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ORIGINAL ARTICLE

Evaluation of the left ventricle in patients with COPD and nocturnal hypoxemia

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ABSTRACT

Objective: To verify association between left ventricular (LV) mass and thickness and the presence of significant nocturnal hypoxemia in patients with COPD with mild diurnal hypoxemia. **Methods:** A cross-sectional study carried out in clinically stable outpatients with COPD and mild hypoxemia (oxygen saturation ≥90 to ≤94%, identified by noninvasive oximetry) in a clinic specialized in the treatment of respiratory diseases in Goiânia-GO. All patients were submitted to clinical evaluation, spirometry, polysomnography, echocardiography, arterial blood gas analysis, 6-minute walk test and chest X-ray. **Results:** Patients with significant nocturnal hypoxemia had echocardiographic parameters associated with increase of LV musculature when compared to patients with mild nocturnal hypoxemia. The LV volume/mass ratio was significantly lower in the group with significant nocturnal hypoxemia (ratio 0.64 ± 0.13 versus 0.72 ± 0.12, p = 0.04), the thickness diastolic diameter of the interventricular septum and the diastolic thickness of the LV posterior wall were significantly higher in this group (9.7 ± 0.92 versus 9.1 ± 0.90 p = 0.03), (9.7 ± 1.0 versus 8.9 ± 1.0, p = 0.01. The time in REM sleep with saturation below 85% significantly predicted septum thickness (adjustment for BMI, age and mean blood pressure, r^2 = 0.20; p = 0.046). **Conclusion:** We observed association between severe REM sleep hypoxemia and echocardiographic parameters indicating increased LV mass in individuals with COPD and significant nocturnal hypoxemia. This suggests that this subgroup of individuals may benefit from an echocardiographic evaluation of the left ventricle.

Keywords: Chronic Obstructive Pulmonary Disease; Left ventricular hypertrophy; Echocardiography.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the main causes of global morbidity and disabilities and, according to the World Health Organization (WHO),[1] more than 210 million people worldwide have COPD, which could become in 2020, the third leading cause of death in the world.[2] In Brazil, it is estimated that there are more than 7 million adults affected.[3]

This disease causes pulmonary and extrapulmonary changes that lead to a decrease in the individual's quality of life, reduction in exercise tolerance, increase in the number of hospitalizations and risk of cardiovascular morbidities.[4] The uncorrected chronic hypoxemia caused by COPD triggers mechanisms that contribute to left ventricular (LV) hypertrophy, through systemic inflammation, release of oxygen radicals and activation of the sympathetic nervous system. LV hypertrophy deserves attention due to the damage caused in patients with this condition, such as: arrhythmias, reduced coronary perfusion, thromboembolic events and a significant 38% increase in mortality in patients with COPD.[5]

Abnormalities caused by mild to severe hypoxemia in the right ventricle are already well described in the literature,[6] but the relationship between chronic respiratory disease and left ventricular disorders is not well established.[7] Thus, the present study aims to verify the association between increased LV mass and/or thickness and significant nocturnal hypoxemia in patients with COPD. Early identification and consequent treatment can have great impact on the prevention of cardiovascular complications in these patients.

METHODS

The present work is a subproject of the research "Association between Night Hypoxemia and Depression in Patients with Chronic Obstructive Pulmonary Disease

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(COPD): A Case-control Study", carried out according to good clinical practices and approved by the Ethics Committee of the Goiânia General Hospital, under protocol nº 198.344/2013. The main research was initially carried out as a cross-sectional study to estimate the prevalence of OSA and nocturnal hypoxemia, followed by a case-control study, comparing patients with COPD and mild hypoxemia with major depression (cases) with patients without major depression (controls). This work evaluates the data collected in a cross-sectional study of the initial sample of patients with COPD and mild hypoxemia.

Study location

The main research study was conducted at the CLARE Clinical Research Center, an outpatient clinic specialized in the care of pulmonary diseases, in Goiânia, Goiás.

Inclusion criteria

Individuals with COPD who were not undergoing home oxygen therapy, clinically stable, aged 40 or over, admitted between April 1 and September 31, 2013 at the CLARE Clinical Research Center.

