ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

Relationship between disease severity and atrial fibrillation in chronic obstructive pulmonary disease

Kronik obstrüktif akciğer hastalığında hastalık şiddeti ile atriyal fibrilasyon arasındaki ilişki

Ekrem Şahan, M.D.[1], Sertan Bulut, M.D.[2]

[1]Department of Cardiology, Atatürk Chest Disease and Thorasic Surgery Training and Research Hospital, Ankara, Turkey
[2]Department of Pulmonology, Atatürk Chest Disease and Thorasic Surgery Training and Research Hospital, Ankara Turkey

ABSTRACT

Objective: The aim of this study was to elucidate the relationship between atrial fibrillation (AF) and chronic obstructive pulmonary disease (COPD) classification based on clinical severity determined in current guidelines. AF is the most common chronic arrhythmia that requires treatment. COPD is one of the risk factors for AF, but this relationship was only explored through respiratory function test results.
Methods: Patients who received inpatient treatment for COPD between November 2019 and January 2017 were screened. Patients with coronary artery disease, heart failure, valvular heart disease, diabetes, chronic kidney disease, hypertension, thyroid dysfunction, and sleep apnea syndrome were excluded. According to the 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, patients with COPD were divided into groups A, B, C, and D, and the relationship between AF and these groups was investigated.
Results: There was no difference between the two groups (depending on the presence of AF) in terms of sex and body mass index. There was a significant difference between the two groups in terms of age, left ventricular ejection fraction (LVEF), left atrium, right atrium, right ventricle, and systolic pulmonary artery pressure. When patients with COPD were classified according to clinical and symptomatic severity, the frequency of AF increased as the clinical severity increased.
Conclusion: Regardless of the forced expiratory volume – first second (FEV_1) value in the respiratory test, the incidence of AF is higher in patients with COPD with a clinically more severe picture.

ÖZET

Amaç: Atriyal fibrilasyon (AF), en sık görülen tedavi gerektiren kronik aritmidir. Kronik obstruktif akciğer hastalığı (KOAH), AF için risk faktörlerinden biridir, ancak bu ilişki sadece solunumu fonksiyon testi sonuçları üzerinden irdelenmiştir. Çalışmadaki amacımız güncel kılavuzlarda belirlenen klinik ciddiyete bağlı KOAH sınıflaması ile AF arasındaki ilişkinin aydınlatılmasıdır.
Yöntemler: Kasım 2019 ve Ocak 2017 arasında KOAH nedeni ile yatarak tedavi alan hastalar tarandı. Koroner arter hastalığı, kalp yetersizliği, kalp kapak hastalığı, diyabet, kronik böbrek hastalığı, hipertansiyon, tiroid disfonksiyonu ve uyku apne sendromu olan hastalar dışlandı. 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) kılavuzuna göre KOAH hastaları A,B,C ve D gruplarına ayrıldı ve bu gruplar ile AF ilişkisi araştırıldı.
Bulgular: Cinsiyet ve beden kitle indeksi açısından iki grup arasında fark yoktu. Yaş, LVEF, sol atrium, sağ atrium, sağ ventrikül ve SPAB açısında her iki grup arasında anlamlı fark mevcuttu. Klinik ve semptomatik ciddiyete göre KOAH hastaları sınıflandırıldığında, klinik ciddiyet arttıkça AF sıklığı artmaktaydı.
Sonuç: Solunum testindeki FEV_1 değerinden bağımsız olarak, klinik olarak daha ciddi tabloya sahip KOAH olgularında AF görülme sıklığı daha fazladır.

