Evaluation of left ventricular function in patients with chronic obstructive pulmonary disease

Elżbieta Suchoń1, Wiesława Tracz1, Piotr Podolec1, Monika Pieculewicz1, Wojciech Płazak1, Anna Prokop3, Piotr Nalepa2

1 Department of Cardiovascular Diseases, Jagiellonian University School of Medicine and the John Paul II Hospital, Kraków, Poland
2 I Department of Pulmonary Diseases, the John Paul II Hospital, Kraków, Poland
3 II Department of Pulmonary Diseases, the John Paul II Hospital, Kraków, Poland

Abstract: Introduction. Patients with right ventricle (RV) pressure overload often have impaired left ventricular (LV) diastolic function. Objectives. The aim of study was to evaluate LV function in patients with chronic obstructive pulmonary disease (COPD). Patients and methods. Thirty-five patients (mean age: 62.1 ± 7.7 yr) with COPD without additional cardiac diseases and 25 age and sex-matched healthy subjects were enrolled into the study. All patients underwent resting ECG tracing, blood pressure measurements thickness of intervent, spirometry, standard and tissue Doppler echocardiography. Results. The mean value of forced expiratory volume in one second (FEV1) in the COPD group was 40 ± 8.9% of the predicted value. We found no significant differences in LV end-diastolic and systolic diastolic function and interventricular septum as well between COPD patients and controls. RV end-diastolic diameter and RV wall thickness were significantly larger and right ventricle systolic pressure – RVSP (38 ± 11.2 vs 20 ± 2.5 mm Hg) significantly higher in the COPD group. Both peak early to peak atrial filling velocities ratio – E/A and peak annular velocity during early diastole to peak annular velocity during atrial contraction – Em/Am were significantly lower in COPD compared to controls. Moreover, there was a strong inverse correlation between Em/Am and RVSP (r = -0.75; p < 0.001) and between E/A (r = -0.6; p < 0.001) as well. We found no significant differences in parameters assessing the LV systolic function between both groups. Conclusions. In COPD patients LV diastolic function is significantly impaired and its magnitude is related with the increase in pulmonary artery pressure, while systolic LV function is well preserved. Key words: chronic obstructive pulmonary disease, left ventricle diastolic function, left ventricle systolic function, spirometry

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the most frequent pulmonary disease in Poland affecting in about 10% of the population aged over 40 years. It is generally known that dyspnea and exercise tolerance reduction in COPD patients occur in the advanced stage of the disease as a result of bronchial patency disturbance progression, and the development of pulmonary arterial hypertension [1]. The significance of the right ventricular performance, is recognized in the bibliography as one of the factors determining the clinical course and prognosis in COPD (independently of the severity of bronchial obstruction), a potential role of the left ventricle is, however, less studied [2]. In several experimental studies and clinical trials, it has been shown that right ventricular overload, as a consequence of the increase of pulmonary vascular tension, can affect the left ventricular filling profile diminishing its compliance by means of the common interventricular septum. [2-5].

The aim of the study was to evaluate the left ventricular systolic and diastolic function in patients with stable COPD.

PATIENTS AND METHODS

Thirty-five patients of mean age: 62.1 ± 7.7 years; 25 (71%) males, 10 (29%) females with COPD without additional cardiac diseases and 25 age and sex-matched healthy subjects were enrolled into the study. All patients underwent resting ECG tracing, blood pressure measurements thickness of intervent, spirometry, standard and tissue Doppler echocardiography, excluded systemic arterial hypertension, ischemic heart disease and organic heart disease were enrolled in the study.

Patients with diagnosed diabetes and those for whom good quality echocardiographic images could not be obtained, have been excluded. The control group consisted of 25 healthy subjects aged: 61.6 ± 10.1; 18 (72%) males and 7 (28%) females with normal spirometry results. In the COPD patient group, typical pharmacological treatment was used: β1 agonists, anticholinergic medications and...
methylxanthins. In 10 (29%) patients inhaled corticosteroids were also used. Controls were not treated pharmacologically.

