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Right Ventricular Dysfunction and Remodeling in Chronic Obstructive Pulmonary Disease Without Pulmonary Hypertension

Janne Mykland Hilde, MD,* Ingunn Skjørten, MD,† Ole Jørgen Grøtta, MD,‡ Viggo Hansteen, MD,* Morten Nissen Melsom, MD, PhD,§ Jonny Hisdal, PhD,‖ Sjur Humerfelt, MD, PhD,† Kjetil Steine, MD, PhD¶

Oslo, Norway

Objectives The aim of the present study was to elucidate right ventricular (RV) function and structure in patients with chronic obstructive pulmonary disease (COPD) without pulmonary hypertension (PH).

Background There is little knowledge of RV function and remodeling in COPD without PH.

Methods Thirty-four controls and 98 patients with COPD were included. The study patients were divided into 2 groups by right heart catheterization: no PH (mean pulmonary artery pressure [mPAP] <25 mm Hg) and PH (mPAP ≥25 mm Hg). The echocardiographic tissue Doppler imaging variables of RV isovolumic acceleration, peak systolic strain, and RV myocardial performance index were measured at the basal free wall, and RV wall thickness and RV internal dimension were measured in the RV outflow tract.

Results The increases in RV wall thickness and RV dimension were more evident when comparing controls with the no PH group (3.5 ± 0.5 mm to 5.5 ± 1.0 mm [$p < 0.01$] and 1.5 cm ± 0.2 to 2.0 ± 0.5 cm [$p < 0.01$]) than comparing the no PH group with the PH group (5.5 ± 1.0 mm to 6.6 ± 1.1 mm [$p < 0.01$] and 2.0 cm ± 0.5 to 2.1 ± 0.3 cm [p = NS]), respectively. Similarly, RV isovolumic acceleration, performance index, and strain deteriorated significantly when comparing controls with the no PH group and comparing the no PH group with the PH group ($p < 0.01$). Significant correlations were observed between mPAP and RV isovolumic acceleration, performance index, strain, and RV wall thickness ($p < 0.01$). RV impairment and increased RV wall thickness and RV dimensions were present even at slight elevations of mPAP (18 ± 3 mm Hg) in the no PH group.

Conclusions The present study showed that impaired RV systolic function, hypertrophy, and dilation were present even at a slight increase of mPAP, which indicates an early impact on RV function and structure in patients with COPD. RV isovolumic acceleration, performance index, and strain could detect subclinical disease and separate controls from those with no PH. (J Am Coll Cardiol 2013;62:1103–11) © 2013 by the American College of Cardiology Foundation

The development of right heart failure in patients with chronic obstructive pulmonary disease (COPD) is linked to worse outcomes with an increased risk of hospital readmissions and mortality (1,2). Thus, noninvasive imaging modalities that provide an accurate measurement of right ventricular (RV) function are crucial in a clinical setting. Several studies have investigated RV function in patients with COPD who have pulmonary hypertension (PH) (3–5). However, little information is available on RV function in patients with COPD who do not have PH.

COPD is associated with structural and mechanical changes in the pulmonary vascular bed that increase RV afterload. Pulmonary vascular remodeling occurs not only in patients with advanced COPD but also in patients with mild disease and even in smokers with normal lung function (6,7). This narrowing and stiffening process occurs in both the proximal and distal pulmonary arteries and results in increased

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From the *Department of Cardiology, Oslo University Hospital, Oslo, Norway; †Department of Pulmonary Medicine, Oslo University Hospital, Oslo, Norway; ‡Department of Radiology, Oslo University Hospital, Oslo, Norway; §Department of Pulmonary Medicine, Akershus University Hospital, Oslo, Norway; ‖Section of Vascular Investigations, Oslo University Hospital, Oslo, Norway; and the ¶Department of Cardiology, Akershus University Hospital, Oslo, Norway. This work was supported by the Eastern Norway Regional Health Authority and the Department of Cardiology, Oslo University Hospital, Oslo, Norway. The authors have reported that they have no relationships relevant to the content of this paper to disclose.

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Abbreviations and Acronyms

CI = confidence interval
COPD = chronic obstructive pulmonary disease
GOLD = Global Initiative for Chronic Obstructive Lung Disease
LV = left ventricular
mPAP = mean pulmonary artery pressure
PA = pulmonary artery
PH = pulmonary hypertension
PVR = pulmonary vascular resistance
PWP = pulmonary wedge pressure
RV = right ventricular
TDI = tissue Doppler imaging

pulmonary vascular resistance (PVR) and reduced pulmonary artery (PA) compliance (8).