After signing the Informed Consent Term (ICF), an oximetry was performed to include only patients with mild daytime hypoxemia (oxygen saturation ≥90% to ≤94%). The patients subsequently underwent clinical evaluation (anamnesis and physical examination), answered validated questionnaires for dyspnea from the Medical Research Council, COPD Assessment Test (CAT) health impairment, socioeconomic level (Associação Brasileira de Empresas de Pesquisa, 2009[8]), and performed spirometry, 6-minute walk test, polysomnography, echocardiogram, arterial blood gas analysis and chest radiography. Individuals with oxygen saturation ≤85% for at least 5 minutes during sleep were considered to have significant nocturnal hypoxemia.[9]

Exclusion criteria

Pregnancy, recent myocardial infarction (less than three months ago), medical history of asthma or any other concomitant lung disease, history of cancer diagnosis, presence of renal failure or dialysis, presence of insulin- dependent, presence of PaO2 <60mmHg at rest, presence of radiographic evidence of any significant abnormality not attributable to COPD and inability to understand or complete all questionnaires, tests and interviews.

Sample size calculation

The t-test was used to determine whether the thickness of the left ventricular (LV) infero-septal wall differs significantly between groups of COPD patients with and without significant nocturnal hypoxemia. The sample was calculated to be able to detect a difference of 15% or more in the thickness of the LV infero-septal wall. A previous study reported that the mean and standard deviation of the LV infero-septal wall thickness in a group of COPD patients was 11 ± 1.9. For α (two-tailed) = 0.05 and power = 0.80, at least 42 individuals with COPD are required.

The results were analyzed using the Stata version 13.1 program (StataCorp, Texas, USA), using a 5% significance level ($p < 0.05$). Shapiro-Wilk test was used to assess the normality of the data. Quantitative variables with normal distribution were described using mean and standard deviation, quantitative variables that did not have normal distribution were described using median and interquartile range, and qualitative variables were described using proportions.

The t-test was used to compare the means; the Wilcoxon test was used for comparisons of medians; and the chi-square test or Fisher's exact-test was used for dichotomous variables. Linear regression was selected to estimate the association between time with saturation below 85% in REM sleep and interventricular septum thickness (IVS), while adjusting for BMI, age and mean arterial pressure.

RESULTS

During the study period, 230 COPD patients were admitted to the CLARE Clinical Research Center outpatient clinic and assessed for eligibility. Of these, 24 patients (10.4%) were excluded due to home oxygen therapy or refusal to participate. Of the remaining patients, 93 patients (40.4%) were excluded because of oximetry ≥ 95% or <90%, 42 patients (18.3%) were excluded due to FEV1/FVC> 70, and 07 patients (3.0%) were excluded due to the presence of radiological evidence of significant changes not attributable to COPD and PaO2 <60mmHg. Figure 1 describes the flow for selecting participants.

The study sample comprised mostly of elderly patients with COPD and advanced disease (GOLD D), with a predominance of males (56.3%), low socioeconomic level, normal Body Mass Index (BMI), the majority of ex-smokers and hypertensive patients (57.8%) with controlled disease. The groups with and without significant nocturnal hypoxemia were different in relation to BMI, PaCO2 and oxygen saturation. There was no statistically significant difference between the two groups, considering blood pressure or percentage of hypertensive patients. The group with significant nocturnal hypoxemia (26.6%) had a higher BMI, higher PaCO2 and less oxygen saturation. (Table 1).

There were more individuals with OSA in the group with significant nocturnal hypoxemia as well as the mean saturation at wake and during sleep were significantly lower in that group (Table 2).

