stage-0, 12.8% for Stage-I, 14.1% for Stage-II, 11.4% for Stage-III, and 17.5% for Stage IV. The success rate of smoking cessation was 67.5% at 3 months and 45.9% at 12 months. At 12 months, the number of non-quitters was 80 (54.1%) (Table 1).

When the baseline parameters of patients were compared according to COPD GOLD stages, the average age of the patients was 40.7 ± 12.0, 45.3 ± 10.1, 45.1 ± 14.3, 62.1 ± 11.2 and 64.8 ± 8.7 years for GOLD Stages-0, I, II, III, and IV, respectively. The average smoking consumption was 19.1 ± 10.5 for Stage-0, 23.5 ± 15.5 pack-years for Stage-I, 31.5 ± 24.6 for Stage-II, 28.4 ± 12.9 for Stage-III, and 32.8 ± 18.5 pack-years for Stage-IV. The distribution of patients' pulmonary function parameters and CAT scores according to groups is shown in Figure 2.

When the initial parameters were compared according to smoking cessation status, there was no statistically significant difference between groups in terms of age, smoking history, level of smoking consumption, FEV_1, FVC, FEV_1/FVC value, FNAQ score, or BMI (Table 2). The CAT score was 18.2 ± 8.8 points in non-quitters, and 21.7 ± 8.9 points in quitters, the difference was statistically significant (P = 0.01). When ROC curve analysis was performed, the cut-off value for smoking cessation was CAT > 20 (sensitivity 60.3%; specificity 63.7%; 95% CI 0.53–0.69; P = 0.01). The CAT score distribution in non-quitters and quitters is given in Figure 3.

Baseline and 12-month FEV_1 values were compared for non-quitters (n = 80) and quitters (n = 68) (Table 3). In non-quitters, the mean FEV_1 values decreased from 2.32 ± 1.14 to 2.24 ± 1.12 (-80 mL, P < 0.001). Particularly in Stage-0, in the early high-risk group of COPD, the reduction in FEV_1 was 90 mL, while the reduction was 70, 60, 40, and 40 mL in Stages-I, -II, -III, and -IV, respectively (Figure 4a). In quitters, the mean FEV_1 levels increased from 2.10 ± 1.19 to 2.19 ± 1.20 mL (+90 ml, P < 0.001). For COPD patients overall, an average increase of 80–110 mL in FEV_1 was observed (Figure 4b). At the end of 12 months' follow-up, 17 (27.5%) of the non-quitters showed deterioration in COPD stage, and five (7.3%) of the quitters showed improvement in COPD stage (Table 4).

DISCUSSION

This study investigated pulmonary function of COPD patients 12-months after quitting smoking, as compared to those who did not quit smoking. Non-quitters generally experienced a reduction of 80 mL in FEV_1 after 12 months. This reduction was seen as 40 mL in GOLD Stage-III and Stage-IV, and

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was less marked than in the other stages. These very low FEV_1 values in patients with COPD may reflect the absence of healthy pulmonary parenchyma due to continued smoking.

In a previous study of a large COPD population, the mean FEV_1 decline was reported to be 47–79 mL/year in GOLD Stage-II, 56–59 mL/year in Stage-III, and 35 mL/year in stage IV [12]. In addition, there was insufficient data on Stage-I, and the smoking status of the patients was not evaluated. In our study, the mean FEV_1 decline in non-quitters and GOLD Stage-I COPD patients was 70 mL/year. However, it has been reported that healthy subjects also have an natural average FEV_1 decline of 25–29 mL/year after the age of 25 years, and an additional 15 mL loss in medium–heavy smokers [13].

In a large study conducted by Scanlon et al. in patients with mild-to-moderate COPD, it was reported that, in those who continue to smoke, there was a decrease of 49 mL and 0.79% in FEV_1 at 1 year, and a decrease of 62 ± 55 mL between 1 and 5 years [14]. They reported that this decrease was two-fold greater than that in quitters. In our study, we noticed a similar decrease in FEV_1, at an average of 80 mL (range 40–80 mL), with rates or reduction varying according to COPD group. Scanlon and his colleagues also examined those who quit smoking, in the same study, and reported that they had an increase of 47 mL or 2% in FEV_1 at 1 year; the FEV_1 decline was 31 ± 41 mL/year or 0.27% in sustained quitters between 1 and 5 years [14]. This suggests that, if the patients quit smoking, the decline in FEV_1 due to the increase in age would return to its natural course. In another study, individuals who followed a short-term cessation program reported a 100-mL increase in FEV_1 after 3 months [15]. In our study, we observed an average increase in FEV_1 of 90 mL (range: 80–110 mL) in COPD patients, of all stages, who quit smoking. This difference between the two studies can be explained by the inhaler treatments that had only just started and continued. Nevertheless, it is clear that quitting smoking resulted in a positive gain for the patients.

