

# ROLE OF COMORBIDITIES IN PULMONARY HYPERTENSION AND CHRONIC PULMONARY HEART DETERMINISM IN PATIENTS WITH MODERATE AND SEVERE COPD

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**Keywords:** moderate and severe COPD, comorbidities, pulmonary hypertension, chronic pulmonary cord

**Abstract:** The objective of this paper is to highlight the presence of comorbidities and their contribution in the determinism of pulmonary hypertension (PH) and chronic pulmonary heart (CPH) in the patients with chronic obstructive pulmonary disease COPD GOLD stage II and III. Methods: The clinical study was conducted on a group of 61 patients with COPD chosen among those who addressed the Pneumophthysiology Hospital of Sibiu, aged between 44 and 78 years old. In terms of the degree of functional respiratory impairment, 38 were diagnosed with COPD GOLD stage II and 23 with GOLD stage III. Gender distribution included 11 female patients and 50 male patients. Based on the anamnestic, clinical and laboratory data, the presence of comorbidities has been established. Transthoracic echocardiography was made to assess the presence of PH, the CPH suggestive elements and the left ventricular damage. The patients with left ventricular failure, atrial fibrillation or valvular heart disease were not included in the study. The patients with difficult ultrasound display were excluded from the study, as well as those who did not record valid echocardiographic measurements. Results: Patients with COPD often associated comorbidities leading to early subclinical echocardiographic systolic and diastolic ventricular dysfunction, uncorrelated with the degree of functional respiratory impairment.

**Cuvinte cheie:** BPOC moderat și sever, comorbidități, hipertensiune pulmonară, cord pulmonar cronic

**Rezumat:** Obiective. Obiectivul acestei lucrări a fost de a evidenția prezența comorbidităților și contribuția acestora în determinismul hipertensiunii pulmonare (HP) și a cordului pulmonar cronic (CPC) la pacienții cu BPOC stadiul II și III GOLD. Metode: Studiul clinic a fost efectuat pe un lot de 61 de pacienți cu BPOC selecționați din rândul celor care s-au adresat Spitalului de Pneumoftiziologie Sibiu, având vârste cuprinse între 44 și 78 de ani. Din punct de vedere a gradului afectării funcționale respiratorii, 38 au fost diagnosticați cu BPOC stadiul II GOLD, iar 23 în stadiul III GOLD. Distribuția pe sexe a fost de 11 pacienți de sex feminin și 50 de pacienți de sex masculin. Pe baza datelor anamnestice, clinice și paraclinice s-a stabilit prezența comorbidităților. Prin ecocardiografie transtoracică s-a evaluat prezența HP, a elementelor sugestive de CPC și a afectării ventriculare stângi. Nu au fost incluși în studiu pacienți care prezentau insuficiență ventriculară stângă, fibrilație atrială sau valvulopatii. Au fost excluși din studiu pacienții care au prezentat fereastră ecografică dificilă și la care nu s-au putut efectua măsurători ecocardiografice valide. Rezultate: Pacienții cu BPOC au asociat frecvent comorbidități care au condus la alterarea ecocardiografică subclinică precoce a funcției sistolice și diastolice a ventriculului drept necorelat cu gradul afectării funcționale respiratorii.

## PURPOSE OF THE STUDY

The objective of this study was to assess the role of comorbidities in PH and CPH determinism in the patients with moderate and severe COPD

## MATERIAL AND METHOD

The clinical study was conducted on a group of 61 patients with moderate and severe COPD, aged between 44 and 78 years old, of which 11 were females and 50 males. By combining the anamnestic, the clinical and the laboratory data, the presence of comorbidities has been established in the study group, that is the chronic ischemic heart disease, hypertension, type II diabetes, obesity and the syndrome of obstructive sleep apnoea (SAS). By the M module echocardiographic method, 2D and pulsed and continuous Doppler, data were obtained regarding the presence of systolic pulmonary arterial hypertension (PAH), the right ventricular free wall thickness, degree of right ventricular dilatation. The impairment of the systolic function of the right ventricle has been assessed by the mode M (TAPSE) technique, 2D (RVEF), as well as the right

ventricular diastolic dysfunction by assessing the diastolic tricuspid flow pattern. The degree of the left ventricular diastolic impairment has been assessed. The existence of statistical correlations between the stages of COPD, the presence of comorbidities and the degree of echocardiographic parameters damage has also been checked.