Atrial fibrillation (AF) is the most common type of chronic arrhythmia that requires treatment in clinical practice. Coronary artery disease, heart failure, valvular heart diseases, hypertension, diabetes, hyperthyroidism, chronic renal failure, obesity are predisposing factors for AF.[1-3] In addition, chronic obstructive pulmonary disease (COPD) is one of the most common diseases of the respiratory system and is a predisposing factor for AF.[4] In a previous study that guided the European Society of Cardiology (ESC) guideline, the relationship between COPD severity and AF was demonstrated with forced expiratory volume – first second (FEV_1) value. The diagnosis and treatment of COPD is made with the recommendations in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[5]

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Correspondence: Ekrem Şahan, M.D., Department of Cardiology, Atatürk Chest Disease and Thorasic Surgery Training and Research Hospital, Ankara, Turkey
Tel: +90 533 353 88 32 e-mail: ekremsahan@hotmail.com

In the GOLD guidelines, determining the severity of COPD disease and treating COPD is performed with A-B-C-D classification as well as FEV_1 values. In ABCD classification, in addition to hospitalization for COPD attacks the patient's symptomatic condition was also assessed. Our aim in this study was to elucidate the relationship between AF and the severity of COPD disease (using the ABCD classification in the GOLD guidelines) by excluding the predisposing factors mentioned above.

METHODS

In this retrospective study, the files of 1454 patients hospitalized with COPD between January 2017 and November 2019 were scanned. Patients who did not have an electrocardiogram (ECG) in their file were excluded from the study. Patients with coronary artery disease, heart failure, valvular heart disease, diabetes, hypertension, obstructive sleep apnea syndrome, thyroid dysfunction, and chronic kidney disease, which are predisposing to AF, were excluded from the study. The study population was evaluated under two groups as those with AF and those without AF.

The Modified Medical Research Council Dyspnea Score and the ABCD classification (Table 1) calculated on the number of COPD exacerbations and hospitalizations were used to assess the severity of the COPD clinical condition. When calculating the Modified Medical Research Council Dyspnea Score, values used were 0=dyspnea only in a severe strenuous exercise; 1=dyspnea when walking fast or climbing uphill; 2=walking slower than a healthy individual in his age, needing rest due to dyspnea; 3=resting due to dyspnea with 100-m walking need; 4=significant dyspnea in daily movements such as dressing. Later, patients were divided into four groups, A, B, C, and D, according to disease attacks, hospitalization, and dyspnea score (Table 1). Based on the number of COPD attacks and hospitalizations, groups A and B were considered as patients with mild COPD, and groups C and D were accepted as patients with severe COPD (Table 2).

Twelve-lead ECG recordings were classified as AF and sinus rhythm. As the study was conducted retrospectively—regardless of whether it was paroxysmal persistent or permanent—patients with AF detected in the 12-lead ECG were included in the AF group. In echocardiography, left ventricular ejection fraction (LVEF) was measured using the modified Simpson method, and pulmonary artery systolic pressure was calculated over the tricuspid regurgitant flow. Right ventricle (RV) basal diameter greater than 41 mm indicates RV enlargement, right atrium (RA) diameter greater than 45 mm indicates RA enlargement, and left atrium (LA) diameter greater than 40 mm indicates LA enlargement.

Abbreviations:

AF	*Atrial fibrillation*
BMI	*Body mass index*
COPD	*Chronic obstructive pulmonary disease*
ECG	*Electrocardiogram*
ESC	*European Society of Cardiology*
FEV_1	*Forced expiratory volume*
GOLD	*Global Initiative for Chronic Obstructive Lung Disease*
LA	*Left atrium*
LVEF	*Left ventricular ejection fraction*
mMRC	*Modified Medical Research Council dyspnea questionnaire*
RA	*Right atrium*
RV	*Right ventricle*
SPAP	*Systolic pulmonary artery pressure*

This retrospective study was conducted in compliance with the regulations and ethical guidelines for retrospective research and approved by the Keçiören Training and Research Hospital Ethical Committee on December 22, 2020 (no: 2012-KAEK-15/2207).

Statistical analysis

SPSS for Windows version 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Normal distribution analysis of the data was interpreted with skewness and kurtosis values. Continuous variables were expressed as mean±standard deviation and categorical variables were expressed as percentages. Continuous data were compared using Student's t test. Categorical data were compared using the chi-square test. Pearson's correlation coefficient was used for correlation analysis. A value of $p<0.05$ was considered statistically significant. Mul-

Table 1. Classification of patients with COPD according to COPD attack, hospitalization, and dyspnea score

	mMRC 0-1	mMRC ≥2
≥2 moderate exacerbations or ≥1 (leading to hospitalization)	C	D
0 or 1 moderate exacerbations (not leading to hospitalization)	A	B

COPD: chronic obstructive pulmonary disease; mMRC: modified Medical Research Council dyspnea questionnaire.