For patients who started inhaler treatment but persisted in smoking, the results are less clear. In our study, we started all GOLD Stage-III and Stage-IV patients on combined inhaler therapy. Non-quitters in Stage-III and IV had a 40 mL reduction in FEV_1; quitters showed an increase of 80 mL and 90 mL in FEV_1 in Stage-III and Stage-IV, respectively. This indicates that the initiation of inhaler treatment (LABA + LAMA) is not very useful for patients who continue to smoke. A recent study of inhaled steroid (ICS) treatment in asthmatic patients found that smokers had eosinophilic airway inflammation plus neutrophilic airway inflammation [16]. In that study, smoking was shown to impair the effectiveness of ICS therapy in the treatment of mild to moderate asthma. In COPD patients, the relationship between smoking status and respiratory outcomes has recently been investigated [17].

That study compared former smokers and current smokers for a 12-month period. Former smokers had a mean difference of 30 mL (range: 9–51 mL) in patients receiving fluticasone furoate, 22 mL (range: 1–43 mL) in patients receiving fluticasone furoate + vilanterol, and no difference in patients using only vilanterol (range: -27 to 15 mL) [17]. However, that study also showed that current smokers had a blunted FEV_1 response with ICS and a smaller decrease in the frequency of exacerbations with ICS/LABA than former smokers. Although these studies also addressed the need for inhaler therapy in patients who smoke, the results remained inconclusive. A more detailed and comprehensive study on this subject is necessary.

Furthermore, smoking cessation outcomes in COPD patients vary widely. In our study, smoking cessation success was 67.5% at 3 months and 45.9% at 12 months. The initial CAT scores of quitters were also higher than those non-quitters (18.2 ± 8.8 vs. 21.7 ± 8.9). Patients with a CAT score < 20, i.e., who were clinically less symptomatic, should be monitored more carefully for smoking cessation. In a recent study, in contrast to our findings, the baseline CAT score in quitters and non-quitters was found to be similar (18.5 vs. 16.5, *P* = not significant), but improvements in quitters (10.5 vs 15.5, *P* < 0.01) were reported in controls [18]. However, in a 2012 study of 739 patients with COPD, smoking cessation success was 60.2% in males and 55.6% in females [19].

The COPD GOLD stage-0 patients in our study constituted an interesting research population. In this group of patients, although parameters such as FEV_1, FVC, and FEV_1/FVC were in the normal range, a mild reduction was detected in PEF and FEF_{25-75} parameters. In a prior study, FEF_{25-75} value less than 80% was an early indicator of small airway impairment [20]. However, a cut-off point of 60% for FEF_{25-75} has been used to identify the presence of small airway disease and increased airway resistance [21,22]. In addition, forced expiration volume in 3 s (FEV_3)/FVC can also be used to identify small airway disease [23]. Our finding indicated a cut-off point of 76.80% for FEF_{25-75}; this may be indicative of the onset of small airway disease in COPD patients. In these patients, mean age (40.7 ± 12.0 vs. 64.8 ± 8.7, *P* < 0.001), baseline FNAQ (4.69 ± 2.31 vs. 6.03 ± 1.98, *P* = 0.01), and baseline CAT score (14.87 ± 7.21 vs. 31.73 ± 4.09, *P* < 0.001) were lower than in GOLD Stage-IV patients. Similarly, in a study conducted by Kömüs et al. involving stage-0 patients, the PEF value was reported as 87.05 ± 19.24% and the FEF_{25-75} value was reported as 56.56 ± 16.59%; these values were lower than those of non-smokers [24]. These findings emphasize the importance of early detection of patients in this risk group, before they begin smoking cessation. Previously, this subclinical phase of COPD was defined as Stage-0 in the first GOLD manual, but it was not included in subsequent guidelines [3,11].

Early detection of this group of patients, and starting the smoking cessation program before end-organ damage occurs, is very important [25]. Some studies have also suggested that this pre-clinical phase should be re-identified as early COPD or Stage-0, and that biomarker screening is required [26].