## RESULTS

### Frequency of comorbidities

Systemic arterial hypertension (AH) was diagnosed in a large number of patients (40 - 81.7%), a significant percentage - 49.18% had stage II and 31.15% had stage III of the disease. It is possible that the increased frequency of hypertension in these patients to be caused by smoking and inactivity, which are characteristic elements of both diseases, as well as by the frequent association of sleep apnoea syndrome, obesity and older age. (1) Coronary artery disease (CAD) was present in 38 patients (62.3%). A similar study found even a history of myocardial infarction in 29% of the patients. Their advanced age, smoking status and the association of obesity, dyslipidemia

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Article received on 30.11.2011 and accepted for publication on 31.01.2012  
ACTA MEDICA TRANSILVANICA March 2012;2(1):183-184

## CLINICAL ASPECTS

and hypertension has an important role in their appearance. (1,2) There has not been demonstrated any significant association between the COPD stage and the presence of ischemic coronary disease ( $\chi^2$  test,  $p = 0.422$ ,  $\alpha = 0.05$ ). A large number of patients recorded high body mass index, respectively 24.59% overweight, 29.5% obesity 1, 8.2% obesity 2 and 6.56% obesity 3, fact noted and in other studies, too. (2) Diabetes mellitus type II was also frequently found in the patients of our study group (15 to 24.59%). There was no statistical significant correlation between COPD stages and the presence of diabetes mellitus. SAS was diagnosed in 36 of the 61 patients with COPD. Of the 36 patients with overlap-syndrome, 7 were diagnosed with mild SAS (IAH 12.37/h), 4 with moderate SAS (AHI 24.5/h), 25 with severe SAS, IAH (48.6/h). We found a significant association between COPD stage and the severity of sleep apnea, measured by apnea hypopnea index (AHI) ( $\chi^2$  test,  $p = 0.048$ ,  $\alpha = 0.05$ ). SAS was a risk factor for lower TAPSE  $<15$  (RR = 1.13), a risk factor for developing HP (RR = 1.25) for the occurrence of right ventricular diastolic dysfunction (RR = 1.2), while for the diastolic dysfunction of the left ventricular, the risk was of 1.44.

### **Echocardiographic data**

Right ventricular wall thickness has a significant prognostic value in evaluating the patients with COPD. In the study batch, the right ventricular wall thickness recorded values above 5 mm in 21 patients (34.42%). The analysis of distribution of cases with right ventricular wall above 5 mm, correlated with the COPD stage showed a presence of 28.95% of the patients with COPD stage II and 43.48% of patients with stage III COPD. There are significant statistical differences between the two stages. It has been proven a significant statistical correlation with the SPAP value ( $r = 0.260$ ,  $p = 0.043$ ) and the RVEF value ( $r = -0.279$ ,  $p = 0.029$ ) but not with the FEV1% value ( $r = -0.190$ ,  $p = 0.142$ ). It showed a slight statistical correlation between the degree of right ventricular dilatation and pulmonary function impairment level represented by FEV1%. We obtained significant correlations of the right ventricular dilatation with SPAP (direct and weak), ( $r = 0.327$ ,  $p = 0.043$ ) with RVEF (reverse and average) ( $r = -0.478$ ,  $p = 0.027$ ) and with the presence of the right ventricular diastolic dysfunction (reverse and average). ( $r = -0.493$ ,  $p = 0, 035$ ).

