Original Article

Access this article online

Quick Response Code:

Website: www.eurasianjpulmonol.com

DOI: 10.4103/ejop.ejop_17_19

The relationship of bronchiectasis to airway obstruction and inflammation in patients with chronic obstructive pulmonary disease

Baris Seker, Burcu Arpinar Yigitbas, Celal Satici, Sibel Yurt, A. Filiz Kosar

Abstract:

BACKGROUND: Chronic obstructive pulmonary disease (COPD) and bronchiectasis are diseases of respiratory tract with significant mortality and morbidity. These two diseases can be seen together occasionally and are thought to change each other's course by adversely affecting the prognosis. The aim of our study was to identify the signs of bronchiectasis in COPD patients, to investigate its possible effects on disease prognosis, and to evaluate these signs for diagnostic convenience.

MATERIALS AND METHODS: This prospective study included a total of stable 60 moderate/severe COPD patients who were admitted to Yedikule Chest Diseases and Chest Surgery Training and Research Hospital between January 2015 and February 2016. The patients were divided into two groups according to the presence of bronchiectasis as confirmed radiologically: 35 patients in the bronchiectasis group and 25 patients in the control group. Demographic data of the patients were questioned and systemic inflammation parameters, spirometric measurements, blood gas analysis, and clinical evaluation findings were recorded.

RESULTS: Bronchiectasis was detected in 58.3% of COPD patients. Patients in two groups are similar in sociodemographical, spirometrical and clinical parameters ($P > 0.05$). Laboratory tests showed similar result in between two groups but carbon dioxide(CO2) values in the blood gas analysis were found to be higher in the bronchiectasis group ($P < 0.05$). The increase in the number of bronchiectasis segments was shown to reduce the FEV_1/FVC ($P < 0.05$). In the overall evaluation, FEV_1%, mMRC, FVC% and CRP levels were found to be associated with exacerbations in COPD ($P < 0.05$). The use of antibiotics increased as FEV_1% and FEV_1/FVC levels of patients decreased ($P < 0.05$). In addition, sputum polymorphonuclear leukocyte (PMNL) values were correlated with spirometric values and as sputum PMNL values increased, spirometric values were found to decrease ($P < 0.05$ for FEV_1% and FVC%).

CONCLUSION: Bronchiectasis is common in COPD patients. In two divided groups, blood gas carbon dioxide values, which affect mortality, were shown to be higher in the bronchiectasis group. This is a new addition to literature that bronchiectatic COPD patients are experiencing different respiratory failure patterns affecting mortality. Diffuse type bronchiectasis has more effect in spirometric results of COPD patients. Also, airway obstruction in COPD is well correlated with elevated sputum PMNL values which represent airway inflammation and if this is combined with high clinical suspicion it guides to a cost effective way for guiding radiological investigations for bronchiectasis.

Keywords:

Bronchiectasis, COPD, diagnosis, inflammation, mortality, prevalance

Department of Chest Disease, Yedikule Research and Training Hospital for Chest Diseases and Chest Surgery, Istanbul, Turkey

Address for correspondence:
Dr. Baris Seker, Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital, Belgradkapi Yolu Street, No:1, Zeytinburnu, Istanbul, Turkey.
E-mail: dr.barisseker@gmail.com

Received: 25-04-2018
Revised: 05-05-2018
Accepted: 13-08-2018

Introduction

Bronchiectasis is permanent dilation of the bronchi and bronchioles caused by permanent destruction of connective tissue, muscular, and elastic elements surrounding the bronchi and bronchioles due to various reasons.[1] It causes the loss of lung function in obstructive and restrictive type.[2] The use of high-resolution computed

How to cite this article: Seker B, Yigitbas BA, Satici C, Yurt S, Kosar AF. The relationship of bronchiectasis to airway obstruction and inflammation in patients with chronic obstructive pulmonary disease. Eurasian J Pulmonol 2019;21:21-8.

tomography (HRCT) has led to a higher number of diagnosis.[3] In advanced chronic obstructive pulmonary disease (COPD) patients, the prevalence of bronchiectasis may vary from 30% to 50%.[1,4,5]

In patients with COPD, the presence of bronchiectasis has been shown to accelerate the loss of pulmonary function.[6,7] Therefore, even distinguishing patients with bronchiectasis is important, as it may cause respiratory failure and the rapid progression of the disease in the course of COPD.[8] This condition may be due to frequent exacerbations, colonization of potential pathogenic microorganisms (PPM), and systemic inflammation.[9] COPD has also been shown to have more severe course in smokers with bronchiectasis.[10,11]

Bronchiectasis is important due to the common association with infections and it is a common pathology secondary to infections in developing countries such as Turkey, and also controversial data were reported about the frequency and course of the disease.