Evaluating the mean saturation of REM sleep versus non-REM sleep, it was found that the median REM

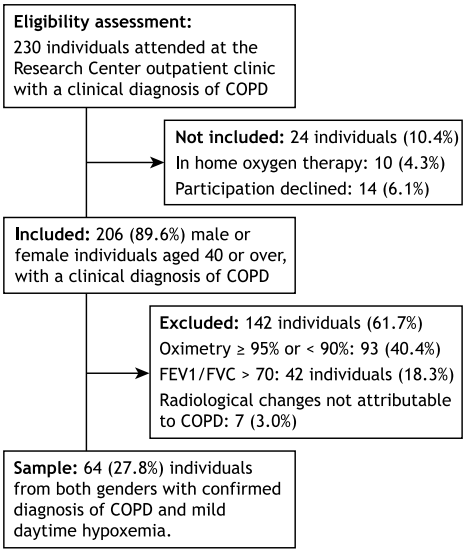

Figure 1. Flow for selecting participants. FEV1 / FVC: forced expiratory volume ratio in the first second and forced vital capacity.

sleep is significantly lower than that of non-REM sleep in both groups: with significant nocturnal hypoxemia (88% versus 91%, respectively p = 0.001) and without significant nocturnal hypoxemia (93% versus 93.5%, respectively p = 0.02).

Regarding echocardiographic parameters, the volume-to-mass ratio was significantly lower in the group with significant nocturnal hypoxemia (ratio 0.64 ± 0.13 versus 0.72 ± 0.12, p = 0.04), the diastolic thickness of the SIV and the LV posterior wall (PP) diastolic thickness were significantly greater in this same group (9.7 ± 0.92 versus 9.1 ± 0.90 p = 0.03), (9.7 ± 1.0 versus 8, 9 ± 1.0, p = 0.01 (Table 3, Figures 2 and 3). The time with saturation below 85% in REM sleep positively correlates to the thickness of the interventricular septum, r = 0.32, p = 0.01, and significantly predicts the interventricular septum thickness (interventricular septum thickness in mm = 8.21 + 0.022 time with saturation ≤85% + 0.03BMI + 0.017 mean arterial pressure -0.02 age, r^2= 0.20; p = 0.046).

Table 1. Characteristics of patients with COPD and mild daytime hypoxemia seen at a clinical center specialized in the treatment of respiratory diseases, Goiânia, Goiás (GO), during the study period.

	All patients	With Significant Nocturnal hypoxemia	Without Significant nocturnal hypoxemia	p
	n = 64	n = 17	n = 47	
Age, years	69.7 ± 8.8	69.4 ± 6.2	69.8 ± 9.6	0.85
Gender male, n (%)	36 (56.3)	7 (41.2)	29 (61.7)	0.15
BMI, kg/m^2	25.1 ± 5.2	27.6 ± 6.6	24.2 ± 4.4	0.02*
Cervical circumference, cm	36.6 ± 4.9	37.4 ± 5.9	36.3 ± 4.4	0.43
Socioeconomic score	17 (14;24)†	16 (16;19)†	17 (14;25)†	0.72
Smoking (packs/year)	47.5 (26;60)†	54 (26;60)†	39 (25;60)†	0.42
Active smoking n (%)	17 (26.6)	5 (29.4)	12 (25.5)	
Ex-smoker n (%)	42 (65.6)	10 (58.8)	32 (68.1)	0.74
Never smoked n (%)	5 (7.8)	2 (11.8)	3 (6.4)	
PAS, mmHg	129.7 ± 18.3	128.2 ± 20.4	130.2 ± 17.6	0.70
DBP, mmHg	74.5 ± 8.3	77.1 ± 9.9	73.6 ± 7.6	0.15
MAP, mmHg	92.9 ± 10.5	94.1 ± 12.6	92.4 ± 9.5	0.57
Hypertension, n (%)	37 (57.8)	11 (64.7)	26 (55.3)	0.50
COPD GOLD A	6 (9.4)	1 (5.9)	5 (10.6)	
n (%) GOLD B	10 (15.6)	3 (17.7)	7 (14.9)	0.76
GOLD C	2 (3.1)	0 (0)	2 (4.3)	
GOLD D	46 (71.9)	13 (76.4)	33 (70.2)	
FEV1 post-Bd (liters)	1.29 ± 0.6	1.21 ± 0.5	1.32 ± 0.6	0.51
FEV1 post -Bd (%)	50.2 ± 18.6	49.6 ± 17.9	50.4 ± 19.0	0.87
FEV1/FVC post -Bd (%)	51.3 ± 12.1	55.7 ± 13.3	49.7 ±11.4	0.08
PaO2, mmHg	71.9 ± 9.8	68.1 ± 11.8	73.4± 8.7	0.06
PaCO2, mmHg	35.1 ± 5.2	37.5 ± 5.7	34.2 ± 4.7	0.03*
Sat O2, blood gas analysis (%)	93.8 ± 2.1	92.9 ± 2.2	94.2 ± 1.9	0.02*
Pulmonary hypertension, n (%)	3 (4.7)	1 (5.9)	2 (4.3)	
PAPs normal, n (%)	30 (46.9)	10 (58.8)	20 (42.6)	0.38
PAPs indeterminate, n (%)	31 (48.4)	6 (35.3)	25 (53.1)	
6MWT distance (% predicted)	92.2 (82.4;107.7)†	95.1 (88.7;107.8)†	89.1 (76.7;107.7)†	0.13
CAT (0-40)	17 ± 7.1	16 ± 6.1	17.3 ± 7.5	0.51

