ORIGINAL RESEARCH

The objective evaluation of obstructive pulmonary diseases with spirometry

Sevket Ozkaya[1]
Adem Dirican[2]
Tibel Tuna[3]

[1]Department of Pulmonary Medicine, Faculty of Medicine, Bahçeşehir University, Istanbul, [2]Department of Pulmonary Medicine, Samsun Medical Park Hospital, [3]Department of Pulmonary Medicine, Samsun Chest Diseases and Thoracic Surgery Hospital, Samsun, Turkey

Abstract: Airway obstruction is variable in asthma, while it is progressive and persistent in chronic bronchitis and emphysema. However, some of the patients presenting with symptoms of chronic airway diseases have clinical features of both asthma and COPD. The group with "Asthma–COPD Overlap Syndrome" (ACOS) phenotype was characterized by definitely irreversible airway obstruction accompanied by symptoms and signs of reversibility. In this study, we aimed to classify obstructive airway diseases by clinical, radiological, and pulmonary function tests. Patients at Samsun Medical Park Hospital Chest Diseases outpatient clinic were evaluated between January 2013 and April 2016, and a total of 235 patients were included in this study. Mean age of the patients was 55.3 ± 14.5 (15–88) years, and the male/female ratio was 45/190. The baseline pulmonary function test results of the patients were as follows: mean forced vital capacity (FVC) values $2,825 \pm 1,108$ (710–6,870) mL and 74.3 ± 22.4 (24–155)%, forced expiratory volume in 1 second (FEV_1) values $1,789 \pm 774$ (480–4,810) mL and 58.1 ± 20.0 (20–130)%, FEV_1/FVC values 62.5 ± 6.8 (39–70)%. Reversibility criteria following bronchodilator treatment were present in 107 (45.5%) patients. We specified five subgroups for patients according to their clinical, radiological, and pulmonary test findings, namely Group 1 (asthma), Group 2 (ACOS), Group 3 (chronic bronchitis), and Group 4 (emphysema). Additionally, a group of patients who had clinical and spirometric features of both asthma and chronic bronchitis in association with underlying emphysema (emphysema with chronic bronchitis and emphysema with asthma) was defined as the undifferentiated obstruction (UNDO) group. Number and percentage distribution of patients by groups were 58 (24.7%) in the asthma group, 70 (29.8%) in the ACOS group, 61 (26%) in the chronic bronchitis group, 32 (13.6%) in the emphysema group, and 14 (6%) in the UNDO group. In conclusion, in our study, the types of obstructive airway diseases could be classified based on clinical, radiological, and pulmonary function test findings into five groups, including asthma, ACOS, chronic bronchitis, emphysema, and both asthma and chronic bronchitis in association with underlying emphysema (emphysema with chronic bronchitis and emphysema with asthma) or the so-called undifferentiated obstruction. We suggest that these patient groups can be determined more accurately by studies that evaluate the association between spirometric FEV_1, FEV_1/FVC values, and reversibility ratios.

Keywords: asthma, COPD, asthma–COPD overlap syndrome, reversibility, spirometry

Introduction

Asthma, chronic bronchitis, and emphysema are the most common pulmonary diseases worldwide characterized by chronic airway inflammation and airway obstruction. Airway obstruction is variable in asthma, while it is progressive and persistent in chronic bronchitis and emphysema. However, some of the patients presenting with symptoms of chronic airway diseases have clinical features of both asthma and COPD. Furthermore, both diseases have overlapping pathological and functional characteristics. Although such patients are commonly described as "asthmatic

Correspondence: Sevket Ozkaya
Cıragan Caddesi, Osmanpasa Mektebi Sokak No 4–6, 34349 Beşiktaş, Istanbul, Turkey
Tel +90 532 474 1309
Email ozkayasevket@yahoo.com

bronchitis" or "asthmatic form of COPD" in the US, the term "Asthma–COPD Overlap Syndrome" (ACOS) is recently being used to describe these patients.[1,2]

In this study, we aimed to classify obstructive airway diseases by clinical, radiological, and pulmonary function tests.