All patients underwent the following procedures: resting ECG tracing, systolic and diastolic blood pressure measurement, echocardiography and resting spirometry. Arterial blood gas was additionally assessed in the COPD patients.

Echocardiography was performed in all patients according to the same protocol with the use of GE Medical System Vivid 7 ultrasound machine equipped with 1.5–4 MHz sector transducer probe. Routine echocardiography with standard projections was done initially and followed by Doppler flow tracing registration at the level of mitral and tricuspid valves. Further, tissue Doppler echocardiography (TDE) obtained images were registered.

Parameters obtained through long-axis parasternal approach in M-mode projection where analyzed: end-diastolic right ventricular diameter (RVD), right ventricular free wall thickness (RVWT), left ventricular end-diastolic (LVD) and end-systolic (LVS) diameter and Interventricular septum thickness (IVS).

In order to assess the left ventricular diastolic function, the isovolumetric relaxation time (IVRT) and the following transmitral inflow parameters were measured (pulsed wave Doppler registration with gate placed at the tip of open mitral valve leaflets): peak velocity of early E-wave transmitral flow (E), peak velocity of early A-wave transmitral flow (A), and the ratio (E/A), was derived. The early diastole (Em) and atrium systole (Am) mitral valve annular velocity was measured at the lateral wall of the left ventricle, by pulsed wave tissue Doppler and similarly the Em/Am ratio was derived.

The assessment of left ventricular systolic function consisted of shortening fraction (FS%), left ventricular ejection fraction (EF %) obtained according to Simpson’s formula, and the mitral valve peak annular velocity measured at the left ventricular lateral wall (Sm).

The right ventricular systolic pressure (RVSP) was obtained from the velocity of tricuspid regurgitation. The value of 10 mmHg, obtained from the modified Bernoullie equation was added to the pressure gradient between the right ventricle and right atrium, as the expected right atrium v wave pressure [6]. As pulmonary stenosis was excluded in all patients, it was agreed that the RVSP value obtained, relates to the pulmonary artery pressure.

Resting spirometry was performed in all patients using a body spiroplethysmograph. The forced expiratory volume in one second (FEV1), expressed as the % of expected normal value and as the percent of vital capacity (VC; FEV1/VC), was analyzed.

In the COPD patient group arterial oxygen blood partial pressure (PaO2), carbon dioxide blood partial pressure (PaCO2); pH by means of radial artery puncture, was additionally obtained.

The results were presented as mean ± standard deviation. The data is presented as mean ± standard deviation. Abbreviations: forced expiratory volume in one second FEV1, FEV1/VC % – forced expiratory volume in one second /vital capacity ratio, HR (1/min) heart rate per minute, NS – statistically nonsignificant, PaCO2 (mmHg) – arterial carbon dioxide blood partial pressure, COPD – chronic obstructive pulmonary disease, PaO2 – arterial oxygen blood partial pressure.

### RESULTS

The clinical characteristics, spirometry and arterial blood gas results are shown in table 1. Statistically important differences with respect to age, sex, mean systolic and diastolic blood pressure values in COPD patients and in the control group, were not found. Sinus rhythm was registered in rest-

