Original Article

Journal of Cardiovascular Medicine and Surgery
Volume 4 Number 2, April - June 2018
DOI: http://dx.doi.org/10.21088/jcms.2454.7123.4218.6

Cardiac Co-morbidities in Patients with Chronic Obstructive Pulmonary Disease: Prospective Observational Study

Nidhi Gupta[1], Gajendra Dubey[2], Citralekha Vora[3], Tarun Madan[4], Pankaj Garg[5], Usha Patel[6]

Authors Affiliation
[1] Assistant Professor [3]Associate Professor [6]Junior Resident, Department of Medicine, B.J. Medical College, Civil Hospital, Asarwa, Ahmedabad, Gujarat 380018, India.
[2]Assistant Professor [4]Associate Professor, Department of Cardiology, [5]Associate Professor, Department of CVTS, U.N. Mehta Institute of Cardiology and Research Center, Ahmedabad, Gujarat 380016.

Corresponding Author:
Nidhi Gupta,
Assistant Professor,
Department of Medicine,
B.J. Medical College, Civil Hospital,
Asarwa, Ahmedabad,
Gujarat 380018, India.
Email: drnidhigupta02@yahoo.com

Received on 16.04.2018
Accepted on 05.05.2018

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a major global health issue. COPD affects pulmonary vasculature as well as heart leading to the development of pulmonary artery hypertension (PAH), cor-pulmonale (COR-P), right and left ventricular dysfunction. Echocardiography is a rapid, noninvasive, portable, and accurate method to evaluate cardiac function in these patients. We performed the echocardiographic evaluation of COPD patients to study the prevalence of heart diseases in these patients. *Materials and Methods:* Ours was observational study. Total 125 patients of moderate to severe COPD according to GOLD guidelines were included in the study. All patients were evaluated with detailed history, chest X-ray postero-anterior view, electrocardiography (ECG), spirometry and trans-thoracic echocardiography (Echo). *Results:* We investigated 89 males and 36 female patients with mean age of 52.54 ± 9.55 years. Fifteen patients had GOLD class I COPD, 45 patients had GOLD class II COPD and 65 patients had GOLD class III and IV COPD. Breathlessness (100%) was most common presenting symptom and tachypnea (73%) was most common presenting sign. ECG was abnormal in 80% patients with right ventricular hypertrophy (53.6%) as most common finding. Eighty percent patients had abnormal echocardiography with PAH (57.6%) and right ventricular dilatation (49.6%) as the most common findings. *Conclusion:* There is significant prevalence of cardiac co-morbidities in patients with COPD. Cardiac screening should be done early in the disease which will be helpful in the assessment of the prognosis and to identify the patients who are likely to suffer increase morbidity and mortality.

Keywords: Chronic Obstructive Pulmonary Disease; Cor-pulmonale; Echocardiography; Left Ventricular Diastolic Dysfunction.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major global health issue and by year 2020, it may be the third most leading cause of mortality and fifth leading cause of morbidity in the world [1]. In a crude estimate, India inhabits nearly 30 million people with COPD, and is responsible for >20% of total deaths annually [2,3].

In COPD, abnormal inflammatory response of the lungs to noxious particles and gases, especially cigarette smoke leads to many pathological changes leading to chronic airflow and gas exchange limitation. Apart from lungs, COPD has significant cardio-vascular effects [4]. The spectrum of cardio-vascular diseases includes ventricular dysfunction, pulmonary artery hypertension (PAH), cor-pulmonale (COR-P), coronary artery disease (CAD), and arrhythmias. Cardiovascular complica-tions even in mild COPD results in significantly increased morbidity and mortality particularly in patients younger than 65 years. Studies have found arrhyth-mia, myocardial infarction, and congestive heart failure (CHF) as the predominant causes of cardio-vascular related mortality in COPD patients however, CAD is the main causes of mortality. Further, co-existence of COPD and CAD is very

common [5.6]. Reduction in forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) ratio is an independent risk factor for coronary events, increasing the risk by 30%. With every 10% decrease in FEV1, all-cause mortality increases by 14% and cardiovascular mortality by 28%. In severe COPD, cardiovascular diseases account for 20-25% deaths [7,8].

In COPD, patients may develop right or left or biventricular systolic and/or diastolic dysfunction independent of associated CAD. Important risk factors for the development of ventricular dysfunction are hypoxia, acidosis, ventricular interdependence, lung hyperinflation, and distension [9-11].

Patients with COPD are also prone to develop PAH. PAH is the common link between lung dysfunction and COR-P. Longstanding PAH in patients with COPD may lead to alteration in the structure and function of the right ventricle called COR-P. COR-P usually has a slow and chronic progression, but can also lead to acute onset and life-threatening complications [12-14].