In the present study, we aimed to evaluate the prevalence and clinical importance of bronchiectasis in moderate-to-very severe COPD patients.

Methods

Study population

This study was designed as a prospective cohort. Moderate-to-severe and very severe COPD patients (forced expiratory volume in 1 s [FEV_1]/forced vital capacity [FVC] <70%, FEV_1 <80% up to FEV_1 <30%) according to the global initiative for obstructive lung disease (GOLD) 2017 COPD airway obstruction classification, with a history of at least 10 packs/year of cigarette smoking, who admitted to our chest diseases outpatient clinic between February 01, 2015, and January 01, 2016 and accepted to participate were included in the study.[12] Patients with COPD, who have had unstable disease in the past 6 weeks (did not take oral/intravenous antibiotics and/or steroids in the past 6 weeks), unstable angina or unstable arrhythmia, previous allergic asthma or bronchiectasis diagnosis, previous stroke history with persistent risk of aspiration, and severe gastroesophageal reflux disease were not included in the study, as those may affect the frequency of exacerbations and the prevalence of bronchiectasis.[13] A total of 74 patients with COPD were included in the study, 14 of them were excluded from the study before registering the patient data, due to the lack of tests and/or telephone contact and/or to refuse to follow-up/test. A total of 60 patients' data were collected. Follow-up period for mortality was 3 years, and ranges from 1 to 10 months for exacerbation and other medical histories.

The study was approved by the Local Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each patient.

Data collection and diagnosis

Patients with COPD, who met the inclusion criteria, were questioned and recorded for age, gender, history of smoking, comorbidities, body mass index, modified medical research council dyspnea score (mMRC), and treatments for COPD (e.g., whether they use respiratory devices). COPD-related comorbidities were grouped and recorded as: (1) Respiratory diseases, (2) cardiovascular diseases, (3) malignancy, (4) endocrine diseases, (5) gastrointestinal diseases, and (6) renal diseases. The frequency of exacerbation was obtained from the history of patient and hospital records. Sputum culture and gram staining were requested from patients within 3 days from the day of admission. In gram staining, <10 epithelial cells (quality sputum sample) were accepted as valuable.[14] Blood gas analysis, hemogram, and biochemical parameters of all patients were collected at admission. Spirometry tests were performed in accordance with the European Respiratory Society guidelines for spirometry.[15,16] Radiological examinations were performed with the HRCT. The existence of bronchiectasis was confirmed and scored by two-blinded radiologists, using the Reid classification and Reiff scoring, in addition, emphysema was also defined.[17-19] Hospital admissions, devices used for respiratory failure, and other clinical data were obtained from the patient during visit or from medical records. After collecting all the data, the patients were interviewed again and the frequency of exacerbation and antibiotic use during the period was questioned. The duration of the follow-up was ranged from 1 to 10 months according to the patients' control examination visit. Fourteen patients were excluded from the study before registering the patient data [Figure 1].

Statistical analysis

Descriptive statistics for numerical variables and frequency distributions for categorical variables were used in the evaluation of the data of the study. Before analyzing data, the suitability of normal distribution of numerical variables

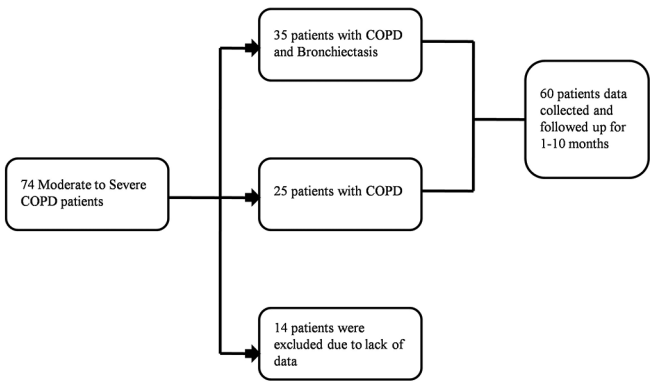

Figure 1: Flow chart of patient inclusion

was investigated, and parametric methods were used to variables with normal distribution, and nonparametric methods were used to variables with abnormal distribution. Pearson correlation and Spearman Rho correlation coefficient were used to determining whether there is a relationship between two numerical variables. The relationship between two categorical variables was examined by the Chi-square test. The difference between the two groups was examined by the independent samples *t*-test and Mann–Whitney U test and the difference between more than two groups was examined by one-way analysis of variance, $P < 0.05$ was considered statistically significant. SPSS version 16.0 software (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.) program is used for analysis.