In addition, we observed stage changes in COPD patients according to smoking cessation status after 12 months. Among patients in the worst stage, 21.5% were non-quitters, while among those in the better stage, 7.3% were quitters. This indicates that the condition of patients who have not quit smoking deteriorate over time, but they do not recover soon after quitting smoking, and that the damage may be permanent.

There are some limitations to our study. Firstly, the study contained historical data and possible involuntary bias, due to its retrospective nature. Secondly, the number of patients in the groups decreased because of the distribution of patients in the various COPD groups. Therefore, attention should be paid to the analysis of distributed data. Thirdly, the obtained data may not be generalizable to COPD patients overall; nevertheless, significant results were obtained.

In this study, FEV_1 decline is accelerated when COPD patients continue to smoke. The treatment of this group of patients with inhaler therapy does not prevent this decline. Another important point is that the GOLD Stage-0 group, which is not included in the current guidelines, needs to be redefined and this group should take priority in the smoking cessation program.

CONCLUSION

FEV_1 decline is accelerated in COPD patients who continue to smoke, and this decline was not prevented by inhaler treatments. However, there was a significant improvement in FEV_1 in all COPD patients who quit. The GOLD Stage-0 group, which is not included in the current guidelines, needs to be redefined, and this group is the most important in terms of prevention of the disease.

Ethics Committee Approval: The study protocol was approved by the local ethics committee in Izmir / Turkey (Nr:198-60, and date:29.10.2014).

Informed Consent: Due to the retrospective design of the study, the informed consent forms were not able to be taken.

Conflict of interest: The author have stated explicitly that there are no conflicts of interest in connection with this article.

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Table 1. Patient demographics at baseline	
Number of Patients	148
Sex (Female/Male), n	68/80
Age, y	48.6 ± 15.1
Age at start smoking, y	18.4 ± 3.9
Level of smoking, pack/years	24.9 ± 16.4
Daily number of cigarettes (cig/day)	19.2 ± 8.6
Mild smoker (0-9)	6 (4.8)
Moderate smoker (10-19)	44 (29.7)
Heavy smoker (>20)	98 (66.2)
FNAQ, points	5.1 ± 2.2
low grade addiction (0-3)	41 (27.7)
Intermediate grade addiction (4-6)	70 (47.2)
high grade addiction (7-10)	37 (25.0)
CAT scores, points	19.8 ± 9.0
Pulmonary function test	
FEV1, L	2.22 ± 1.17
FEV1, %	67.9 ± 29.1
FVC, L	3.17 ± 1.38
FVC, %	81.24 ± 27.97
FEV1/FVC, %	67.49 ± 12.80
PEF,	3.22 ± 2.17
PEF (%)	43.64 ± 23.25

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FEF25-75, L FEF25-75, %	2.37 ± 1.05 53.38 ± 26.04
COPD GOLD-status Stage-0 Stage-I Stage-II Stage-III Stage-IV	 65/148 –(43.9) 19/148 –(12.8) 21/148 –(14.1) 17/148 –(11.4) 26/148 –(17.5)
Smoking cessation treatments Only NRT NRT + Varenicline Patients with initial inhaler treatment Successfull smoking cessation at 3-M Quitters at 12-M Non-quitters at 12-M	 50 (75.7) 36 (24.3) 43 (29.0) 100 (67.5) 68 (45.9) 80 (54.1)
Data are presented mean ± SD or n (%). FEV_1, a forced expiration volume in 1 s; FVC, forced vital capacity; PEF, peak expiratory flow; FEF_{25-75}, forced expiratory flow between 25% and 75% of vital capacity; COPD GOLD, Global Initiative for Chronic Obstructive Lung Disease; FNAQ, Fagerström Nicotine Addiction Questionnaire; CAT, COPD assessment test; M, month; L, liter; NRT, nicotine replacement treatment.	