A more increased frequency of the diastolic dysfunction of the right ventricle has been registered in 20 patients with severe COPD, as against those patients with moderate COPD, where it has been identified in 21 patients (55.26%), being a significant correlation between the COPD stage and the diastolic dysfunction ( $\chi^2$  test,  $p = 0.024$ ). By applying the linear correlation analysis, the Pearson correlation coefficient was measured, obtaining statistically significant correlations of the right ventricular dysfunction assessed by the E / A SPAP ratio ( $r = -0.433$ ,  $p = 0.015s$ ) and FEV1% ( $r = -0.303$ ,  $p = 0.046$ ). The statistical correlations between the FEV1% and SPAP, RVEF values had been studied, as well as the systolic dysfunction of the right ventricle. No significant correlation has been registered between the SPAP and FEV1% ( $p=0,720$ ), but significant correlations were observed between the diastolic dysfunction of the right ventricle ( $r=0,303$ ,  $p=0,046$ ) and the ejection fraction of the right ventricle (weak and inverse correlation) ( $r=-0,311$ ,  $p=0,015$ ). In our study, there were 9 patients who had values for TAPSE below 15 mm (14.8%). Of these, the majority (8 patients), have stage III COPD, the  $\chi^2$  test showing a significant association between COPD stage and TAPS ( $\chi^2$  test,  $p = 0.002$ ,  $\alpha = 0.01$ ). We identified the presence of FEVD below 44% in 29 patients, 14 patients with COPD stage II (36,8%) and 15 patients with COPD stage III (65,2%) registered vales of RVEF below 45%. It seemed that the percentage of those with COPD stage III is

significantly increased in relation to the percentage of those with stage II (test Z,  $p=0.038$ ,  $\alpha=0.05$ ). A statistical significant correlation has been observed between the values of the ejection fraction of the right ventricle and FEV1% ( $r=0.339$ ,  $p=0.008$ ), as well as with SPAP ( $r=-0,031$ ,  $p=0,015$ ). We registered values of SPAP above 35 mmHg in 7 patients with moderate COPD (18,42%), while in the patients with severe COPD, in 7 patients out of 23 (30,43%). There has been no significant association between the COPD stage and the systolic PAP (test  $\chi^2$ ,  $p=0.351$ ). This result may be explained by the presence of other factors such as those genetic, which are responsible for the presence of PH in the patients with COPD, fact that was demonstrated in other specialised studies and justified by the fact that the PH knows a multiple factor-dependence. FEV1% did not significantly correlated from the statistical point of view with the SPAP values ( $p=0,720$ ). Other specialised studies proved a statistically significant correlation of the value of the pulmonary arterial pressure with age and VEMS (3), even a recent retrospective study showed that the presence of pulmonary hypertension, echocardiographically highlighted correlated with the decrease of the survival rate to one year in the case of the patients with COPD, irrespective of age or FEV1%. (4) The study of comorbidities in the patients with COPD plays an important part in the diagnostic and therapeutic approach of the patients, even from the GOLD stages II and III.

## CONCLUSIONS

At the same time with the progressive worsening of COPD, the secondary aggravation of the pulmonary arterial systolic pressure also occurs with the subclinical damage of the diastolic and systolic function of the right ventricle. VEF has a role in evaluating the degree of functional respiratory impairment, as well as in the assessment of comorbidities and the presence of HP and CPH even from the II<sup>nd</sup> and III<sup>rd</sup> stage of COPD. The studied echocardiographic parameters which are important in the development of CPC, secondary to COPD, did not have a statistically significant correlation with FEV1%. Morbid associations common in patients with COPD, especially obesity and SASO are responsible for further increase of the obstructive sleep apnea syndrome (OSAS). The study of the presence of PH in the patients with COPD plays a very important part due to the clinical implications and prognostic significance in terms of the survival rate. The active search of comorbidities is justified, as well as the echocardiographic and polygraphic night evaluation in the patients with COPD even from stages II and III.

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