Data are presented as mean ± SD, n (%) or median (interquartile range: p25; p75) †. BMI: Body Mass Index; PAS: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; GOLD: Global Initiative for Chronic Obstructive Lung Disease; FEV1: forced expiratory volume in one second; post-BD: post-bronchodilator; FVC: forced vital capacity; PAPs: pulmonary artery systolic pressure; 6MWT: 6-minute walk test; CAT: COPD Assessment Test. Pulmonary hypertension: PAPs> 40. Undetermined PAP: patients without tricuspid regurgitation. *Statistically significant difference.

Table 2. Sleep parameters of patients with COPD and mild daytime hypoxemia seen at a clinical center specializing in respiratory diseases, Goiânia, Goiás (GO), during the study period.

	Significant nocturnal hypoxemia		p
	Yes	No	
	n = 17	n = 47	
Epworth sleepiness scale	8.3 ± 4.2	7.5 ± 4.4	0.55
Total time in bed, min	432.4 ± 46.6	422.5 ± 52.6	0.49
Sleep period, min	404.8 ± 41.4	386.8 ± 42.8	0.17
Wake up before sleep, min	33.5 (17-40)†	30.5 (18-39)†	0.92
Wakefulness after sleep onset, min	38 (18-51)†	29.5 (17-38)†	0.46
Sleep efficiency	69.7 (63.7-79.4)†	70.6 (58.5-82.5)†	0.66
Sleep latency REM, min	152 (59-226.5)†	108.3 (67.5-152.5)†	0.48
Micro wake-up/TTS hour	20.4 (7-28.7)†	10.4 (6.1-19.8)†	0.21
REM sleep duration, min	70.6 ± 20.6	54.3 ± 25.9	0.04*
Duration of non-REM sleep, min	254.6 ± 46.4	237.8 ± 51.8	0.28
Sleep stage I (% of TTS)	5.3 (3.3-6.5)†	5.7 (4.1-6.7)†	0.57
Sleep stage II (% of TTS)	59.3 ± 11.1	59.4 ± 12.3	0.96
Sleep stage III/IV (% of TTS)	15.3 ± 8.4	16.2 ± 9.0	0.70
REM stage (% of TTS)	20.1 ± 5.8	18.6 ± 8.4	0.49
Apnea/hypopnea index (TTS)	15.3 (10.2-30.5)†	5.9 (3.2-9.8)†	0.0002*
Presence of OSA (%) (AIH≥15)	9 (64.3)	5 (35.7)	0.0001*
Mean saturation, wakefulness (%)	92 (90-93)†	94 (93-95)†	0.0002*
Mean sleep saturation (%) (TTS)	91 (89-92)†	94 (92-95)†	0.0001*
Mean sleep saturation (%) (REM)	88 (85-89)†	93 (91-94)†	<0.00001*
Mean sleep saturation (%)(n-REM)	91 (88-92)†	93.5 (91-95)†	0.001*
Minimum sleep saturation (%) (TTS)	73 (72-77)†	87 (83-91)†	<0.00001*

Data are presented as mean ± SD, n (%) or median (interquartile range: p25; p75)†. TTS: total sleep time; OSA: obstructive sleep apnea. REM: *rapid eye movement*; AIH: *the apnea-hypopnea index*. *Statistically significant difference.