Table 2. Demographic and echocardiographic characteristics of the study groups

Variable	Without AF (n=132)	With AF (n=38)	*p*	GOLD A+B group (n=90)	GOLD C+D group (n=80)	*p*
Age, years	68.83±10.53	74.55±8.52	0.002	69.97±10.22	70.26±10.60	0.853
Gender						
Male	97 (73.5)	23 (60.5)	0.122	61 (67.8)	59 (73.8)	0.394
Female	35 (26.5)	15 (39.5)		29 (32.2)	21 (26.2)	
BMI (kg/m^2)	26.16±5.23	27.81±5.30	0.090	26.69±4.78	26.34±5.81	0.670
LVEF (%)	58.09±3.71	54.34±4.82	<0.001	57.72±3.68	56.70±4.80	0.119
SPAP (mmHg)	38.75±17.52	49.00±13.65	0.001	37.57±15.25	44.95±18.55	0.005
LA enlargement	36 (27.3)	28 (73.7)	<0.001	34 (37.8)	30 (37.5)	0.970
RA enlargement	60 (45.5)	31 (81.6)	<0.001	45 (50.0)	46 (57.5)	0.328
RV enlargement	59 (44.7)	31 (81.6)	<0.001	45 (50.0)	45 (56.3)	0.415
FEV_1 (L)	1.34±0.44	1.23±0.36	0.190	1.35±0.43	1.27±0.42	0.249
FEV_1 (%)	50.82±13.98	49.66±9.92	0.663	52.82±13.42	48.01±12.47	0.017

Data are expressed as mean+SD or n (%).
AF: atrial fibrillation; BMI: body mass index; FEV1: forced expiratory volume – first second; LA: left atrium; LVEF: left ventricular ejection fraction; RA: right atrium; RV: right ventricle; SPAP: systolic pulmonary artery pressure.

Table 3. Frequencies of AF in groups combined according to hospitalization and number of COPD attacks

COPD groups (combined)	Without AF (n=132), n (%)	With AF (n=38), n (%)	*p*
A+B (n=90)	77 (58.3)	13 (34.2)	0.009
C+D (n=80)	55 (41.7)	25 (65.8)	

AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease.

tiple logistic regression analysis was used with all of the prespecified factors with p<0.25 in the univariate analysis. Statistical significance in the multivariate analysis was accepted at p<0.05.

RESULTS

Of 1454 inpatients with a diagnosis of COPD, 170 patients who were in compliance with the methodology of the study were included in the study. The average age of the entire study population was 70.11±10.37 years. The number of female patients in the whole study population was 50 (29.4%). There was no statistically significant difference between mild COPD (A + B group) and severe COPD (C + D group) groups in terms of age, sex, body mass index, LVEF, RA enlargement, RV enlargement, RA enlargement, and FEV_1 (L) (Table 2). In terms of disease severity, there was a significant difference in systolic pulmonary artery pressure (p=0.005) and FEV_1 (%) (p=0.017) between mild COPD (A + B group) and severe COPD (C + D group) groups (Table 2). When the patients were evaluated as groups with and without AF, a statistically significant difference was found between the two groups in terms of age (p=0.002), and there was no significant difference between the two groups in terms of sex and body mass index (Table 2). In terms of echocardiographic findings, LVEF (p<0.001), systolic pulmonary artery pressure (p=0.001), LA enlargement (p<0.001), RA enlargement (p<0.001), and RV enlargement (p<0.001), there was a significant difference between the two groups. For FEV1 values, there was no statistically significant difference between the two groups (Table 2). When the diagnosis of AF was examined in the mild COPD (A + B group) and severe COPD (C + D) groups, AF was more common in the group with a higher number of disease attacks and/or hospitalization (p=0.009) (Table 3).

In the study population, the effects of variables included in the study on the diagnosis of AF were examined. When multivariate regression analysis is done; LVEF (Odds ratio: 0.842, 95% CI: 0.758-0.936; p≤0.001), LA enlargement (Odds ratio: 4.690, 95% CI: 1.359-16.185; p=0.014), and COPD disease severity (Odds ratio: 2.697, 95% CI: 1.046-6.951; p=0.040) were associated with AF (Table 4).