Results

Bronchiectasis was detected in 58.3% of COPD patients and patients were divided into groups as COPD patients with bronchiectasis (n = 35) and without bronchiectasis (n = 25). The two groups had a similar distribution in terms of sociodemographic data. Other demographic data of the patients are summarized in Table 1. Radiological examination showed that the most common type of bronchiectasis was cylindrical (97%) and both emphysema and bronchiectasis were present in 54% of patients.

Patients completing research is 60 and during 3 years mortality follow-up, 13 patients died, and 8 of them had bronchiectasis and COPD together. Mortality risk in COPD patients is significantly increased in the presence of bronchiectasis with an odds ratio (OR) of 1.18 (95% of confidence interval = 0.33–4.17).

When comparing two groups in terms of spirometric values, all values were similar, including those particularly reflect obstruction as FEV_1% and FEV_1/FVC (P = 0.27, P = 0.25, respectively). The mean of FEV_1/FVC was observed to be decreased as the

Table 1: Demographic, clinical and laboratory characteristics of the patients included in the study

	COPD patients with bronchiectasis (*n*=35; 58.3%)	COPD patients without bronchiectasis (control) (*n*=25; 41.7%)	*P*
Age, mean±SD	62.09±10.758	61.12±8.918	0.715
Gender, *n* (%)			
Male	32 (53)	22 (13)	N/A
Female	3 (2)	3 (2)	
BMI	24.66±4.755	27.1±5.224	0.297
Smoking periods (pack year), *n* (%)			
<20	3 (2)	None	N/A
>20	32 (53)	25 (15)	
mMRC, mean±SD	1.94±1.327	1.68±1.249	0.442
Comorbidity, *n* (%)			
CVS	12 (7)	14 (8)	N/A
Other	6 (4)	4 (2)	
FEV_1 ml, mean±SD	1.39±0.613	1.50±0.436	0.439
FEV_1%, mean±SD	46.87±21.909	52.54±15.778	0.274
FEV_1/FVC %, mean±SD	58.07±11.573	61.44±10.484	0.253
FVC (ml), mean±SD	2.20±0.737	2.26±0.639	0.742
FVC %, mean±SD	58.33±21.454	62.45±14.979	0.412
Hct %, mean±SD	43.72±6.29	43.74±5.85	N/A
Plt (k/mm³), mean±SD	220.77±62.301	236.32±56.984	N/A
Leukocyte (k/mm³), median (minimum–maximum)	9.3 (4–19)	9.4 (3.7–33)	0.970
Albumin mean (g/dL)±SD	4.21±0.34	4.25±0.372	0.649
Sedimentation (mm/h), median (minimum–maximum)	15 (1–67)	15 (2–58)	0.563
CRP (mg/dl), median (minimum–maximum)	6.1 (0–70)	4.8 (0–48)	0.869
pH, mean±SD	7.42±0.038	7.43±0.037	0.388
pO_2 (mmHg), mean±SD	84.59±16.874	78.96±16.356	0.202
pCO_2 (mmHg), median (minimum–maximum)	41 (30–67)	37 (30–51)	0.038*
HCO_3 (mEq/L), mean±SD	26.68±4.243	25.36±3.041	0.189
Tuberculosis sequelae, *n* (%)			
Present	23 (65)	7 (28)	N/A
Absent	12 (35)	18 (72)	

*P<0.05. Parameters with normal distribution are shown with mean±SD, parameters with abnormal distribution are shown with median, minimum–maximum. BMI: Body mass index, mMRC: Modified medical research council dyspnea score, FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity volume, FEV_1%: The ratio of FEV_1 to predicted values, FVC %: The ratio of FVC to predicted values, FEV_1/FVC: The ratio of FEV_1 to FVC, CVS: Cardiovascular system, Hct: Hematocrit, Plt: Platelet, CRP: C-reactive protein, pO_2: Partial oxygen pressure, pCO_2: Partial carbon dioxide pressure, pH: Blood acid-base level, HCO_3: Blood bicarbonate level mEq/L, SD: Standard deviation, N/A: Not applicable, COPD: Chronic obstructive pulmonary disease

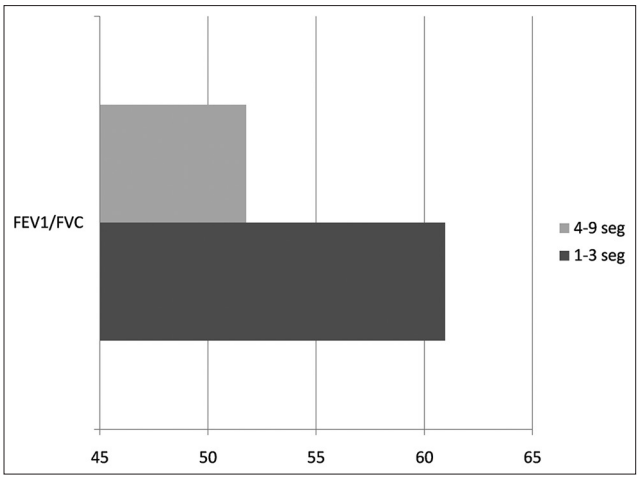

Figure 2: The demonstration of increasing degrees of obstruction with bronchiectasis extension

number of involved bronchiectatic bronchial segments increased ($P < 0.05$) [Figure 2].