Table 3. Echocardiographic variables of patients with COPD and mild daytime hypoxemia seen at a clinical center specializing in respiratory diseases, Goiânia, Goiás (GO), during the study period.

	Significant nocturnal hypoxemia		p
	Yes	No	
	n = 17	n =47	
Left atrial diameter (mm)	33.8 ± 3.7	32.1 ± 3.8	0.13
Right ventricular diameter (mm)	21 (20-21)†	21 (20-21)†	0.14
Diastolic left ventricular diameter (mm)	46 (40-51)†	46 (42-50)†	0.73
Systolic left ventricular diameter (mm)	27 (26-30)†	29 (25-31)†	0.70
Diastolic thickness of the interventricular septum (mm)	9.7 ± 0.92	9.1 ± 0.90	0.03*
Diastolic thickness of the LV posterior wall (mm)	9.7 ± 1.0	8.9 ± 1.0	0.01*
Volume/mass ratio	0.64 ± 0.13	0.72 ± 0.12	0.04*
Left atrium/aorta relationship	1.2 ± 0.2	1.1 ± 0.2	0.16
Left ventricular mass (g)	154.3 ± 39.4	143.8 ± 39.3	0.35
LV ejection fraction (%)	70 (64-74)†	69 (65-72)†	0.33
LV mass/body surface ratio (g/m^2)	91.2 (69.5-101.2)†	81.3 (69.4-106.3)†	0.80
LV cavity shortening (%)	40 (35-43)†	39 (36-41)†	0.64
LV septum/posterior wall thickness ratio	1 (1-1)†	1 (1-1.1)†	0.42
LV end diastolic volume (ml)	97 (70-124)†	97 (79-118)†	0.73
LV stroke volume (ml)	68.1 ± 20.7	67.7 ± 20.1	0.95
LV end stroke volume (ml)	27 (25-35)†	32 (22-38)†	0.70
LV systolic dysfunction, n (%)	0 (0)	2 (4.3)	0.54
LV diastolic dysfunction, n (%)	14 (82.4)	32 (68.1)	0.21

Data are presented as mean ± SD, n (%) or median (interquartile range: p25; p75)†. LV: left ventricle. *Statistically significant difference.

DISCUSSION

Our COPD sample showed characteristics representative of these patients in Brazil, corroborating the data published by the PLATINO study in Brazil, in which 18% of men and 14% of women were affected with COPD.[10] Thus, both the study by Mueller et al.,[11] who evaluated the systemic effects of nocturnal hypoxemia in COPD patients without obstructive sleep apnea syndrome (male gender corresponded to 71.4% of the total sample), and the present study (male gender corresponded to 56.3% of the sample) showed predominance of males.

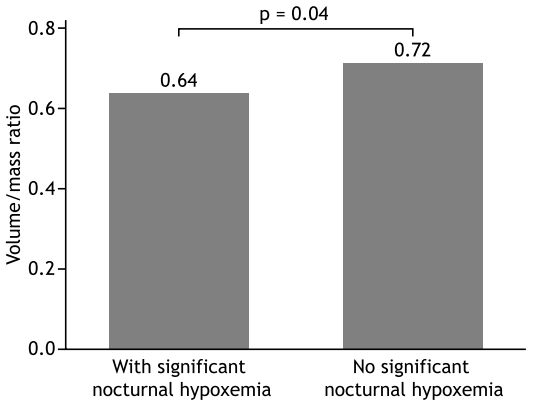

Figure 2. Mean volume/mass ratio of patients with COPD and mild daytime hypoxemia seen at a clinical center specializing in respiratory diseases, Goiânia, Goiás (GO), during the study period.

The same was observed regarding the socio-economic level of the sample. Tando,[12] states that low socioeconomic conditions are a risk factor for COPD. Likewise, Prescott et al.,[13] reinforces that the negative impact of socioeconomic status on the pulmonary function of patients with COPD is only second to the impact of smoking. In the socioeconomic score used in the present study, patients with significant nocturnal hypoxemia reached 16 points and those without significant nocturnal hypoxemia reached 17 point, both in class C2 (mean family income of 726 reais), reinforcing the influence of socioeconomic status in COPD.