Table 2. Comparison of baseline parameters according to smoking cessation status

Characteristic	Non-quitters (n=80)	Quitters (n=68)	*P* value
Age	48.8 ± 15.1	48.3 ± 15.2	0.83
Age of start smoking, y	18.5 ± 4.4	18.2 ± 3.3	0.68
Smoking history, py	27.9 ± 19.1	25.8 ± 21.8	0.53
Body mass index	25.9 ± 5.5	26.1 ± 4.7	0.78
Daily number of cigarettes (cig/day)	20.1 ± 9.1	18.1 ± 7.8	0,18
Light smoker (≤ 10 cig/day)	9.3 ± 1.7	9.4 ± 1.5	0.34
Heavy smoker (≥ 11 cig/day)	23.0 ± 8.1	22.1 ± 6.1	0.89
Very Heavy smoker (≥ 20 cig/day)	24.1 ± 8.0	22.9 ± 5.9	0.04
FEV1, L	2.32 ± 1.14	2.10 ± 1.19	0.25
FVC, L	3.25 ± 1.34	3.08 ± 1.43	0.45
FEV1/FVC, %	68.52 ± 12.81	66.41 ± 12.86	0.32
FNAQ, p	5.1 ± 2.2	5.0 ± 2.2	0.85
CAT, p	18.2 ± 8.8	21.7 ± 8.9	0.01

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Data are presented as mean ± SD.
See Table 1 legend for expansion of other abbreviation.

Table 3. Changes in FEV_1 values at baseline and at 12 months

	Non-Quitter					Quitter				
GOLD Status	**n**	**Baseline**	**12-month**	**Δ, L**	***P***	**n**	**Baseline**	**12-month**	**Δ, L**	***P***
Stage-0	36	3.14 ± 0.79	3.05 ± 0.78	-0.08	<.001	29	3.08 ± 0.73	3.18 ± 0.72	+0.10	<.001
Stage-I	14	2.62 ± 0.65	2.55 ± 0.64	-0.07	<.001	5	2.94 ± 0.68	3.05 ± 0.69	+0.11	<.001
Stage-II	11	1.88 ± 0.49	1.82 ± 0.50	-0.06	<.001	10	2.02 ± 0.63	2.11 ± 0.62	+0.09	<.001
Stage-III		0.96 ±	0.92 ±	-0.04	0.10		1.00 ±	1.08 ±	+0.0	<.001

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	8	0.27	0.28			9	0.14	0.13	8	
Stage IV	11	0.65 ± 0.13	0.61 ± 0.14	-0.04	<.001	15	0.62 ± 0.13	0.71 ± 0.15	+0.09	<.001
Total	80	2.32 ± 1.14	2.24 ± 1.12	-0.08	<.001	68	2.10 ± 1.19	2.19 ± 1.20	+0.09	<.001
Mean (median) ± SD; **Δ**, change; L, liters.										

Table 4. Change of GOLD Stages within 12 months

Non-quitters (n=80)		**Quitters (n=68)**	
GOLD Status	**n**	**GOLD Status**	**n**
Stage-0 to Stage-I	5	Stage-I to Stage-0	1
Stage-I to Stage-II	9	Stage-II to Stage-I	0
Stage-II to Stage-III	1	Stage-III to Stage-II	1
Stage-III to Stage-IV	2	Stage-IV to Stage-III	3
Total worsening	17 – 21.5%	Total improved	5 –7.3%