Table 4. Univariate and multivariate regression analysis for AF incidence in COPD

	Univariate regression analysis			Multivariate regression analysis		
	Odds Ratio	CI 95%	*p*	Odds Ratio	CI 95%	*p*
Age	1.059	1.019-1.101	0.003	1.031	0.975-1.089	0.283
Gender	1.807	0.848-3.852	0.122	0.665	0.214-2.069	0.481
BMI	1.059	0.991-1.133	0.093	1.081	0.991-1.180	0.080
LVEF	0.813	0.741-0.892	<0.001	0.842	0.758-0.936	0.001
SPAP (mmHg)	1.033	1.012-1.055	0.002	1.018	0.987-1.050	0.251
LA enlargement	7.467	3.297-16.908	<0.001	4.690	1.359-16.185	0.014
RA enlargement	5.314	2.185-12.926	<0.001	0.540	0.055-5.256	0.596
RV enlargement	5.479	2.252-13.331	<0.001	1.927	0.201-18.437	0.569
FEV_1 (L)	0.554	0.229-1.341	0.190	0.722	0.228-2.287	0.580
FEV_1 (%)	0.993	0.967-1.021	0.631	-	-	-
COPD group A+B/C+D	2.692	1.266-5.724	0.010	2.697	1.046-6.951	0.040

AF: atrial fibrillation; BMI: body mass index; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume – first second; LA: left atrium; LVEF: left ventricular ejection fraction; RA: right atrium; RV: right ventricle; SPAP: systolic pulmonary artery pressure.

DISCUSSION

In this study, we investigated the possible effect of the clinical severity of COPD on the frequency of AF and found that the frequency of AF increases as the disease severity increases. COPD severity was previously determined from the FEV_1 value obtained from the pulmonary function test. The GOLD guidelines used in the diagnosis and treatment of COPD included not only the FEV_1 value but also the clinical status and symptomatic severity of the disease. The study on COPD-AF based on the ESC guidelines has been conducted on the FEV_1 value, and it has been shown that the frequency of AF increases as the FEV_1 value decreases. When the study population was grouped according to the clinical and symptomatic severity of COPD, there was no difference in FEV_1 (L) value between the AB and CD groups, but there was a difference between the two groups in terms of FEV_1 (%). In our study, when FEV_1 values were taken into consideration, no statistically significant difference was found between patients with and without AF. However, there was a relationship between the clinical and symptomatic severity of COPD and the frequency of AF. The frequency of AF was higher in the group with a more severe COPD clinic.[6] As COPD disease progresses, an increase in hypoxia, pulmonary hypertension, and an adaptation process in the right cavities occurs due to these conditions.[7,8] These physio-pathological conditions also increase the frequency of AF in COPD patients. In addition, β-agonist bronchodilators and anticholinergic agents used in the treatment of COPD increase the risk of AF and tachyarrhythmias.[9,10] As these agents were used in all patients in the study group, their effect on the results of this study was considered neutral.

Although many predisposing factors affecting the incidence of AF were excluded in the study plan, age and structural changes in the heart may also have affected the incidence of AF. In multivariate regression analysis, it was revealed that advanced age, LA enlargement, and the severity of COPD disease affect the presence of AF in the study population. The relationship between age and increased frequency of AF and structural changes in the heart and the presence of AF is known.[11] Age and LA growth may have affected the frequency of AF in the study population in this respect. When the AB and CD groups were compared according to the severity of COPD, the absence of a significant difference in age and LA enlargement between the two groups may suggest that this effect may be less.

Limitations

The retrospective nature of the study is one of the limitations. Another limitation is the number of patients included in the study. Had the number of patients included in the study been higher, it could have increased the statistical power of the study.

Conclusion

The frequency of AF is higher in patients with COPD with clinically more severe presentations, independent of the FEV_1 value in the respiratory test. It may be recommended that patients with severe COPD should be followed more closely in terms of AF.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Keçiören Training and Research Hospital (Approval Date: December 22, 2020; Approval Number: 2012-KAEK-15/2207).

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