Patients and methods

Patients at Samsun Medical Park Hospital Chest Diseases outpatient clinic were evaluated between January 2013 and April 2016 and included in this study. The inclusion criteria were symptomatic patients (cough, dyspnea, and/or wheezing); presence of airway obstruction in spirometry (forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] $\leq$70% of expected); patients who had never used bronchodilators before; or patients who had not received short- or long-acting inhaled bronchodilator therapy within the recent 12 hours. The basal and postbronchodilator FVC, FEV_1, and FEV_1/FVC values were measured using the MIR MiniSpir PC-Based USB Spirometer by the same physician (SO) following a 30-minute resting period in an outpatient clinic setting. The test must be performed in the seated position, when the nose is clamped and nasal respiration is hindered. The patients performed the forced expiratory maneuver at least three times and the maximum FEV_1 value was recorded as the basal value. Reversibility levels were evaluated as the absolute change in FEV_1 and the percentage of change from the initial FEV_1, calculated as FEV_1%Δinit: post-FEV_1 − pre-FEV_1/pre-FEV_1 ×100 (according to American Thoracic Society guidelines), and bronchial reversibility is defined as a drug-induced increase in FEV_1 of $\geq$200 mL and $\geq$12% baseline. Results are presented as mean ± standard errors of mean values.

Ethical statement

The study was performed in accordance with the ethical principles of the Good Clinical Practice guidelines and with applicable local regulatory requirements. The protocol was approved by Medical Park Hospital Institutional Review Board. All patients read the patient information form about the study procedure, and written informed consents were obtained.

Results

A total of 235 patients were included in this study. Patient characteristics are presented in Table 1. Mean age of the patients was 55.3±14.5 (15–88) years, and male/female ratio was 190/45. Mean body mass index values were 27.3±5.2 (15.1–44.3). Nonsmokers constituted 19.6% of the patients, while 34% were ex-smokers and 46.4% were current smokers. The baseline pulmonary function test results of

Table 1 Characteristics of patients

Characteristics	Values
Age (years), mean ± SD (min–max)	55.3±14.5 (15–88)
Male/female	190 (80.9%)/45 (19.1%)
BMI; mean ± SD (min–max)	27.3±5.2 (15.1–44.3)
Smoking status	
Nonsmoker, n (%)	46 (19.6)
Current smoker, n (%)	109 (46.4)
Ex-smoker, n (%)	80 (34)
Baseline spirometry	
FVC (mL)	
Mean ± SD (min–max)	2,825±1,108 (710–6,870)
%Predicted ± SD (min–max)	74.3±22.4 (24–155)
FEV_1 (mL)	
Mean ± SD (min–max)	1,789±774 (480–4,810)
%Pred ± SD (min–max)	58.1±20.0 (20–130)
FEV_1/FVC	
%Pred ± SD (min–max)	62.5±6.8 (39–70)

Abbreviations: BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; min, minimum; max, maximum; Pred, Predicted.

the patients were as follows: mean FVC values 2,825±1,108 (710–6,870) mL and 74.3±22.4 (24–155)%, FEV_1 values 1,789±774 (480–4,810) mL and 58.1±20.0 (20–130)%, and FEV_1/FVC values 62.5±6.8 (39–70)%. Reversibility criteria following bronchodilator treatment were present in 107 (45.5%) patients. We specified five subgroups for patients according to their clinical, radiological, and pulmonary test findings, namely Group 1 (asthma), Group 2 (ACOS), Group 3 (chronic bronchitis), and Group 4 (emphysema). Additionally, a group of patients who had clinical and spirometric features of both asthma and chronic bronchitis in association with underlying emphysema (emphysema with chronic bronchitis [EWCB] and emphysema with asthma [EWA]) was defined as the undifferentiated obstruction (UNDO) group. Number and percentage distribution of patients by groups were 58 (24.7%) in the asthma group, 70 (29.8%) in the ACOS group, 61 (26%) in the chronic bronchitis group, 32 (13.6%) in the emphysema group, and 14 (6%) in the UNDO group (Table 2). The epidemiological and