| Table 1. Clinical characteristics, spirometry and arterial blood gas results in COPD patients and in control group |
|---------------------------------------------------------------|
| COPD group n = 35                                           | Control group n = 25                                      |
| Age (years)                                                 |                                                        |
| 62.1 ± 7.7                                                  | 61.8 ± 10.1                                             |
| Male                                                        |                                                        |
| 25 (71%)                                                    | 18 (72%)                                               |
| Female                                                      |                                                        |
| 10 (29%)                                                    | 7 (28%)                                                |
| Systolic pressure (mm Hg)                                   |                                                        |
| 125 ±10.8                                                   | 127  ±10.4                                             |
| Diastolic pressure (mm Hg)                                  |                                                        |
| 76 ± 7.7                                                    | 77 ± 8.1                                               |
| HR (1/min)                                                  |                                                        |
| 79 ± 9.8                                                    | 74 ± 10.2                                              |
| FEV1(%)                                                     |                                                        |
| 40 ± 8.9                                                    | 98 ± 4.9                                               |
| FEV1/VC(%)                                                  |                                                        |
| 54.9 ±5.1                                                   | 84 ±2.8                                                |
| pH                                                          |                                                        |
| 7.35 ± 0.02                                                 |                                                        |
| PaO2 (mm Hg)                                                |                                                        |
| 71 ±10.3                                                    |                                                        |
| PaCO2 (mm Hg)                                               |                                                        |
| 49 ±7.1                                                     |                                                        |
Table 2. Echocardiographic parameters assessing the left and right ventricular dimensions, interventricular septum thickness, right ventricular free wall thickness, right ventricular systolic pressure

| Parameter                              | COPD group n = 35 | Control group n = 25 | p    |
|----------------------------------------|--------------------|----------------------|------|
| LVD (mm)                               | 49.1 ±7.6          | 50.2 ±5.4            | NS   |
| LVS (mm)                               | 32.3 ±5.6          | 32.7 ±6.1            | NS   |
| IVS (mm)                               | 10.2 ±6.6          | 9.8 ±0.8             | NS   |
| RVD (mm)                               | 27.2 ±2.6          | 20 ±2.9              | <0.001|
| RVWT (mm)                              | 7.1 ±1.8           | 3.6 ±1.5             | <0.001|
| RVSP (mm Hg)                           | 38 ±11.2           | 20 ±2.5              | <0.001|

IVS – interventricular septum thickness, LVD – left ventricular end-diastolic diameter, LVS – left ventricular end-systolic diameter, RVD – right ventricular end-diastolic diameter, RVWT – right ventricular systolic pressure, RVSP – right ventricular free wall thickness, other – see table 1

Table 3. Echocardiographic parameters assessing right ventricular diastolic function in COPD patients group and in control group.

| Parameter   | COPD group n = 35 | Control group n = 25 | p    |
|-------------|--------------------|----------------------|------|
| E/A         | 0.69 ±0.12         | 1.1 ±0.1             | <0.001|
| Em/Am       | 0.7 ±0.14          | 1.1 ±0.1             | <0.001|
| IVRT (ms)   | 112 ±6.7           | 79 ±9.8              | <0.001|

E/A – peak velocity of early E-wave transmitral flow (E) to peak velocity of early A-wave transmitral flow (A) ratio, Em/Am – early diastole mitral valve annular velocity at the lateral left ventricular wall (Em) to atrium systole mitral valve annular velocity (Am) ratio, IVRT – isovolumetric relaxation time, other – see table 1

Table 4. Echocardiographic parameters assessing left ventricular systolic function in COPD patients group and in control group.

| Parameter   | COPD group n = 35 | Control group n = 25 | p    |
|-------------|--------------------|----------------------|------|
| EF (%)      | 65.2 ±8.7          | 66 ±5.4              | NS   |
| FS (%)      | 36 ±6.7            | 37 ±7.2              | NS   |
| Sm (cm/s)   | 10.3 ±1.2          | 11 ±1.2              | NS   |

EF – left ventricle ejection fraction, FS – left ventricle shortening fraction, Sm – mitral valve systolic peak annular velocity measured at the left ventricular lateral wall, other – see table 1

The influence of the right ventricular volume or pressure overload on the left ventricular function is known as the reverse Bernheim phenomenon, and is associated with the existence of a common wall such as the interventricular septum, and the common pericardium holding the cavities of the heart [3]. In the case of right ventricular long-standing pressure overload the dominant role is played by the interventricular hypertension indices.