Systemic arterial hypertension (SAH) was observed in 57% of the individuals evaluated. It was considered the most frequent comorbidity in patients with COPD in Costa's et al.[14] research, and it affects 42.2% of the participants in this study. Also, we observed no statistically significant difference between the groups with and without significant nocturnal hypoxemia in relation to the level of blood pressure, and in relation to the prevalence of hypertensive patients. Thus, the LV hypertrophy found in the group with nocturnal hypoxemia was not due to inadequate control of blood pressure or the greater amount of hypertension in the group with significant nocturnal hypoxemia, as arterial hypertension is a well-established risk factor for LV hypertrophy.[15]

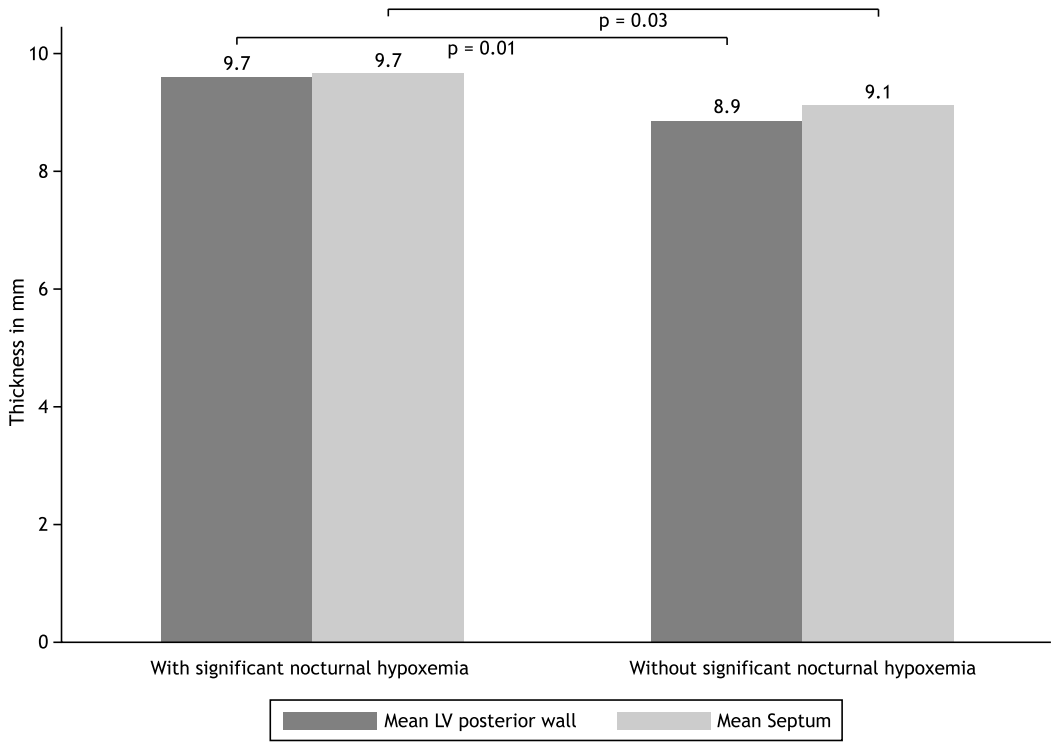

Figure 3. Mean posterior wall of the LV and interventricular septum of patients with COPD and mild daytime hypoxemia seen at the clinical center specialized in the treatment of respiratory diseases, Goiânia, Goiás (GO), during the study period. LV: left ventricle.