Table 2 Groups and reversibility ratios of patients

Types	n (%)
Asthma	58 (24.7)
ACOS	70 (29.8)
Chronic bronchitis	61 (26)
Emphysema	32 (13.6)
UNDO	14 (6)
EWA	4 (28.6)
EWCB	10 (71.4)
Reversibility	
Yes	107 (45.5)
No	128 (54.5)

Abbreviations: ACOS, Asthma–COPD Overlap Syndrome; UNDO, undifferentiated obstruction; EWA, emphysema with asthma; EWCB, emphysema with chronic bronchitis.

Table 3 The demographic and spirometric results of groups

Characteristics	Asthma	ACOS	Chronic bronchitis	Emphysema	UNDO
Age (years), mean ± SD	39.1±14.5	57.9±10.4	59.1±8.3	66.2±9.6	67.9±6.1
Male/female	37/21	62/8	47/14	32/0	12/2
BMI; mean ± SD	27.2±5.4	28.3±4.9	27.5±5	24.5±4.2	27.5±7.3
Smoking status					
Nonsmoker, n (%)	26 (44.8)	6 (8.6)	12 (19.7)	0	2 (14.3)
Current smoker, n (%)	29 (50)	38 (54.3)	28 (45.9)	11 (34.4)	3 (21.4)
Ex-smoker, n (%)	3 (5.2)	26 (37.1)	21 (34.4)	21 (65.6)	9 (64.3)
Baseline spirometry					
FVC (mL)					
Mean ± SD	3,442±1,294	2,777±1,047	2,719±881	2,331±783	2,105±989
%Pred ± SD	83±22.1	72±21.3	76.2±23.4	64.8±19.2	63.5±19
FEV_1 (mL)					
Mean ± SD	2,248±894	1,724±690	1,765±662	1,374±588	1,273±685
%Pred ± SD	64.6±19.0	55.7±18	61.9±21.7	48.5±18.5	48.7±18.4
FEV_1/FVC					
%Pred ± SD	64.7±5.7	61.7±6.3	64.4±6.1	57.5±7.7	59.6±7.1

Abbreviations: ACOS, Asthma–COPD Overlap Syndrome; UNDO, undifferentiated obstruction; BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; Pred, Predicted.

spirometric features of each group are presented in Table 3. The reversibility rates of the patients were 19%±13.3% for the asthma group, 26.4%±16.1% for the ACOS group, 8.2%±10.1% for the chronic bronchitis group, 6.5%±12.5% for the emphysema group, and 15.7%±10.4% for the UNDO group. Postbronchodilator FEV_1 values were as follows: asthma group 75.5%±20.2%, ACOS group 68.5%±17.7%, chronic bronchitis group 65.9%±22.3%, emphysema group 50.4%±18.8%, and UNDO group 55.5%±19%. Postbronchodilator FEV_1/FVC values were as follows: asthma group 70%±11.1%, ACOS group 66.7%±8.1%, chronic bronchitis group 66.6%±7.5%, emphysema group 57.0%±10.4%, and UNDO group 58.5%±10.2% (Table 4). Figures 1 and 2 present the distribution of patients according to the relationship between postbronchodilator change in FEV_1% and basal FEV_1% in groups and the relationship between postbronchodilator change in FEV_1/FVC% and basal FEV_1/FVC in groups. We aimed for an objective classification of patients according to spirometric results in diagrams and hence created

3D MATLAB diagrams. Basal and postbronchodilator spirometric results are presented in Figures 3–5.