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LEGENDS OF FIGURE

Figure 1. The flow of the study

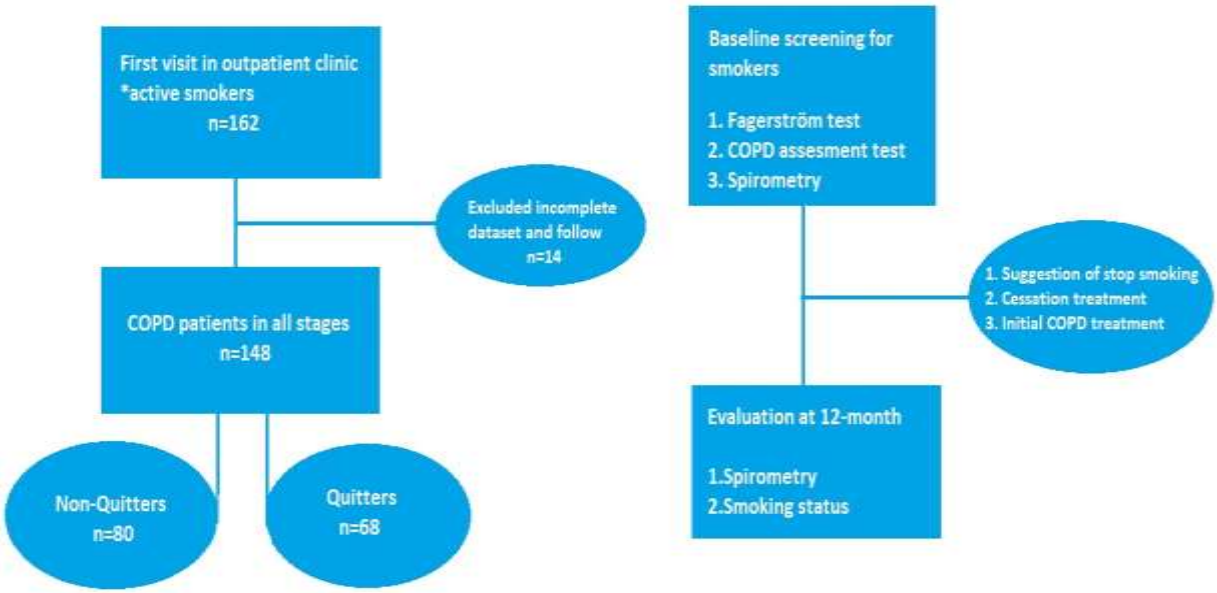

Figure 1. The flow of the study

Figure 2. Comparison of baseline pulmonary function parameters according to COPD severity

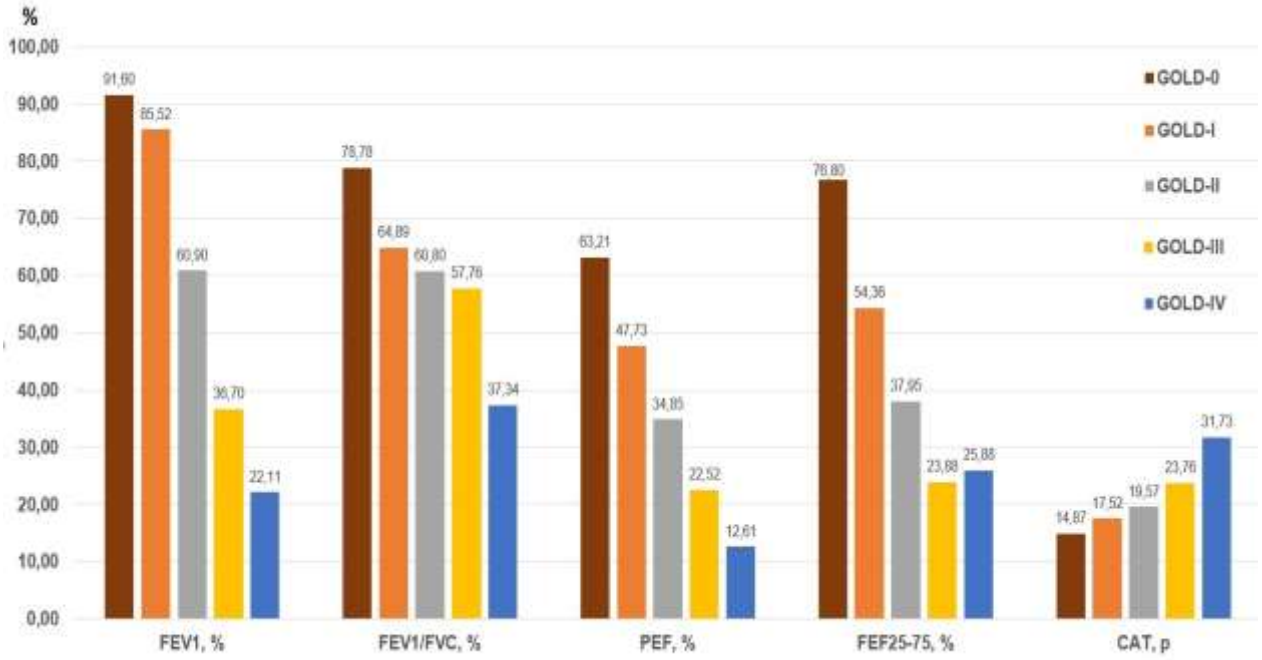

Figure 2. Comparison of baseline pulmonary function parameters according to COPD severity