In addition, inflammation markers (platelet and leukocyte level, albumin, sedimentation, C-reactive protein [CRP]) were found at similar levels between two groups ($P > 0.05$). Furthermore, exacerbation frequency and follow-up antibiotic usage were not different ($P > 0.05$). mMRC value in patients with bronchiectasis (1.92) was higher than the control group (1.68), but this was not statistically significant. In arterial blood gas examination, CO_2 was found to be significantly higher in the bronchiectasis group than the control group ($P < 0.05$).

In the evaluation of the determinants of exacerbations in all patients; the mMRC score, was higher and the FEV_1% and FVC% were lower in patients with exacerbation history ($P < 0.05$) [Table 2]. The patients with a lower mean of FEV_1/FVC and FEV_1% were found to use more antibiotics than the higher ones when the antibiotic usage was evaluated in the follow-up of all COPD patients ($P < 0.05$) [Table 3].

When the sputum polymorphonuclear leukocyte (PMNL) values were examined together with spirometric data for all patients in terms of airway inflammation and obstruction all spirometric values were found to be worse in patients with sputum PMNL values > 10 ($P < 0.05$) [Figure 3]. Furthermore, in the sputum culture examination, 46 patients were able to give sputum and bacterial growth was observed in 9 of them. In patients with bacterial growth, 6 of them had bronchiectasis.

Discussion

In the present study, the prevalence of bronchiectasis in patients with moderate-to-severe COPD (%58) was found compatible with the meta-analysis (54%).[5]

Table 2: The investigation of the difference between exacerbation history in terms of modified medical research council dyspnea score and spirometry values for all chronic obstructive pulmonary disease patients

	n	Mean±SD	*P*
mMRC			
Without exacerbation	24	1.38±1.209	0.023*
With exacerbation	36	2.14±1.268	
FEV_1			
Without exacerbation	24	1.59±0.519	0.075
With exacerbation	36	1.33±0.544	
FEV_1/FVC			
Without exacerbation	24	62.38±8.060	0.074
With exacerbation	36	57.54±12.564	
FEV_1%			
Without exacerbation	24	55.91±20.000	0.030*
With exacerbation	36	44.77±18.343	
FVC			
Without exacerbation	24	2.35±0.756	0.226
With exacerbation	36	2.13±0.643	
FVC %			
Without exacerbation	24	66.24±21.481	0.038*
With exacerbation	36	55.92±16.155	

*P<0.05. mMRC: Modified medical research council dyspnea score, FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity volume, FEV_1%: The ratio of FEV_1 to predicted values, FVC %: The ratio of FVC to predicted values, FEV_1/FVC: The ratio of FEV_1 to FVC, SD: Standard deviation

Table 3: The investigation of the difference between follow-up antibiotic usage status in terms of spirometric values (independent sample *t*-test)

	n	Mean±SD	*P*
FEV_1			
Not used	34	1.57±0.529	0.079
Used	17	1.28±0.612	
FEV_1/FVC			
Not used	34	62.20±10.556	0.008**
Used	17	53.40±11.233	
FEV_1%			
Not used	34	54.56±19.693	0.046*
Used	17	42.48±20.247	
FVC			
Not used	34	2.34±0.674	0.379
Used	17	2.16±0.740	
FVC %			
Not used	34	64.40±18.444	0.148
Used	17	56.17±19.688	

*P<0.05, **P<0.01. FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity volume, FEV_1%: The ratio of FEV_1 to predicted values, FVC %: The ratio of FVC to predicted values, FEV_1/FVC: The ratio of FEV_1 to FVC, SD: Standard deviation

Despite having the same inflammation and spirometric parameters, in respiratory failure evaluation, partial carbon dioxide levels (pCO_2) were higher in COPD patients with bronchiectasis ($P < 0.05$). Studies in COPD patients have shown the effect of carbon dioxide levels on mortality.[20] However, there was no significant change