Discussion

Obstructive lung diseases are characterized by reduced airflow related to increased resistance caused by airway narrowing. Such obstructions cause respiratory symptoms including dyspnea, cough, sputum, and wheezing and may occur either directly by narrowing of the airway lumen or by decreased elasticity of the parenchyma surrounding the airways. FEV_1 and FEV_1/FVC values of the spirometric test are the best indicators for airway obstruction.[3] Asthma is diagnosed based on characteristic symptoms including wheezing, dyspnea, and cough and presence of variable airway obstruction, while COPD is characterized by definitely irreversible and progressive airway obstruction.[4] Spirometry is required for the diagnosis and evaluation of COPD. In COPD-suspected patients, if the ratio of FEV_1 to FVC following bronchodilator administration is <70%, airway

Table 4 The reversibility and postbronchodilator results of groups

Characteristics	Asthma	ACOS	Chronic bronchitis	Emphysema	UNDO
Reversibillity					
Yes, n (%)	42 (72.4)	60 (85.7)	1 (1.6)	0	4 (28.5)
Change (mL), mean ± SD	375±227	382±168	106±62	51±44	172±109
Change, %pred ± SD	19±13.3	26.4±16.1	8.2±10.1	6.5±12.5	15.7±10.4
Postbronchodilator values					
FEV_1, %pred ± SD	75.5±20.2	68.5±17.7	65.9±22.3	50.4±18.8	55.5±19
FEV_1/FVC, %pred ± SD	70±11.1	66.7±8.1	66.6±7.5	57.0±10.4	58.5±10.2