Although invasive hemodynamic measurements of RV function still remain the gold standard, echocardiography is the standard clinical method to assess RV function. However, echocardiographic assessment of RV function is often difficult using conventional methods because of the complexity of the anatomy of the right ventricle. Novel techniques such as 3-dimensional evaluation of RV ejection fraction, tissue Doppler imaging (TDI) velocities, and strain have emerged and enable identification of impaired RV function at an earlier stage.

Thus, the present study sought to identify subclinical RV systolic dysfunction at rest, before hemodynamic decompensation, by applying modern echocardiographic imaging in a cohort of patients with stable COPD. We hypothesized that remodeling of the pulmonary arteries, increased steady state, and pulsatile RV afterload would have a secondary impact on RV geometry and function in patients with COPD who had a mean pulmonary artery pressure (mPAP) below the current guideline definition of PH.

Methods

Study patients. Ninety-eight outpatients with stable COPD of varying severity and free of overt cardiovascular disease were consecutively included in this study from 2006 to 2010 (Table 1). The diagnosis of COPD was based on a history of cigarette smoking of at least 10 pack-years and spirometric irreversible airway obstruction according to current guidelines (9). Spirometry, diffusion capacity for carbon monoxide, and measurement of arterial blood gases were performed according to guidelines. Patients were classified according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (9).

White patients who were 40 to 75 years of age with spirometric confirmed COPD in GOLD stages II to IV were included. They had to be free of exacerbations of COPD for the 2 months before inclusion in the study. A small number of these patients were treated with supplemental oxygen, administered as long-term treatment with oxygen in 8 patients and as ambulatory oxygen support in 4 patients. All participants underwent preinclusion screening, including resting electrocardiogram and a dynamic exercise test on a cycle ergometer. Patients with left ventricular (LV) disease, treated arterial hypertension with blood pressure >160/90 mm Hg, arrhythmias (including atrial fibrillation), other acute or

Table 1 Demographics, LV Systolic/Diastolic Functional Indices, and Pulmonary Function in Patients With COPD With and Without PH Compared With Healthy Controls

Variables	Healthy Controls (n = 34)	No PH (n = 72)	PH (n = 26)	p Value
Age (yrs)	63 ± 7	64 ± 6	62 ± 8	NS
Female (n)	19	34	15	NS
Body mass index (kg/m^2)	25 ± 3	24 ± 5	25 ± 6	NS
Body surface area (m^2)	1.9 ± 0.2	1.8 ± 0.2	1.8 ± 0.3	NS
Heart rate (beats/min)	66 ± 11	87 ± 14*	95 ± 18*†	<0.01
Systolic blood pressure (mm Hg)	120 ± 17	139 ± 22*	140 ± 18*	<0.01
Diastolic blood pressure (mm Hg)	76 ± 12	69 ± 12*	68 ± 13*	<0.01
N-terminal pro-hormone of brain natriuretic peptide (pmol/l)‡	N/A	9.3 (2.1–40.4)	9.9 (1.4–68.7)	NS
LV ejection fraction (%)	61 ± 5	57 ± 4*	58 ± 5*	<0.01
LV transmitral early diastolic velocity/late diastolic velocity ratio	1.07 ± 0.29	1.04 ± 0.25	1.03 ± 0.26	NS
LV transmitral early diastolic velocity/septal mitral annular early diastolic tissue velocity	7.7 ± 1.5	8.6 ± 2.1	10.3 ± 2.2*†	<0.01
Left atrial volume (ml/m^2)	21 ± 4	24 ± 5*	21 ± 5	<0.01
Smoking habits (n)§	2/13/19	23/49/0*	8/18/0*	<0.01
Pack-years of smoking	8 ± 9	41 ± 19*	39 ± 20*	<0.01
FEV_1 % predicted	98 ± 10	46 ± 15*	32 ± 12*†	<0.01
FVC % predicted	105 ± 11	76 ± 20*	61 ± 16*†	<0.01
FEV_1/FVC (%)	76 ± 4	49 ± 11*	43 ± 13*†	<0.01
Diffusion capacity for carbon monoxide of the lungs % predicted	100 ± 15	57 ± 19*	36 ± 20*†	<0.01
Residual volume % predicted	119 ± 16	192 ± 59	241 ± 60*†	<0.01
Inspiratory capacity/total lung capacity	0.44 ± 0.08	0.32 ± 0.11	0.23 ± 0.12*†	<0.01
6-min walk distance (m)	N/A	489 ± 113	343 ± 149†	<0.01

Values are mean ± SD or n. *Significantly different from controls. †Significantly different from no PH. ‡Geometric mean (95% confidence interval). §Current, former, and never smokers, respectively.
COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; LV = left ventricular ejection fraction; N/A = not measured; PH = pulmonary hypertension.