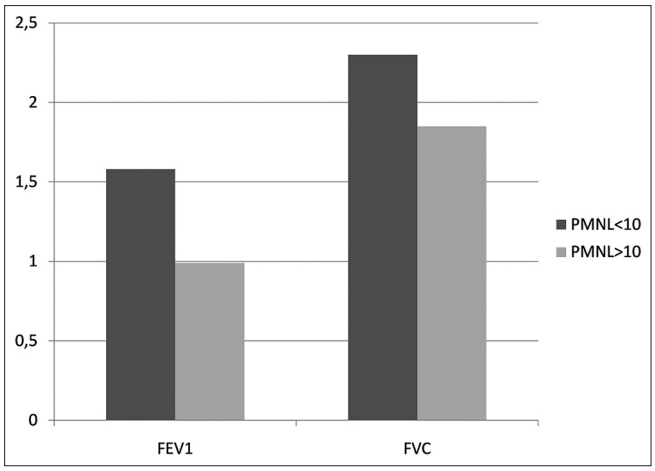

Figure 3: Demonstration of association between airway obstruction and sputum inflammation marker polymorphonuclear leukocyte count ($P < 0.05$)

in partial oxygen levels, which has been shown in other researches ($P > 0.05$).[21,22] Furthermore, mortality risk in COPD was significantly increased with an OR of 1.18, in the presence of bronchiectasis. It is considered with this combined data obtained from the study that bronchiectasis may increase mortality.

In addition, we showed that in both groups of patients, more sputum PMNL counts means more inflammation and obstruction, and more obstruction means more antibiotic usage, and for bronchiectasis group, if involved segments are increased, spirometric values are decreased.

According to this study in light of these data, we deduce that, an increase in the number of bronchiectatic segments and sputum PMNL levels were correlated with lower spirometric values which are associated with the frequency of exacerbations in COPD, and obstruction was thought to be more prominent, and these patients were more likely to use antibiotics supporting other studies.[18] In similar studies, radiological scoring systems including the status of segments have been used.[23] These scoring systems were found to be consistent with the spirometric staging of COPD. In the scoring system developed by Bhalla *et al*.[24] which was used as a modified version in the mentioned study; grade and extent of bronchiectasis, mucus plug formation, peribronchial thickening, and level of division which bronchiectasis extends are evaluated. The HRCT score was found to be negatively correlated with spirometric FEV_1, FVC and FEV_1/FVC by the scoring system used in the mentioned study ($P < 0.001$). In another study, it was showed that FEV_1 was decreased as the number of lobe with bronchiectasis was increased.[25] In this study, a significant relation was found between sputum PMNL values and spirometry values, and this was in parallel with interleukin-6 (IL-6), IL-8, and total cell counts in a similar study reflecting airway inflammation and frequent exacerbation.[26] With this data, we suggest, sputum PMNL level to be used for the follow-up of bronchiectasis or as a screening parameter for the radiologic investigation of the presence of bronchiectasis in patients with COPD. This condition may be evaluated with other further supporting studies and may be considered as a cost-effective test, particularly in developing countries with a high prevalence of bronchiectasis and disease burden.

Bronchiectasis as a tuberculosis sequelae was included in the study due to the frequent observation of tuberculosis in Turkey, although upper lobe bronchiectasis due to tuberculous sequelae was excluded in some studies.[22,23] It is considered that this condition may explain the difference in the spirometric data, inflammation levels and other parameters between our study and other studies. Because we know that bronchiectasis due to tuberculous sequelae has different localization than other types of infectious sequelae as tuberculosis most commonly affecting upper lobes or upper portions of lower lobes that has better drainage and low risk of mucus plugging.[27]

For discussion about radiological examination and obstruction levels, the most common type of bronchiectasis was cylindrical, widespread involvement was present in 46% of patients. Only upper lobe and only lower lobe involvement ratios were similar. In similar studies, the ratio of cylindrical bronchiectasis was reported as 91%, and localization was mostly in lower lobes.[28] In this study, the rate of detection of emphysema was 54% in patients with bronchiectasis which was 76%, 82%, and 80% in similar studies, respectively.[21,23,29] The mean of FEV_1% was 47 ± 22 standard deviation (SD) in bronchiectasis group and 52.5 ± 16 SD in the control group in the evaluation of spirometric values. The nearest study to these values was conducted with 99 COPD patients and mean FEV_1% difference was found to be similar. FEV_1 was found 45% in patients with bronchiectasis and COPD, and 54% in isolated COPD patients, this was statistically significant ($P < 0.001$).[21] In contrast to this, we found that FEV_1% was not significantly different between the two groups despite numbers ($P > 0.05$). In similar studies, mean FEV_1% was lower in COPD patients with bronchiectasis, FEV_1 42% (Tulek *et al*.), FEV_1 45% (Garcia *et al*.) when compared to COPD only patients ($P < 0.01$).[21,23,28] In this study, FEV_1/FVC value was found to be 58% in the bronchiectasis group and 61.4% in the control group, and in contrast to similar studies, this difference was not statistically significant ($P > 0.05$). As mentioned previously, spirometric values were thought to be related to the