Abbreviations: ACOS, Asthma–COPD Overlap Syndrome; UNDO, undifferentiated obstruction; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; pred, predicted.
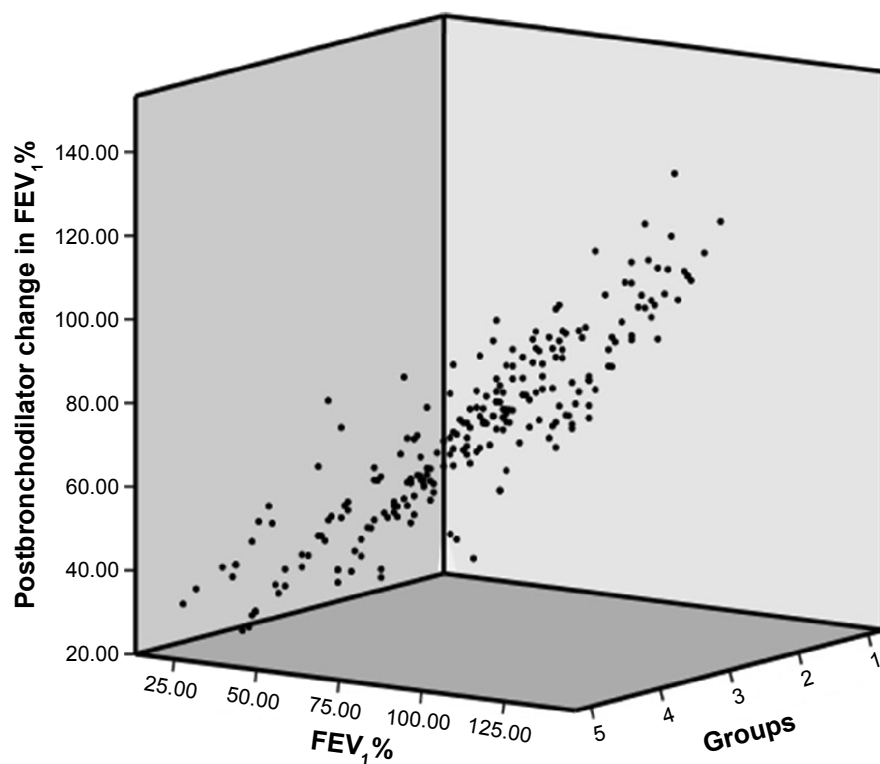
Figure 1 Distribution of patients.
Notes: The relationship between postbronchodilator change in FEV_1% and basal FEV_1% in groups: Group 1 (asthma), Group 2 (ACOS), Group 3 (chronic bronchitis), Group 4 (emphysema), and Group 5 (UNDO).
Abbreviations: ACOS, Asthma–COPD Overlap Syndrome; UNDO, undifferentiated obstruction; FEV_1, forced expiratory volume in 1 second.
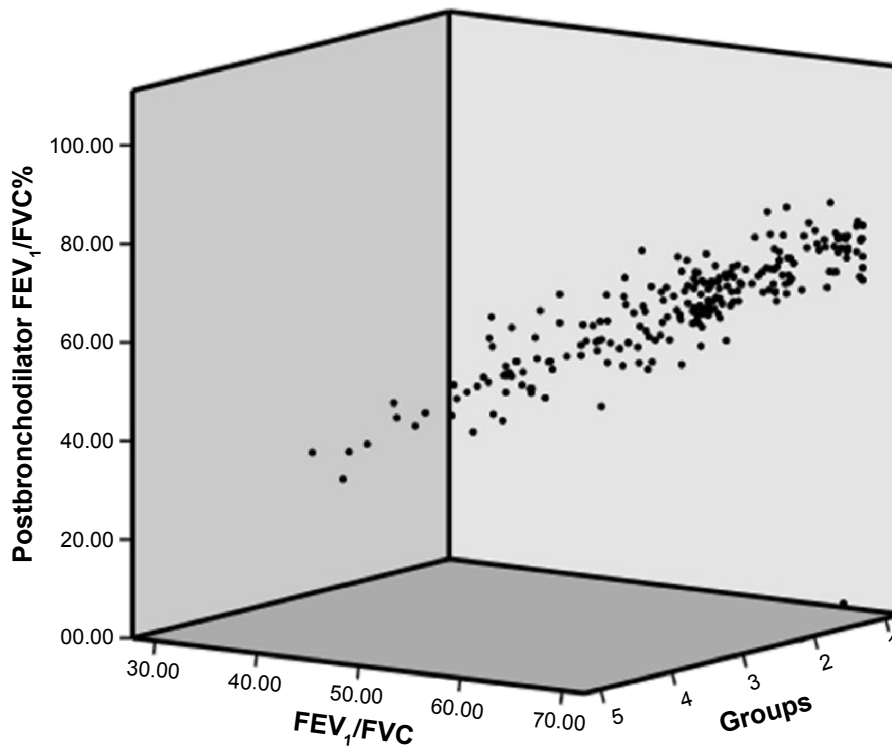

Figure 2 Distribution of patients.
Notes: The relationship between postbronchodilator change in FEV_1/FVC% and basal FEV_1/FVC in groups: Group 1 (asthma), Group 2 (ACOS), Group 3 (chronic bronchitis), Group 4 (emphysema), and Group 5 (UNDO).
Abbreviations: ACOS, Asthma–COPD Overlap Syndrome; UNDO, undifferentiated obstruction; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
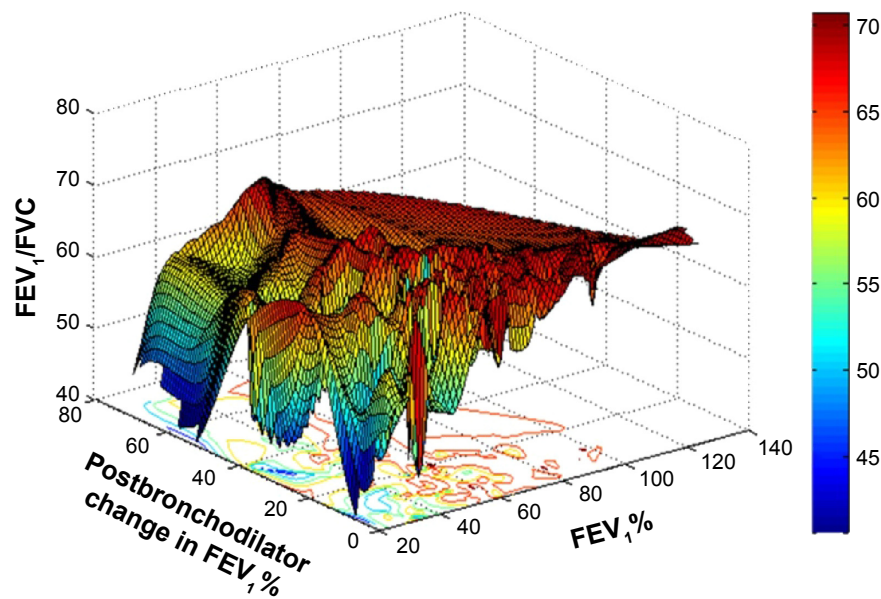
Figure 3 The MATLAB 3D figure showing the relationship between FEV_1, postbronchodilator change in FEV_1%, and basal FEV_1% of patients.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

