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Factors Associated with the Development of Atrial Fibrillation in Chronic Obstructive Pulmonary Disease

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Abstract

Background. It is well established that atrial fibrillation (AF) could develop in patients with chronic obstructive pulmonary disease (COPD); however, its predictors are not quite clear. The aim of this study was to investigate the cardiovascular, hormonal and bronchial obstruction markers and their possible relation to AF risk in COPD. **Methods.** Echocardiographic data, resting pulmonary artery mean pressure (PAP) by Doppler ultrasound assessment, N-terminal B-type natriuretic peptide (NT-pro-BNP), aldosteronee levels, plasma renin activity, and spirometry parameters in 153 patients with COPD was carefully studied. During follow up, between 8 and 26 months, 18 patients developed an outcome event of atrial fibrillation (AF). **Results.** On univariate analysis, renin activity (p=0.007), left atrium (p=0.015), right atrium (p=0.028) and right ventricle (p=0.001), left ventricle systolic (p=0.012) and diastolic (p=0.010) diameters were noted to be predictors of AF, although PAP, NT-pro-BNP levels or FEV1 (p>0.05) were not. However, on multivariate analysis, renin activity (1.14 [1.03; 1.24], p=0.006) and right ventricular diameter (1.39 [1.11; 1.72], p=0.003) were found to be AF predictors. **Conclusion:** The plasma renin activity and right ventricular diameter were found to be the most reliable markers of AF risk in COPD patients from among all the investigated echocardiographic and biochemical parameters. IJBM 2011; 1(2):71-73.
Key words: *COPD, atrial fibrillation, plasma renin activity.*

Introduction

Although earlier studies had been done supporting increased risk of atrial fibrillation (AF) in chronic obstructive pulmonary disease (COPD) patients [1-2], the data on its prevalence, clinical correlates and predictors are controversial [2-5]. Further studies need to be undertaken to confirm whether pulmonary hypertension, right heart remodeling, neurohormonal markers and bronchial obstruction significantly affect the risk of atrial fibrillation in COPD patients. The aim of this study is to investigate the cardiovascular, hormonal, bronchial obstruction markers and their possible relation to AF risk in COPD patients.

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Methods

This study included 153 patients with COPD, in the age group of 42 to 78 years. The initial spirometry parameters, echocardiography data, resting pulmonary artery mean pressure (PAP), N-terminal B-type natriuretic peptide (NT-pro-BNP), plasma aldosteronee concentration (PAC) and plasma renin activity (PRA) were thoroughly investigated. During follow-up, between 8 and 26 months, 18 patients developed an outcome event – AF (group 2) whereas the others showed no such development (group 1, n=135) (Fig. 1). In group 2, paroxysmal AF was detected in 12 patients, whereas persistent AF was observed in 6 individuals.

Groups 1 and 2 did not differ in certain parameters like age (60.1±12.49 and 59.2±6.61 years, p=0.78), gender (male patients proportion – 60.7% and 77.8%, respectively, p=0.12), and COPD severity (2.7±0.84 and 2.8±0.94, p=0.68), whereas body mass index (BMI, 26.5±5.36 and 29.5±6.72, p=0.035) and arterial hypertension prevalence

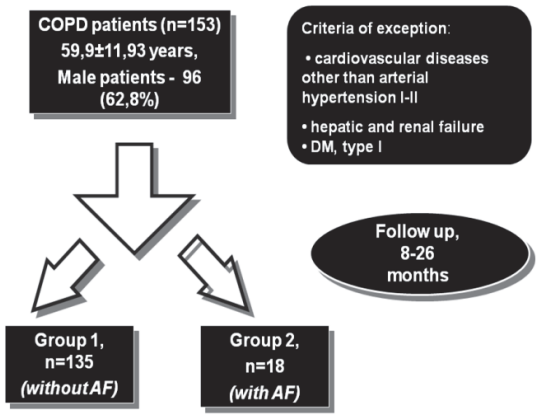

Fig. 1
Study design

(37% and 61.1%, p=0.045) were greater in group 2.

In this study, PAP was estimated by Doppler ultrasound using the Kitabatake A. [8] method. End-systolic size, end-diastolic size, ejection fraction of the left ventricle (LV ESS, LV EDS and LVEF), right ventricular end-diastolic diameter (RVD), left and right atrium diastolic diameter (LAD, RAD) were also assessed with echocardiography. LV myocardial mass (LV MM) was investigated by the Devereux R.B. method [9].

Plasma aldosterone concentration and renin activity were investigated by radioimmune assay, whereas NT-pro-BNP was assessed by the immunochemical method. Laboratory testing was performed using “Immunotech” and "Roche diagnostics" reagent sets.

The initial parameters in both groups at the beginning of the testing were compared using the Mann-Whitney test. Univariate and multivariate logistic regression analysis was also applied in the AF predictors’ assessment.

