RIGHT ATRIUM VOLUME INDEX IN NON-SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract. Introduction: Right atrium volume index (RAVI) has recently been reported as a quantitative echocardiographic parameter associated with right ventricular systolic dysfunction (RVSD) in patients with pulmonary arterial hypertension (PAH) due to chronic obstructive pulmonary disease (COPD). **Aims:** The aim of the current study was to assess right atrium remodeling (RAVI) in COPD patients without echocardiographic parameters of RVSD or PAH at rest and to analyse its association with right ventricular diastolic dysfunction (RVDD) at rest and after exercise – stress-induced RVDD. **Methods:** The study was conducted in 104 COPD patients. Pulmonary function tests, blood gas analysis, incremental, symptom-limited cardio-pulmonary test (CPET) protocol and detailed echocardiographic examinations before and 2-3 minutes after peak CPET were applied. The cut-off values for stress-induced RVDD were $E/e' > 6.0$. **Results:** Patients were divided into two groups: patients with stress-induced RVDD (82/104 – 78%) and those without stress-RVDD (22/104 – 22%). RAVI was significantly higher in the group with stress-induced RVDD (23.04 ± 2.67 ml/m² vs 18.02 ± 2.69 ml/m²) in comparison to those without it. Correlation analysis showed that RAVI was associated with stress-induced RVDD (E/e') and the distance from the 6 minute walk test (6-MWT), but was not an independent predictor for any of them. **Conclusions:** RAVI correlates with stress-induced RVDD parameters (E/e') in non-severe COPD patients without pulmonary arterial hypertension at rest. It corresponds to the diminished distance from the 6-MWT, but was not an independent factor of reduced physical activity.

Key words: stress-echocardiography, right ventricular diastolic dysfunction, right atrium remodeling, non-severe chronic obstructive pulmonary disease, cardio-pulmonary testing

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INTRODUCTION

In COPD patients, pulmonary vascular disease, pulmonary arterial hypertension and RV dysfunction may develop either as a consequence of the systemic effects of COPD (hypoxia, inflammation, oxidative stress, endothelial dysfunction), [1] or may be the result of intermittent (nocturnal desaturations;

desaturations during exercise or exacerbations) [2, 3] or chronic vasoconstriction [4]. The invasiveness of right heart catheterization protrudes the early detection of RV dysfunction [5, 6]. Similarly to left heart dysfunction, changes of right atrium area (RA) and right atrium volume index (RAVI) reflect the pathophysiological consequences of right ventricular dysfunction [7, 8]. In non-severe COPD patients, with-

out pulmonary arterial hypertension, right atrium (RA) area is enlarged [9]. Right atrium volume index (RAVI) has recently been associated with pulmonary hypertension and right ventricular systolic and diastolic dysfunction, secondary to COPD [10].

The aims of the current study are to reveal: 1) whether RAVI may be predictive of RVDD at rest; 2) whether it correlates to early stages of stress-induced RVDD; 3) whether RAVI is associated to 6-minute walk distance test.

MATERIAL AND METHODS

Material

It was a retrospective study that was performed in 224 clinically stable outpatients, diagnosed with COPD at the University Hospital for Respiratory Diseases "St. Sophia", Sofia. All the subjects had exertional dyspnoea, but a total of 104 patients (64 men, 40 women; mean age of 62.9 ± 7.5 years) were considered eligible, assuming the exclusion criteria.

The following exclusion criteria were considered: 1) left ventricular ejection fraction (LVEF) < 50%; 2) left ventricular diastolic dysfunction at rest more than first grade; 3) presence of echocardiographic criteria of pulmonary hypertension (systolic pulmonary arterial pressure > 36 mm Hg, maximum velocity of the tricuspid regurgitation jet > 2.8 m/s; 4) valvular heart disease; 5) documented cardiomyopathy; 6) severe uncontrolled hypertension (systolic pressure > 180 mm Hg and diastolic pressure > 90 mm Hg); 7) atrial fibrillation or malignant ventricular arrhythmia; 8) anaemia; 9) cancer; 10) chronic kidney disease;

11) recent chest or abdominal surgery; 12) recent exacerbation (during the last three months); 13) recent change (during the last three months) in medical therapy.

Methods

All subjects underwent preliminary clinical examination which included chest X-ray, spirometry, electrocardiogram, echocardiography. Only patients with mild/ moderate airway obstruction ($FEV_1 > 50\%$) were selected. They performed spirometry on Vyntus, cardiopulmonary exercise testing (Carefusion, Germany) in accordance with ERS guidelines [11-13]. Stress-induced RV diastolic dysfunction was considered if stress induced E/e' ratio > 6 [14]. Patients with and without RVDD were compared to each other. Normally distributed continuous variables were compared by unpaired t-test, whereas Mann-Whitney-U test was used in other cases. Categorical variables were compared by the χ^2 test. The Spearman's ρ rank correlation was applied. In all cases a p value of less than 0.05 was considered significant as determined with SPSS® 13.0 Software (SPSS, Inc, Chicago, Ill) statistics.

RESULTS

According to RV parameters, the two groups differed significantly regarding RAVI, RVWT, TAPSE at rest, E/A at rest, E/A after stress, E/e' after stress, AT and systolic pulmonary arterial pressure after stress (Table 1).

Association was noted between RAVI and stress induced E/e' ratio, as well as RAVI and 6-MWT (Table 2).