Trans-thoracic echocardiography (TTE) provides a rapid, noninvasive, portable, and almost accurate method to evaluate the bi-ventricular function, ventricular filling pressure, valvular function and PAP [15]. It has been studied that echocardiography measured pulmonary arterial pressure closely correlates with pressure measured by right heart catheterization [16,17].

Present study was undertaken prospectively to evaluate the prevalence of cardiac co-morbidities in patients with COPD who presented to our hospital.

Materials and Methods

Ours was a prospective observational study. Between January 2017 and December 2017, consecutive patients with diagnosis of COPD according to GOLD guideline who attended the out-patient department of our hospital were included in the study. The study was approved by ethics committee of our hospital and informed and written consent was obtained from all the patients.

Exclusion criteria were associated acute or chronic respiratory infections, bronchial asthma, interstitial lung disease, carcinoma lungs, and other lung pathologies. Other exclusion criteria were history of cardiac diseases like ischemic heart disease, valvular heart diseases, and congenital heart disease. Patients with other associated co-morbidities like diabetes mellitus, non-pulmonary malignancy, collagen vascular diseases, HIV and other immunosuppressive diseases were also excluded from the study.

All the patients included in the study were evaluated by detailed history of respiratory and cardiovascular symptoms and were clinically examined. Further, a chest X-ray, electrocardiography (ECG), and detailed two-dimensional (2D) and M Mode trans-thoracic echocardiography (TTE) (VIVID 7 (GE healthcare) with a multi-frequency probe (range 2–4.3 MHz)) were performed in all the patients.

On TTE, PAH was defined as systolic pulmonary artery pressure (sPAP)≥30 mmHg. PAH was classified into mild, moderate, and severe category as sPAP 30-50, 50-70, >70 mmHg, respectively (using Chemla formula) [13,14]. Right ventricle dimension was measured by M-mode. COR-P was said to be present when RV dimension was >2.6cm (normal range 0.9-2.6 cm). Note was also made for right ventricle contractility. Left ventricular diastolic dysfunction was diagnosed by E/A ratio. E/A ratio is ratio of the peak mitral flow velocity of the early rapid filling wave (E) and peak velocity of the late filling wave caused by atrial contraction (A). E/A ratio >1.3 was taken as normal. E/A ratio <1.3 was taken as a sign of LVDD in age group 45-49 years, <1.2 in age group 50-59 years, <1.0 in age group 60-69 years, and <0.8 in age group ≥ 70 years [15].

Statistical Analysis

The data was presented as mean±SD. Between the groups' comparison was done by ANOVA. P value ≤ 0.05 was taken as significant. Correlation between the cardiac parameters on echocardiography findings and pulmonary parameters on spirometry findings was done to find out the relation and to estimate the risk of morbidity.

Results

Our study included 125 patients (89 males) with COPD. Fifteen patients had GOLD class I COPD, 45 patients had GOLD class II COPD and 65 patients had GOLD class III and IV COPD. Demographic profile of the patients is given in Table 1. Mean age of the patients was 52.54±9.55 years and age ranged from 33 years to 74 years. Ninety (72%) patients were older than 50 years. Mean BMI was 20.12±2.24 kg/m^2. Fifty four (43.2%) patients were underweight. 80% patients had history of smoking and 80.3% smokers had >15 pack-years smoking history. 48% patients were symptomatic for >5 years. Among various symptoms, breathlessness was the

commonest symptom while tachypnea was the commonest sign.

Table 1: Demographic profile of the patients.

Variables	No of patients (N=125)
Age (Years)	52.54 ± 9.55
Sex (Male) (n)	89 (71.2%)
Body Mass Index (kg/m^2)	20.12 ± 2.24
History of smoking (n)	86 (68.8%)
Duration of smoking (pack-years)	23.55 ± 5.34
COPD Severity (n)	
• Mild	15 (12%)
• Moderate	45 (36%)
• Severe	65 (52%)
Duration of symptoms (years)	7.58 ± 2.83
Symptoms	
• Breathlessness	125(100%)
• Cough and expectoration	118 (94.4%)
• RHC pain	10 (8%)
Signs	
• Tachypnea	91 (72.8%)
• Barrel shaped chest	75 (60%)
• Pedal edema	48 (38.5%)
• RHC Tenderness	5 (4%)
FEV1 (%)	47.67 ± 16.34

COPD- chronic obstructive pulmonary disease, RHC- right hypochondrium, FEV1- forced expiratory volume in 1 second.

In chest X-ray, 100 (80%) patients had features of emphysema while 85 (68%) patients had increased Broncho-vascular marking suggestive of chronic bronchitis. X-ray evidence of PAH i.e. prominent right descending pulmonary artery was present in 44 (35%) patients. Cardiomegaly on chest X-ray was noted in 26 (21%) patients.