Results and discussion

A comparative study of the laboratory parameters of the control and AF groups revealed that there was no difference at all between the two groups in the initial NT-pro-BNP and PAC levels at the start; however, plasma renin activity showed a significant increase in the AF group (Table 1) suggesting the possible activation of the renin-angiotensin-aldosterone system (RAAS) triggering the development of arrhythmia in COPD patients. Plasma aldosterone concentration also showed minimal increase. Natriuretic peptide has been shown to be less useful in the diagnosis and prognosis of AF in COPD.

Echocardiography data are presented in Table 1. Echocardiography detected LV systolic dysfunction in AF patients by displaying alterations in LVEF (p=0.034) but showing no difference in the initial PAP (p=0.13). Compared with the control group, patients with arrhythmia also exhibited an increase in size of the heart chambers and LV mass parameters suggesting more significant structural damage to the myocardium ($p<0.05$).Cardiac dilatation, as found to play an important role in the development of AF, although pulmonary hypertension severity showed no such effect.

No difference was found between the groups regarding the vital capacity (VC), forced expiratory volume in one second (FEV1) and its ratio (FEV1/VC) values. However, most spirometry parameters were noted to be slightly lower in AF patients. This suggests that bronchial obstruction has a less significant role in the development of AF in COPD patients (Table 1).

On univariate analysis, renin activity (p=0.007), left atrium (p=0.015), right atrium (p=0.028) and right ventricular (p=0.001) diameters were found to be definite predictors of AF, although PAP, NT-pro-BNP levels or FEV1 ($p>0.05$, Table 2) showed no such role.

Table 1
Initial laboratory, echocardiography and spirometry parameters in groups 1 and 2

Parameter	Group 1	Group 2	P
NT-pro-BNP (pg/ml)	68.9 [28.4; 192.2]	134.85 [39.4; 240.2]	0.22
PAC (pg/ml)	40.8 [22.30; 125.80]	67.0 [38.65; 105.40]	0.14
PRA (ng/ml/h)	4.6 [2.89; 5.81]	11.7 [4.52; 11.65]	0.005
PAP (mm Hg)	30.5±9.73	32.7±11.36	0.13
LV ESS (mm)	35.8±7.10	40.4±5.50	0.005
LV EDS (mm)	51.5±6.53	55.9±5.51	0.004
RVD (mm)	32.3±3.65	35.5±3.21	0.001
LAD (mm)	37.9±4.58	41.5±3.13	0.004
RAD (mm)	36.2±6.59	41.0±6.65	0.030
LVEF (%)	57.8±10.35	53.2±6.68	0.034
LV MM (g)	222.7±73.57	273.3±82.90	0.016
VC (% of predicted N)	70.6±18.36	65.0±25.86	0.43
FEV1 (% of predicted N)	53.8±21.16	49.1±25.34	0.50
FEV1/VC (%)	59.1±12.89	56.3±12.56	0.57

Table 2
Predictors of AF in COPD patients according to univariate data analysis

Parameter	OR [95% CI]	P
BMI	1.08 [1.00; 1.18]	0.045
Arterial hypertension	3.47 [1.21; 9.91]	0.015
PRA	1.13 [1.05; 1.20]	0.007
LV EDS	1.11 [1.03; 1.21]	0.010
LV ESS	1.09 [1.02; 1.18]	0.012
PAP	1.02 [0.97; 1.07]	0.41
LAD	1.17 [1.01; 1.34]	0.015
RAD	1.10 [1.01; 1.21]	0.028
RVD	1.25 [1.09; 1.24]	0.001
FEV1	0.99 [0.96; 1.01]	0.15

However, renin activity (1.14 [1.03; 1.24], p=0.006) and right ventricular diameter (1.39 [1.11; 1.72], p=0.003) were revealed to be independent predictors of AF development by multivariate analysis. Thus, COPD patients exhibiting cardiac dilatation and RAAS alterations also demonstrated greater risk of developing arrhythmia. Interestingly, COPD patients with obesity and a past medical history of systemic hypertension were also predisposed to AF. However, pulmonary hypertension and bronchial obstruction appeared to play a less significant role compared with other risk factors.

Conclusions

Among COPD patients, the greater risk of developing AF was detected in subjects with obesity, systemic arterial hypertension, enlarged heart chamber size at baseline and elevated initial RAAS values. Pulmonary hypertension and bronchial obstruction also appeared to exert less influence compared with other investigated parameters. Plasma renin activity and right ventricular diameter were found to be the most reliable markers of AF risk in COPD patients. Awareness of the risks coupled with optimized treatment of COPD to minimize myocardial remodeling, and thus, cardiac dilatation, could be of great advantage in treatment. The suppression of RAAS components could also greatly reduce the risk of AF in such patients. Further study is warranted to confirm the efficacy of RAAS blockers for the prevention of AF in COPD patients.

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