obstruction is confirmed and the patient is considered to have COPD. COPD is primarily classified as chronic bronchitis or emphysema. "Chronic bronchitis" phenotype, in accordance with the manifestations of chronic bronchitis, describes the patients who had expectoration and cough for 3 months or longer particularly in winter months of two consecutive years. Mucous secretions in COPD lead to excessive airway inflammation and thus cause respiratory infections, which

results in further exacerbations in the chronic bronchitis phenotype. "Emphysema" phenotype patients are those who have clinical, radiological, and functional findings of emphysema and whose primary complaints are dyspnea and activity limitation. Emphysema patients generally have low body mass index, as determined in our study. This phenotype description and radiological emphysema diagnosis should be separated as various degrees of emphysema can
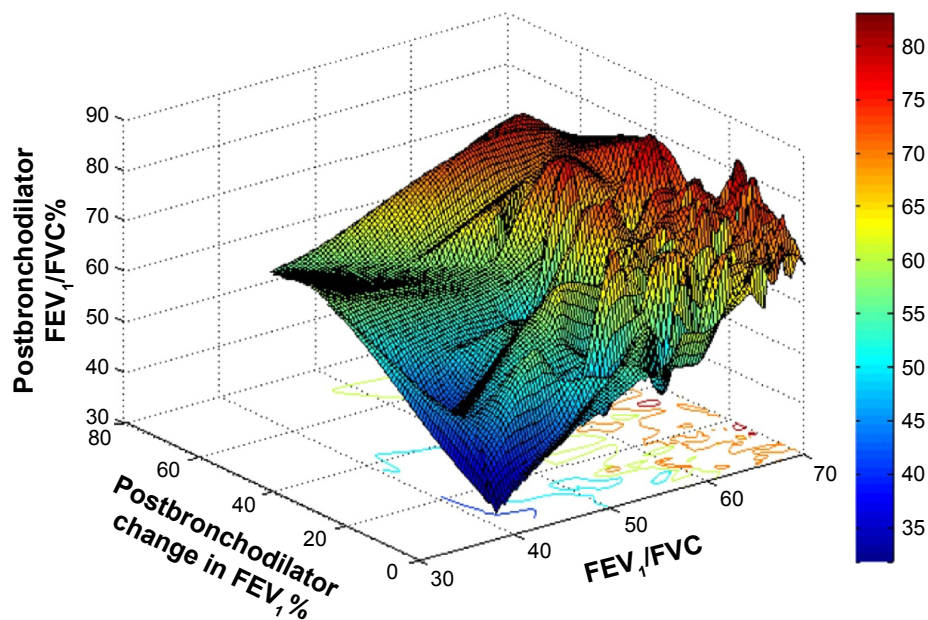