Table 1. Echocardiographic characteristics of the patients with and without RVDD

Mean $\pm$ SD	Patients w/o stress RVDD (22)	Patients with stress RVDD (82)	p-value
RV structural parameters			
RAVI, ml/m ²	18.02 $\pm$ 2.69	23.04 $\pm$ 2.67	< 0.0001*
RVWT, mm	5.42 $\pm$ 1.10	6.53 $\pm$ 0.54	< 0.0001*
RV functional parameters at rest			
E/A ratio	0.91 $\pm$ 0.31	0.67 $\pm$ 0.14	0.312*
E/e' aver	5.72 $\pm$ 2.42	4.64 $\pm$ 2.01	0.340*
sPAP, mm Hg	26.85 $\pm$ 2.44	27.92 $\pm$ 2.99	0.260*
RV functional parameters after exercise stress test			
E/A ratio	1.4 $\pm$ 0.25	1.37 $\pm$ 0.21	0.290*
E/e' aver	4.73 $\pm$ 1.4	9.45 $\pm$ 2.18	< 0.0001*
sPAP, mm Hg	31.77 $\pm$ 2.20	38.27 $\pm$ 4.19	< 0.0001*

Results are presented as mean $\pm$ SD. *Mann-Whitney U test; Abbreviations: RVDD: right ventricular diastolic dysfunction

Table 2. Correlations between functional echocardiographic parameters at rest and after exercise stress with RAVI and 6MWT in patients with stress RVDD

	RAVI	6 MWT
RAVI		0.256* 0.027†
E/A ratio at rest	0.856* 0.384†	0.528* 0.561†
E/e' ratio at rest	0.186* 0.420†	0.607* 0.731†
S peak velocity m/sec	0.194* 0.400†	0.209* 0.475†
TAPSE, mm	0.077* 0.739†	0.087* 0.309†
AT at rest, msec	-0.523* 0.015†	0.083* 0.517†
sPAP at rest	0.598* 0.004†	0.047* 0.228†
AT, msec exercise	0.321* 0.156†	0.311* 0.041†
sPAP exercise	0.033* 0.887†	0.038* 0.832†
E/A ratio after exercise	0.052* 0.824†	0.071* 0.762†
E/e' ratio after exercise	0.445* 0.025†	0.207* 0.034†

*Spearman ρ correlation coefficient; † p – value;
‡Abbreviations AT – acceleration time

DISCUSSION

The main findings of our study are: 1) there is a high prevalence of stress-induced RVDD in non-severe COPD patients without PH at rest (78%); 2) the average value of RAVI in these patients is higher compared to those without stress-induced RVDD; 3) RAVI is associated with haemodynamic parameters at rest (acceleration time, systolic pulmonary arterial pressure), stress-induced RVDD (E/e') and diminished physical activity (6-MWT). The increased values of RAVI are associated with higher systolic blood pressure, stressed induced ratio E/e, shorter acceleration time and shorter distance, when performing 6MWT.

Having in mind the anatomical position and peculiarities of the right chambers, a satisfactory description of cardiac remodeling is often a challenge to clinicians, even more in patients with hyperinflation and COPD. RAVI has been reported as more easily

accomplished and reproducible measurement. Cioffi et al, studied patients with respiratory diseases and echocardiographic data of PH [15]. They found that RA size may be an early sign of the negative impact of the right ventricular-arterial decoupling in PH. Similar is the data from Agoston Coldea, et al [16]. They investigated that RAVI correlated to indices of RV systolic dysfunction (TAPSE, RVFAC or RVEF) and its progressive elevation corresponded to advanced RV systolic and diastolic dysfunction (E/e'). Our results from non-severe COPD patients without PH at rest also confirm these observations - we established that stress-induced diastolic dysfunction (E/e') is associated with right heart structural parameters (RAVI and RWT). Obviously, the relation between RAVI and diastolic function is debatable. The different results are probably due to the drawbacks of the echocardiography of the right ventricle, but may also be influenced by the different stages of COPD, where different degrees of diastolic dysfunction develop. The conditions under which RVDD is established (stress echocardiography or echocardiography at rest) could also be a possible explanation to the discrepancy. We established that RV diastolic dysfunction contributes to diminished physical activity. Patients with RVDD achieve a lower work load at CPET and a lower 6 minute distance. RAVI and stress-induced E/e' ratio are associated with the 6-MWT, but in a multivariate analysis they do not remain as independent predictors.

Data, regarding the role of RVDD in physical activity, is contradictory. Cuttica et al, found a correlation between RWT and diminished 6 MWT, independent from the lung function [9]. Schoos et al. report that tricuspid regurgitation is the only predictor of exercise tolerance [16]. Gokdenis et al, state that RVFW-S is the only marker responsible for 6-MWT [17]. The diversial results may probably be due to the different study populations and their clinical characteristics.

The main limitations of this study are: 1) the relatively small sample size; 2) COPD patients experience enhanced pressure swings during the respiratory cycle and measurements were performed at the end of expiration, which may influence the results; 3) we do not have invasive measurement of mPAP; 4) measurements were acquired in the early recovery period (approximately 2 min) after symptom-limited exercise and underestimation is possible.

CONCLUSION

We demonstrate that non-severe COPD patients have a high prevalence of exercise stress-induced right ventricular diastolic dysfunction (78%). It con-

tributes to exacerbation, disease progression and physical disability in COPD, and thus requires timely detection and management. RAVI corresponds to stress-induced RVDD (E/e') and diminished physical activity (6 MWT), but is not an independent predictor for any of them.

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