The study sample had normal BMI; however, the mean BMI of the group with significant nocturnal hypoxemia was higher than in the group without abnormal sleep (27.6 kg/m^2 versus 24.2 kg/m^2). This was also observed in the study Chaouat et al.,[16] which found an association between high BMI and nocturnal desaturation. Pujante et al.[17] found a high prevalence (76.2%) of OSA in patients with morbid obesity, as well as a high prevalence (78.6%) of changes in LV mass in morbidly obese patients affected by OSA. In other studies, Avelar et al.,[18] Mirzaaghazadeh et al.,[19] Papachatzakis et al.,[20] Gupta et al. [21], most patients with OSA presented significantly higher BMI and waist circumference, since obesity is an important risk factor for OSA, which in turn leads to nocturnal hypoxemia.[22]

However, OSA is not the exclusive cause of significant nocturnal hypoxemia, which can also be caused by COPD, by decreased functional residual capacity due to hypotonia of the intercostal muscles, decreased ventilatory response to hypoxia and hypercapnia, and by worsening ventilation/perfusion disproportion at night.[23] We observed OSA in 64.3% of patients with significant nocturnal hypoxemia, and in 35.7% of patients without significant nocturnal hypoxemia. According to Senaratna et al.,[24] in the general population, the prevalence ranges from 9 to 38%, and Tufik et al.[25] found OSA index in 32.8%, which was similar to that found in the sample without hypoxemia. This shows that the prevalence of OSA in the general population and in COPD patients without nocturnal hypoxemia remained very close, while the excess of OSA in the group with hypoxemia partially justifies the greater nocturnal desaturation in this group.

Zanchet and Viegas[26] found that 52% of the patients studied (with COPD, without sleep apnea and with mild hypoxemia during wakefulness) presented nocturnal desaturation. This was also seen in the present study since, even in the group without significant hypoxemia, the minimum sleep saturation was low (87%). We also observed that the mean wakefulness saturation was significantly lower in individuals with significant nocturnal hypoxemia (92% versus 94%), and this reproduced during sleep (88% versus 93% in REM sleep). Thus, we conclude that the presence of mild hypoxemia during wakefulness is a predictive factor of lower levels of the mean saturation during sleep, as demonstrated by Lewis et al.[27] A decrease in oxygen saturation was observed when in REM sleep compared to non-REM sleep in both groups. This drop in both groups is probably due to physiological changes in respiratory mechanics during sleep. The decrease in the sensitivity of the chemoreceptors, the respiratory motor drive and muscle contraction cause changes in the ventilation/perfusion ratio and increase in resistance to airflow. Although unimportant in healthy individuals, these changes can lead to pronounced nocturnal hypoxemia in REM sleep in patients with COPD.[4]

Regarding the daytime PaO2 and PaCO2 values, Plywaczewski et al.[28] demonstrated that patients with PaO2 values below 65 mmHg and PaCO2 above 45 mmHg were more likely to have nocturnal desaturation. We found similar results. The group with significant nocturnal hypoxemia had significantly lower levels of saturation (92.9% versus 94.2%) and higher PaCO2 (37.5 versus 34.2) compared to the group without significant nocturnal hypoxemia.

According to Mendes,[29] studies on the relationship between pulmonary function and cardiac remodeling in hypertensive individuals are still scarce. Vonk-Noordegraaf et al.[6] did not find an increase in LV mass or changes in their imaging parameters when comparing a group of 25 COPD patients with mild hypoxemia with healthy controls, however, nuclear magnetic resonance was used to assess the heart and not echocardiography. In post-mortem studies, left hypertrophy and its magnitude have been shown to be well correlated with the duration of right ventricular (RV) pressure overload.[30] In addition, due to ventricular interdependence, structural changes in the RV also change the structures of the LV.[6] The present study brings important findings to reinforce this scientific evidence regarding the LV changes that can be produced by respiratory diseases.