The left ventricular diastolic function parameters in studied groups are shown in table 3. The mitral inflow velocities ratio (E/A), mitral early diastolic and late diastolic annular velocities ratio (Em/Am), were significantly lower in COPD patients and the isovolumetric relaxation time (IVRT) was significantly longer in relation to control group. An important correlation between the above mentioned parameters and the right ventricular pressure was found in COPD patients. The strongest inverse correlation was observed between RVSP and the mitral valve annular velocities Em/Am ratio; r = –0.75; p <0.001 (fig. 1). A weaker correlation was observed between RVSP and the mitral valve inflow velocities (E/A) ratio; r = –0.61; p <0.001 (fig. 2). The weakest, but still important, correlation was observed between RVSP and the isovolumetric relaxation time (IVRT; r = 0.39; p <0.05).

The analysis of systolic function parameters (FS%, EF%) and left ventricular mitral valve annular velocity (Sm) has not shown any significant difference between the studied groups (tab. 4).

No correlation between left ventricular diastolic function parameters, spirometry and arterial blood gas results was found.

DISCUSSION

The influence of the right ventricular volume or pressure overload on the left ventricular function is known as the reverse Bernheim phenomenon, and is associated with the existence of a common wall such as the interventricular septum, and the common pericardium holding the cavities of the heart [3]. In the case of right ventricular long-standing pressure overload the dominant role is played by the interventricular pressure overload.
septum shift into the left ventricular cavity and this may result in the limitation of left ventricular cavity dimensions, its contractility and compliance and in consequence in the rise of the left ventricular diastolic pressure [3-5]. This phenomenon has been described in detail with respect to patients with severe primary pulmonary arterial hypertension [5].

The results presented in this study clearly indicate the impaired diastolic function in the studied patient group. Moreover, there was a strong correlation between the level of impairment of diastolic function and the level of pressure in the pulmonary artery what correlates with other investigators findings [4,7-9]. Tutar et al [8] described the left ventricular diastolic function impairment in COPD patients, and a similar correlation between right ventricular pressure and E/A ratio, and IVRT. Schena et al [4] also demonstrated that the right ventricular pressure correlates with left ventricular eccentricity indexes; the distorted ventricular geometry results in its abnormal filling pattern in turn. The relation between right ventricular pressure and left ventricular diastolic dysfunction in a large group of cor pulmonale patients of different etiology (including COPD patients), was confirmed by Mustapha et al. [10]. The development of relaxation diastolic dysfunction is most probable in patients with severe pulmonary hypertension as suggested by the authors.

Hypertension in the course of COPD is usually of a mild or moderate grade as confirmed by results of the present study [11, 12]. In the studied group of patients, the right ventricular pressure ranged from 22–64 mmHg; mean 38 ±11.1 mm Hg. It is known, however, that in this group of patients, a rapid pulmonary artery pressure rise may occur with light exercise or in the event of infectious exacerbations [11-13]. It is to be expected that the diastolic function impairment which increases proportionally to right ventricular rise in pressure, will substantially augment during physical exercise. It is therefore possible that apart from the respiratory tests results, and right ventricular performance the right ventricular diastolic performance, may play a major role in the clinical setting of the COPD. The potential rise in left ventricular filling pressure passively transmitted to the pulmonary, capillary vascular system, may add up to the already augmented precapillary pressure and cause dyspnea exacerbation in these patients.

In the presented study the left ventricular systolic function impairment in the course of COPD, was not found. Ejection fraction, shortening fraction and lateral mitral annular peak velocity (Sm) in patients, was in the normal value range and did not differ significantly from control group. Similar results were obtained by other investigators [4,16]. As suggested in the bibliography, in the absence of conditions primarily leading to left ventricular systolic function impairment (ischemic heart disease, systemic arterial hypertension etc.), the derangement of systolic function in the course of COPD is rarely found, usually in severe pulmonary hypertension, in patients with right ventricular dysfunction [13-15]. With normal ejection fraction, and normal left ventricular shortening fraction found, some investigators, however, suggest the presence of subclinical systolic dysfunction in the COPD patients [17]. According to the authors the significantly increased left ventricular performance index (TEI index), that evaluates global systolic and diastolic functions of the myocardium, provides evidence for this dysfunction [18].