groups with emphysema and bronchiectasis included in the study. In this study, the patients with emphysema together with bronchiectasis are less frequent than similar studies. It was considered that this condition may affect FEV_1% and FEV_1/FVC values. There is a study that suggests FEV_1 decline is more prominent in the emphysema group, and the presence of emphysema has been associated with lower lung functions ($P < 0.001$).[29] It is also considered that cases with tuberculosis sequelae could affect the spirometry in the study. In a study related to this situation, it was stated that FEV_1 was lower in patients with bronchiectasis due to tuberculosis; although, this study did not identify the group of COPD patients.[30]

There are three studies about COPD and bronchiectasis in Turkey. The first of these was conducted in 2006. In this study, the prevalence of bronchiectasis in COPD patients was 31% (93 patients in total) and it was stated that the duration of stay in intensive care unit and hospitalization could be prolonged in COPD patients with bronchiectasis, and did not affect mortality.[31] Another study was conducted in 2013. This study noted the importance of the HRCT for phenotyping and disease management in COPD patients and that bronchiectasis may be a distinct phenotype of COPD.[23] The last study is a review, written in 2014. In this review, based on the data from many references, it has been reported that widespread use of the HRCT increased the rate of bronchiectasis detection, and COPD patients with bronchiectasis have a worse prognosis, longer duration of exacerbations, and a higher rate of PPM colonization.[32] There is no follow-up study of patients with COPD and bronchiectasis in Turkey, and by this study, we showed the mortality effect of bronchiectasis and the importance of follow-up. Furthermore, we suggest including bronchiectasis due to tuberculosis sequelae patients for research purposes because of disease burden.

The "exacerbator" group in the phenotypes of COPD, defined in the studies of COPD disease, includes the patients with 2 or more exacerbations per year.[33,34] In these patients, risk factors for exacerbation were detected as senility, low FEV_1 and oxygen requirement, previous exacerbation history, more severe systemic and airway inflammation, bacterial load of sputum in stable phase, chronic bronchitis, and some comorbid diseases (cardiovascular system, anxiety-depression, myopathy, and reflux disease)[34] and when bronchiectasis patients are examined the level of inflammation in sputum specimens was found to be high, even in the stable phase.[35] We can get a conclusion from these two studies that bronchiectasis causes an airway inflammation that causes an exacerbator phenotyped COPD patient. In this study, PMNL count in Gram staining that reflects the level of airway inflammation; CRP, albumin, sedimentation, Plt, leukocyte that reflect the systemic inflammatory response; and symptom query, mMRC value, and follow-up antibiotic usage which are clinical reflections of these conditions were obtained from the patient data.[36-39] We examined these values to get a conclusion about bronchiectasis if present causes an exacerbator phenotype in COPD. The number of patients who had 2 or more exacerbations was 17, and 12 of them had bronchiectasis, but this was not significant enough to define bronchiectasis as an exacerbator COPD phenotype ($P > 0.05$). In a meta-analysis, patients with bronchiectasis had 1.5 times more exacerbations than COPD only patients.[5]

Similar studies have examined PPM colonization, which has been reported to be associated with bronchiectasis and also *Pseudomonas* colonization was more frequent in COPD patients with bronchiectasis.[21,28,40] In this study, patients with bronchiectasis were more likely to need antibiotics during the follow-up, but sufficient data could not be obtained on this issue. The reason of this condition was considered as requirement for larger sampling and longer follow-up.

To tell more about examining these two groups differences clinically, it was considered that using COPD assessment test (CAT) scoring which also evaluates the sputum condition may be more appropriate in these patients, as the increase in sputum frequency is more suitable for reflecting the score of the disease status of patients with bronchiectasis. In similar studies, CAT scoring was not used as seen in the meta-analysis. We suggest using the CAT score for assessing the clinical condition of these patients.

In this study, sample size and research duration were our limitations. Some patients did not want to complete the study because of social problems and patients with more severe COPD were not suitable to include, because of improper medical records or severe disease status. We conducted this study in a preset schedule, and this was also a limitation, because some patients may have more attacks during this unfollowed period.