Figure 4 The MATLAB 3D figure showing the relationship between postbronchodilator FEV_1/FVC%, postbronchodilator change in FEV_1%, and basal FEV_1/FVC% of patients.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
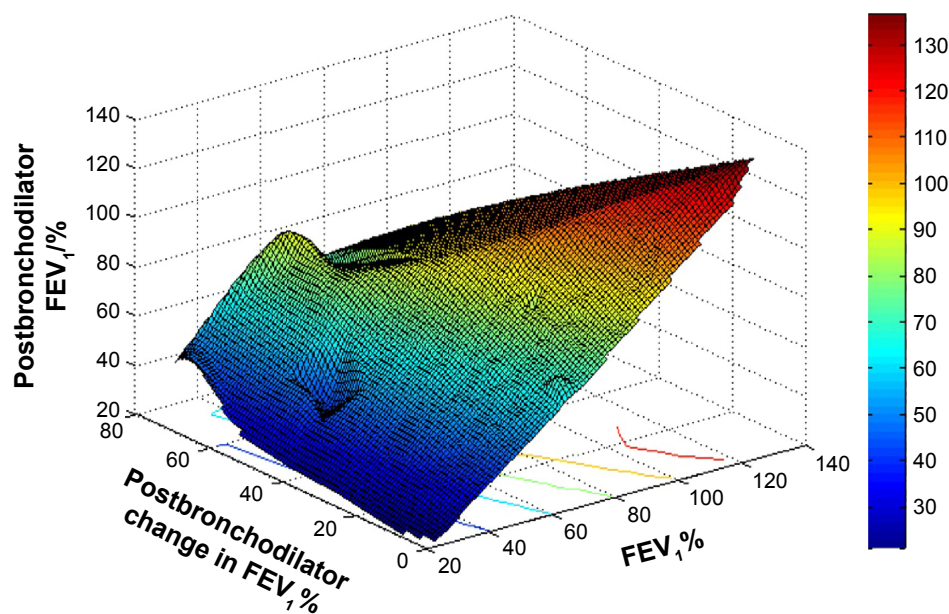
Figure 5 The MATLAB 3D figure showing the relationship between postbronchodilator FEV$_1$%, postbronchodilator change in FEV$_1$%, and basal FEV$_1$% of patients.
Abbreviation: FEV$_1$, forced expiratory volume in 1 second.

be detected on radiological examinations in patients who have airway obstruction.[3] In our patient series, the patients who had clinical and spirometric features of both asthma and chronic bronchitis in association with underlying emphysema were described as the UNDO group, which constituted 6% of the patients. The patients in this group (UNDO) have severe parenchymal damage, airway obstruction, and disability.

The group with "ACOS" phenotype was characterized by definitely irreversible airway obstruction accompanied by symptoms and signs of reversibility. Various guidelines have also described significant asthma component in COPD patients or asthma-complicated COPD. The terms "Asthmatiform Bronchitis" and "Asthmatic form of COPD" were used to describe such patients in the US, and the term "Asthma–COPD Overlap Syndrome" (ACOS) is recently being used. In our study, this group included the largest number of patients who had the highest value and ratio of reversibility. Despite high reversibility values, postbronchodilator mean FEV$_1$ value was <80% and FEV$_1$/FVC value was <70%.[5–8] In 2012, Soler-Cataluña et al have described the "COPD–asthma overlap" phenotype with the presence of at least two of the major and minor criteria: major criteria were very high reversibility test (FEV$_1$ ≥15%; ≥400 mL), eosinophilia in sputum, and history of asthma. Minor criteria included positive reversibility test (FEV$_1$ ≥12%; ≥200 mL), increased IgE, and history of atopy.[9]

The major criteria for ACOS described by Louie et al[10] in 2013 included both asthma and COPD diagnosed in the patient by the same doctor, presence or history of atopy (eg, allergic rhinitis), increased IgE, age ≥40 years, >10 pack-years smoking, postbronchodilator FEV$_1$ <80% predicted, and FEV$_1$/FVC <70%, while the minor criteria were postbronchodilator ≥15%, ≥12%, and >200 mL increase in FEV$_1$. Results of our study were compatible with these results. The relation between FEV$_1$, FEV$_1$/FVC values, and reversibility by the patient groups is presented in Figures 1–5. The objective classifications of obstructive pulmonary diseases can be done by formulating more than two spirometric variables according to basal and postbronchodilator results.