Figure 3. CAT score distribution in quitters and non-quitters

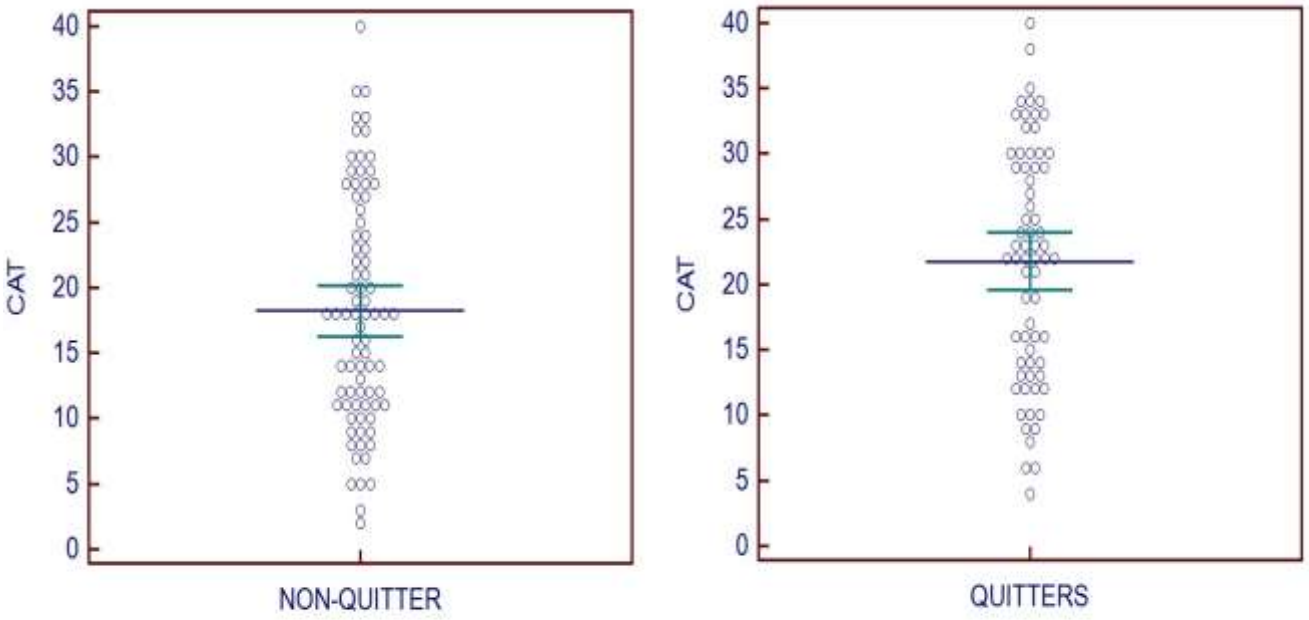

Figure 3. CAT score distribution in quitters and non-quitters

Figure 4. Changes in FEV1 value of non-quitters, and quitters

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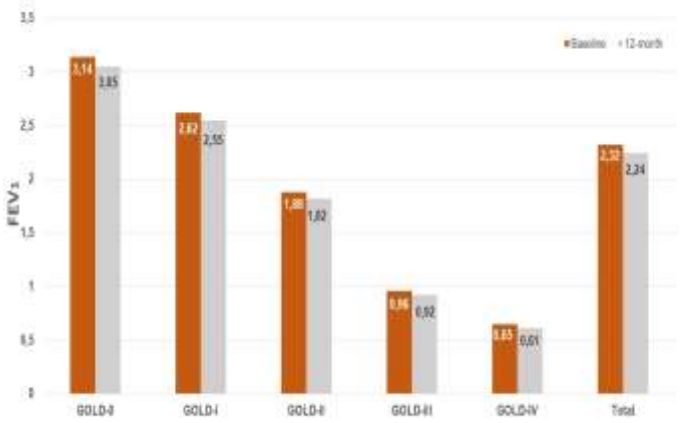

Figure 4a. Changes in FEV_1 value of non-quitters

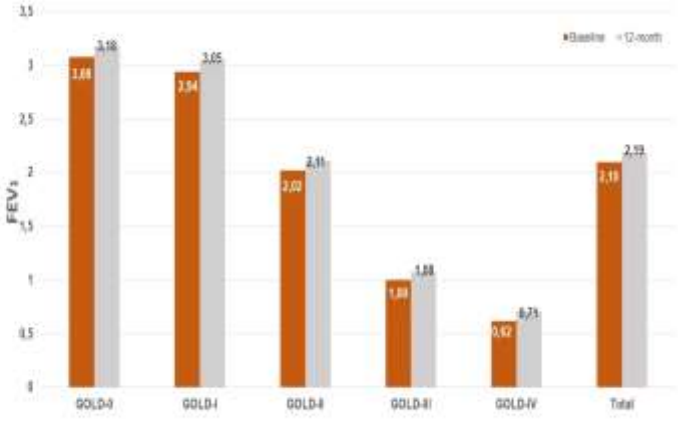

Figure 4b. Changes in FEV_1 value of quitters