Conclusion

Significant proportion of patients with COPD is associated with bronchiectasis. This shows us that many patients with COPD, especially severe patients, need further evaluation for other respiratory problems because they may effect some important clinical parameters and so the mortality. Furthermore, bronchiectasis is an independent mortality risk factor for patients with COPD as expressed in meta-analyses.[5,41]

Patients with bronchiectasis and COPD, when bronchiectasis associated with tuberculosis were

included, were considered to have similar behaviors with the current GOLD staging of COPD in terms of spirometric values and exacerbation. We suggest using also bronchiectasis due to tuberculosis patients in studies and meta-analysis for developing countries and tuberculosis prevalent countries. This may reflect better diversity of COPD patients with bronchiectasis in these countries.

COPD with diffuse bronchiectasis causes worse spirometric values. This causes more functional loss and respiratory failure. In this type of patients, we have more inflammation in the airway as pathology of bronchiectasis also suggest this and these patients have more exacerbation and more antibiotic usage.

We suggest more patients should be included in new studies with more follow-up times, and patients should be assessed with CAT score that better reflects their sputum production. Tuberculosis-prevalant countries need to evaluate bronchiectasis due to tuberculosis sequelae and integrate research according to needs. Furthermore, it is also considered that in frequent exacerbator patients with suspected bronchiectasis, sputum PMNL value which reflects airway inflammation should be checked, and if it is detected high, detailed radiological investigations should be done, and this should be used as a cost-effective screening test.

Acknowledgment

The authors would like to thank to Doctor Mehmet Tutar and TUSAD(Turkey Respiratory Research Society) Academy for contribution about radiologic evaluation; statistical analysis, technical support and language support respectively.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Rademacher J, Welte T. Bronchiectasis – Diagnosis and treatment. Dtsch Arztebl Int 2011;108:809-15.
2. Pande JN, Jain BP, Gupta RG, Guleria JS. Pulmonary ventilation and gas exchange in bronchiectasis. Thorax 1971;26:727-33.
3. Goeminne P, Dupont L. Non-cystic fibrosis bronchiectasis: Diagnosis and management in 21st century. Postgrad Med J 2010;86:493-501.
4. O'Donnell AE. Bronchiectasis in patients with COPD: A distinct COPD phenotype? Chest 2011;140:1107-8.
5. Ni Y, Shi G, Yu Y, Hao J, Chen T, Song H. Clinical characteristics of patients with chronic obstructive pulmonary disease with comorbid bronchiectasis: A systemic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2015;10:1465-75.
6. Jordan TS, Spencer EM, Davies P. Tuberculosis, bronchiectasis and chronic airflow obstruction. Respirology 2010;15:623-8.
7. Roberts HR, Wells AU, Milne DG, Rubens MB, Kolbe J, Cole PJ, *et al*. Airflow obstruction in bronchiectasis: Correlation between computed tomography features and pulmonary function tests. Thorax 2000;55:198-204.
8. Keistinen T, Säynäjäkangas O, Tuuponen T, Kivelä SL. Bronchiectasis: An orphan disease with a poorly-understood prognosis. Eur Respir J 1997;10:2784-7.
9. Evans SA, Turner SM, Bosch BJ, Hardy CC, Woodhead MA. Lung function in bronchiectasis: The influence of pseudomonas aeruginosa. Eur Respir J 1996;9:1601-4.
10. Nicotra MB, Rivera M, Dale AM, Shepherd R, Carter R. Clinical, pathophysiologic, and microbiologic characterization of bronchiectasis in an aging cohort. Chest 1995;108:955-61.
11. King PT, Holdsworth SR, Freezer NJ, Villanueva E, Gallagher M, Holmes PW, *et al*. Outcome in adult bronchiectasis. COPD 2005;2:27-34.
12. Global Strategy for the Diagnosis, Management and Prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Available from: http://www.goldcopd.org/2017. [Last accessed on 2016 Nov 28].
13. Kim JK, Lee SH, Lee BH, Lee CY, Kim do J, Min KH, *et al*. Factors associated with exacerbation in mild- to-moderate COPD patients. Int J Chron Obstruct Pulmon Dis 2016;11:1327-33.
14. Bartlett JG, Ryan KJ, Smith TF, Wilson WR. Laboratory Diagnosis of Lower Respiratory Tract İnfections. Cumitech 7A. Washington, DC: American Society for Microbiology; 1987. p. 9-10.
15. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al*. Standardisation of spirometry. Eur Respir J 2005;26:319-38.
16. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, european community for steel and coal. Official statement of the european respiratory society. Eur Respir J Suppl 1993;16:5-40.
17. Al-Jahdali H, Alshimemeri A, Mobeireek A, Albanna AS, Al Shirawi NN, Wali S, *et al*. The Saudi thoracic society guidelines for diagnosis and management of noncystic fibrosis bronchiectasis. Ann Thorac Med 2017;12:135-61.
18. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, *et al*. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med 2014;189:576-85.
19. Takahashi M, Fukuoka J, Nitta N, Takazakura R, Nagatani Y, Murakami Y, *et al*. Imaging of pulmonary emphysema: A pictorial review. Int J Chron Obstruct Pulmon Dis 2008;3:193-204.
20. Zielinski J, MacNee W, Wedzicha J, Ambrosino N, Braghiroli A, Dolensky J, *et al*. Causes of death in patients with COPD and chronic respiratory failure. Monaldi Arch Chest Dis 1997;52:43-7.
21. Martínez-García MA, de la Rosa Carrillo D, Soler-Cataluña JJ, Donat-Sanz Y, Serra PC, Lerma MA, *et al*. Prognostic value of bronchiectasis in patients with moderate-to-severe chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2013;187:823-31.
22. Kitaguchi Y, Fujimoto K, Kubo K, Honda T. Characteristics of COPD phenotypes classified according to the findings of HRCT. Respir Med 2006;100:1742-52.
23. Tulek B, Kivrak AS, Ozbek S, Kanat F, Suerdem M. Phenotyping of chronic obstructive pulmonary disease using the modified Bhalla scoring system for high-resolution computed tomography. Can Respir J 2013;20:91-6.
24. Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman BS, McCauley DI, *et al*. Cystic fibrosis: Scoring system with thin-section CT. Radiology 1991;179:783-8.
25. Guan WJ, Gao YH, Xu G, Lin ZY, Tang Y, Li HM, *et al*. Characterization of lung function impairment in adults with bronchiectasis. PLoS One 2014;9:e113373.