According to Global initiative for chronic Obstructive Lung Disease (GOLD) consensus, four different phenotypes including combinations of emphysema, chronic bronchitis, frequently exacerbating, and COPD–asthma co-occurrence were described in the Spanish COPD Guidelines published in 2012: 1) chronic bronchitis or emphysema co-occurrence without frequent exacerbations, 2) COPD–asthma co-occurrence, 3) emphysema domination with frequent exacerbations, and 4) chronic bronchitis domination with frequent exacerbations. Patients who were described within as COPD–asthma co-occurrence phenotype were first described under the term "Asthma–COPD Overlap Syndrome" in GOLD 2014; although this syndrome was described for patients

with this co-occurrence, having frequent exacerbations, reduced quality of life, and faster lung function loss, the definitive criteria are not clear.[3] Postbronchodilator spirometry is required for diagnosis and grading disease severity. Reversibility testing is not recommended since measuring reversibility has not contributed to differential diagnosis from asthma or determining long-term response to bronchodilator or corticosteroid treatments. However, in relation to the new definition of ACOS, we believe reversibility level could be a significant determinant and should be performed for patients with airway obstruction.

Conclusion

In our study, the types of obstructive airway diseases could be classified based on clinical, radiological, and pulmonary function test findings into five groups including asthma, ACOS, chronic bronchitis, emphysema, and both asthma and chronic bronchitis in association with underlying emphysema (EWCB and EWA) or the so-called undifferentiated obstruction (UNDO). We suggest that these patient groups can be determined more accurately by studies that evaluate the association between spirometric FEV_1, FEV_1/FVC values, and reversibility ratios.

Disclosure

The authors report no conflicts of interest in this work.

References

1. GOLD [homepage on the Internet]. *Diagnosis of Diseases of Chronic Airflow Limitation: Asthma, COPD and Asthma-COPD Overlap Syndrome (ACOS) GINA*. GOLD; 2016. Available from: http://www.goldcopd.org. Accessed July 23, 2016.
2. Nakawah MO, Hawkins C, Barbandi F. Asthma, chronic obstructive pulmonary disease (COPD), and the overlap syndrome. *J Am Board Fam Med*. 2013;26(4):470–477.
3. GOLD [homepage on the Internet]. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2014. Available from: http://www.goldcopd.org/. Accessed July 23, 2016.
4. Global Initiative for Asthma [homepage on the Internet]. *Global Strategy for Asthma Management and Prevention*. 2014. Available from: www.ginasthma. Accessed July 23, 2016.
5. Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it? *Thorax*. 2009;64(8): 728–735.
6. Miravitlles M. The overlap syndrome between asthma and COPD: implications for management. *Hot Top Respir Med*. 2011;16:15–20.
7. Qaseem A, Wilt TJ, Weinberger SE, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med*. 2011;155(3):179–191.
8. Albert P, Agusti A, Edwards L, et al. Bronchodilator responsiveness as a phenotypic characteristic of established chronic obstructive pulmonary disease. *Thorax*. 2012;67(8):701–708.
9. Soler-Cataluña JJ, Cosío B, Izquierdo JL, et al. Consensus document on the overlap phenotype COPD-asthma in COPD. *Arch Bronconeumol*. 2012;48(9):331–337.
10. Louie S, Zeki AA, Schivo M, et al. The asthma-chronic obstructive pulmonary disease overlap syndrome: pharmacotherapeutic considerations. *Expert Rev Clin Pharmacol*. 2013;6(2):197–219.