Three parameters that are related to left ventricular hypertrophy were altered in a group of patients experiencing significant hypoxemia at night (mass volume ratio, diastolic thickness of the interventricular septum and diastolic thickness of the posterior LV wall). As explained in the study by Dempsey et al.,[22] severe hypoxia induces increases in sympathetic nervous activity, including sympathetic nervous activity in the renal system, activating the Renin-Angiotensin-Aldosterone System. This stimulation of the mineralocorticoid receptor induces not only inflammation, but also oxidative stress, which leads to endothelial dysfunction and vascular remodeling, important mechanisms in the pathogenesis of cardiac hypertrophy. Even in healthy individuals, REM sleep is associated with intense sympathetic activation, up to 226% of the baseline value in wakefulness, possibly linked to changes in muscle tone.[31] In patients with nocturnal hypoxemia, such as those with OSA, this sympathetic nervous system hyperactivity can persist even when the individual is awake, being directly or indirectly involved in several other effects of hypoxemia, including oxidative stress, lipid dysfunction, inflammation systemic, endothelial dysfunction and accelerated atherosclerosis.[32] The increase in hypoxemia during REM sleep in patients with COPD is caused by a reduction in the minute volume secondary to depression of the ventilatory response to chemical stimuli associated with reduced activity of the accessory musculature of ventilation, that occurs at this stage of sleep. With the diaphragmatic function compromised by possible hyperinflation and the reduction of accessory respiratory muscle activity, there is a reduction in the functional residual capacity, which increases the closing volume, alters the ventilation-perfusion ratio and causes a decrease in oxygenation.[33] The intensification of hypoxemia, in turn, accentuates the activation of the sympathetic

nervous system, which leads to hemodynamic changes during REM sleep, playing an important role in the production of left ventricular hypertrophy.[34]

Left ventricular characteristics were analyzed in patients with significant nocturnal hypoxemia with COPD and mild daytime hypoxemia and data were found that indicate an increase in LV mass when compared with a group without significant nocturnal hypoxemia. Left ventricular mass has been shown to be an important predictor of cardiovascular outcomes, such as heart failure and coronary artery disease, with a higher cardiovascular risk with increased LV muscle, regardless of the presence of ventricular hypertrophy criteria.[35,36] In addition, randomized clinical trials demonstrate that a therapeutic intervention that reduces LV mass results in a decrease in mortality and morbidity.[3,4] Thus, by showing a greater LV mass in the group with significant hypoxemia during sleep, we identify the presence of greater cardiovascular risk in these patients.[37,38]

In the literature, data from studies relating COPD and left ventricular cardiac function are scarce and not conclusive. Thus, as a significant portion of COPD patients present nocturnal hypoxemia, our findings have relevant clinical implications for the prognosis of these patients, since LV hypertrophy in its uncompensated phase can result in left ventricular dysfunction, constituting an important factor in increasing cardiovascular morbidity and mortality. Thus, in addition to the clinician's usual concern with treating the hemodynamic consequences of lung disease in the right ventricle, we show that, in a subgroup of patients (with significant nocturnal hypoxemia), it is important to consider whether the respiratory disease affects the left ventricle to avoid the complications associated with your dysfunction.

We evaluated COPD patients with mild hypoxemia (oxygen saturation ≥90 to ≤94%) since isolated nocturnal hypoxemia in individuals with oxygen saturation ≥ 95% at rest is unlikely,[27] suggesting that this subgroup of patients would not need to be evaluated for nocturnal hypoxemia. Considering that COPD patients with oxygen saturation <90% are more likely to have PaO2 <60 mmHg at rest and come to need home oxygen therapy in case of pulmonary hypertension or cor pulmonale, this group of patients must have an echocardiogram. Thus, a subgroup of individuals with COPD is formed with oxygen saturation between 90 and 94%, of which there is little publication on the presence of nocturnal hypoxemia. This nocturnal hypoxemia could generate a higher cardiovascular risk, since patients with mild daytime hypoxemia may present disproportionate drops in oxygen saturation during sleep, which can cause arrhythmias and pulmonary hypertension, increasing the risk for heart and cerebrovascular disease.[39]

The present study has several limitations. The use of sedative medications was not included as an exclusion criterion and its use could accentuate a hypoxemia present during sleep. However, as the study design was not concerned with diagnosing the cause of nocturnal hypoxemia, but its consequence (significant left ventricular hypertrophy), the cause of severe hypoxemia, whether isolated night hypoxemia, apnea sleep, or chronic use of sedatives (since they are usually chronic medications) would not matter. The result would still be nocturnal hypoxemia, which, if significant, would produce an increase in ventricular mass. In addition, as the study has a relatively small sample size and cross-sectional character, it is necessary to carry out new prospective studies with larger samples that include participants with different severities of COPD to confirm the results found, and to verify the applicability of the evaluation of these parameters of left ventricular hypertrophy in daily clinical practice.

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