26. Bhowmik A, Seemungal TA, Sapsford RJ, Wedzicha JA. Relation of sputum inflammatory markers to symptoms and lung function changes in COPD exacerbations. Thorax 2000;55:114-20.
27. Salkın D. Tuberculosis as a cause of upper lobe bronchiectasis. Calif Med 1950;73:577-80.
28. Martínez-García MÁ, Soler-Cataluña JJ, Donat Sanz Y, Catalán Serra P, Agramunt Lerma M, Ballestín Vicente J, *et al.* Factors associated with bronchiectasis in patients with COPD. Chest 2011;140:1130-7.
29. Bafadhel M, Umar I, Gupta S, Raj JV, Vara DD, Entwisle JJ, *et al.* The role of CT scanning in multidimensional phenotyping of COPD. Chest 2011;140:634-42.
30. Lopes AJ, Camilo GB, de Menezes SL, Guimarães FS. Impact of different etiologies of bronchiectasis on the pulmonary function tests. Clin Med Res 2015;13:12-9.
31. Gursel G. Does coexistence with bronchiectasis influence intensive care unit outcome in patients with chronic obstructive pulmonary disease? Heart Lung 2006;35:58-65.
32. Tulek B. Co-occurrence of chronic obstructive pulmonary disease and bronchiectasis: Is ıt a new phenotype of chronic obstructive pulmonary disease? Eurasian J Pulmonol 2014;16:8-12.
33. Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, *et al.* Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med 2010;363:1128-38.
34. Miravitlles M, Calle M, Soler-Cataluña JJ. Clinical phenotypes of COPD: Identification, definition and implications for guidelines. Arch Bronconeumol 2012;48:86-98.
35. Patel IS, Seemungal TA, Wilks M, Lloyd-Owen SJ, Donaldson GC, Wedzicha JA. Relationship between bacterial colonisation and the frequency, character, and severity of COPD exacerbations. Thorax 2002;57:759-64.
36. Tatar D, Senol G, Anar C, Tibet G. Markers of lower respiratory tract infections in emergency departments. Multidiscip Respir Med 2013;8:20.
37. Engel MF, Paling FP, Hoepelman AI, van der Meer V, Oosterheert JJ. Evaluating the evidence for the implementation of C-reactive protein measurement in adult patients with suspected lower respiratory tract infection in primary care: A systematic review. Fam Pract 2012;29:383-93.
38. Celli BR, Barnes PJ. Exacerbations of chronic obstructive pulmonary disease. Eur Respir J 2007;29:1224-38.
39. Burge S, Wedzicha JA. COPD exacerbations: Definitions and classifications. Eur Respir J Suppl 2003;41:46s-53s.
40. Gatheral T, Kumar N, Sansom B, Lai D, Nair A, Vlahos I, *et al.* COPD-related bronchiectasis; independent impact on disease course and outcomes. COPD 2014;11:605-14.
41. Du Q, Jin J, Liu X, Sun Y. Bronchiectasis as a comorbidity of chronic obstructive pulmonary disease: A systematic review and meta-analysis. PLoS One 2016;11:e0150532.