In conclusion, the left ventricular diastolic function in patients with advanced COPD is impaired. The level of diastolic impairment is proportional to the right ventricular pressure. Impairment of left ventricular systolic function has not not found in COPD patients.
REFERENCES

1. Kasibowska-Kuzniar K, Jankowska R, Kuzniar T. Chronic obstructive pulmonary disease exacerbation – effects on quality of life. Pol Arch Med Wewn. 2005; 114: 1010-1015.
2. Burgess M, Mogulkoc N, Wright-Thomas R, et al. Comparison of echocardiographic markers of right ventricular function in determining prognosis in chronic pulmonary disease. J Am Soc Echocardiogr. 2002; 15: 633-639.
3. Alpert SA. The effect of right ventricular dysfunction on left ventricular form and function. Chest. 2001; 119: 1632-1633.
4. Scherf M, Clini E, Errera D, et al. Echo-Doppler evaluation of left ventricular impairment in chronic cor pulmonale. Chest. 1996; 109: 1446-1451.
5. Louie EK, Rich S, Brundage BH. Doppler echocardiographic assessment of impaired left ventricular filling in patients with right ventricular pressure overload due to primary pulmonary hypertension. J Am Coll Cardiol. 1986; 6: 1298-1306.
6. Rydlewska-Sadowska W. Echokardiograficzna metoda Dopplera. In: Rydlewska-Sadowska W, eds. Echokardiografia kliniczna. Warszawa, Biblioteka Instytutu Kardiologii, 1991.
7. Boussuges A, Pinet C, Molenat F, et al. Left atrial and ventricular filling in chronic obstructive pulmonary disease. An echocardiographic and Doppler study. Am J Respir Crit Care Med. 2000; 162: 670-675.
8. Tutar E, Kaya A, Gulec S, et al. Echocardiographic evaluation of left ventricular diastolic function in chronic cor pulmonale. Am J Cardiol. 1999; 83: 1414-1417.
9. Ozer N, Tolgozoula L, Coplu L, et al. Echocardiographic evaluation of left and right ventricular diastolic function in patients with chronic obstructive pulmonary disease. J Am Soc Echocardiogr. 2001; 14: 557-561.
10. Moustapha A, Kaushik V, Diaz S, et al. Echocardiographic evaluation of left ventricular diastolic function in patients with chronic pulmonary hypertension. Cardiology. 2001; 95: 96-100.
11. Chaoat A, Bugnet AS, Kadaoui N. Severe pulmonary hypertension and chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2005; 172: 189-194.
12. Weizhenblum E, Chaoat A. Right ventricular function in COPD. Can it be assessed reliably by the measurements of right ventricular ejection fraction? Chest. 1998; 113: 567-568.
13. Matthias R, Berger H, Davis R, et al. Right and left ventricular exercise performance in chronic obstructive pulmonary disease: Radionuclide assessment. Ann Int Med. 1980; 93: 234-239.
14. Render ML, Einstein AS, Blaustein A. Left ventricular dysfunction in deteriorating patients with chronic obstructive pulmonary disease. Chest. 1995; 107: 162-168.
15. Yilmaz R, Gencer M, Ceylan E, et al. Impact of chronic obstructive pulmonary disease with pulmonary hypertension on both left ventricular systolic and diastolic performance. J Am Soc Echocardiogr. 2005; 18: 873-881.
16. Vonk-Noordergraaf A, Marcus T, Holvenda S, et al. Early changes of cardiac structure and function in COPD patients with mild hypoxemia. Chest. 2005; 127: 1898-1902.
17. Vizza CD, Lynch JP, Ochoa LL, et al. Right and left ventricular impairment in patients with severe pulmonary disease. Chest. 1998; 113: 576-583.
18. Tei C, Nishimura RA, Seward JB, et al. Noninvasive Doppler derived myocardial performance index: correlation with simultaneous measurements of cardiac catheterisation measurements. J Am Soc Echocardiogr. 1997; 10: 169-178.