ECG findings

Table 2 shows ECG changes in patients with varying severity of COPD. Total 67 (53.6%) patients had an ECG evidence of right ventricular hypertrophy (RVH). The most common finding suggestive of RVH was right axis deviation (47.2% patients), followed by R/S <1 in lead V5 and V6, followed by R/S >1 in lead V1 (40% patients). After RVH, other common findings were P pulmonale (46.4% patients) and poor progression of R wave (30.4% patients). Uncommon ECG finding was incomplete right bundle branch block (RBBB) (6.4% patients). 20% patients had a normal ECG.

On comparing the ECG changes as per COPD severity, ECG was abnormal in all the patients with severe COPD compared to 60% in patients with moderate COPD and 53% in patients with mild COPD. In patients with severe COPD, RVH (72.3% patients) was most common while in patients with moderate COPD, 'p' pulmonale (46.7% patients) was most common ECG finding. In patients with mild COPD, 53% patients had low voltage complexes while 47% patients had normal ECG. As shown in Table 1, incidence of right axis deviation, RVH, 'p' pulmonale ($p<0.001$) and Poor progression of 'r' wave ($p<0.05$) increased significantly with increasing severity of COPD. Among atrial arrhythmias, 7 (5.6%) patients had atrial fibrillation and 6 (4.8%) patients had multifocal atrial tachycardia.

Table 2: Electrocardiographic (ECG) Findings with Severity of the COPD.

	Mild (n=15)	Moderate (n=45)	Severe (n=65)	% of patients	P value
'p' pulmonale	1 (6.7%)	21(46.7%)	36 (55.4%)	58 (46.4%)	**0.003**
Low voltage complex	8 (53%)	11 (24.4%)	20 (30.7%)	39 (31.2%)	0.112
Right axis deviation	0	17 (37.7%)	42 (64.6%)	59 (47.2%)	**<0.0001**
Poor 'r' wave progression	0	16 (35.5%)	22 (33.8%)	38 (30.4%)	**0.023**
In complete RBBB	0	0	8 (12.3%)	8 (6.4%)	**<0.0001**
RVH	0	20 (44.4%)	47 (72.3%)	67 (53.6%)	**<0.0001**
AF	0	2 (4.4%)	5 (7.7%)	7 (5.6%)	0.463
MAT	0	2 (4.4%)	4 (6.1%)	6 (4.8%)	0.597
Normal	7 (47%)	18 (40%)	0	25 (20%)	**<0.0001**

RBBB- right bundle branch block, RVH- right ventricular hypertrophy, AF- atrial fibrillation, MAT- multifocal atrial tachycardia.

Echocardiographic findings

As shown in Table 3, most common echocardiography finding was PAH (57.6% patients) followed by RV dilatation (49.6% patients). Comparing the patients with varying severity of COPD, in patients with severe COPD, RV dilatation (78.4% patients) was most common findings while in patients with moderate COPD, PAH (40% patients) was most common. In patients with mild COPD, 66.6% patients had normal echocardiography while 33.4% patients had PAH. The incidence of RA (41.6%) and RV (49.6%) enlargement and PAH (57.6%) increased significantly with increasing severity of the COPD (Table 3).

In ventricular dysfunction, most common finding was LVDD (36% patients) followed by LVSD (15.2%

patients). Of 45 patients with LVDD, 32 (71.1%) patients had Grade 1, 12 (26.7%) patients had Grade 2 and 1 (2.2%) patient had Grade 3 LVDD. Incidence of LVDD and LVSD increased with increasing severity of COPD. Total 15.2% patients had RV dysfunction. RV dysfunction was seen only in patients with severe COPD. LVH was present in 4.8% patients.

In our study, 72 (57.6%) patients had PAH. Incidence of PAH increased significantly with increasing severity of COPD (p<0.0001). Mean PA pressures was 37.63 ± 17.36 mmHg. Out of 72 patients, 35 patients had mild PAH, 25 patients had moderate PAH and 12 patients had severe PAH. All the patients with severe PAH were in moderate (n=4) or severe COPD (n=8) group. Out of 12 patients with severe PAH, 7 patients had other associated lesion as a cause of PAH (chronic pulmonary thromboem-bolism (n=3), obstructive sleep apnea (n=3) and collagen vascular disease (n=1)). In 5 patients, severe PAH was attributable to COPD. Total 39.2% patients had COR-P. As with PAH, incidence of COR-P increased significantly with increasing severity of COPD.

Table 3: Correlation of echocardiographic Findings with Severity of COPD

	Mild (n=15)	Moderate (n=45)	Severe (n=65)	No of patients (%)	P value
RA dilatation	0	9 (20%)	43 (66.1%)	52 (41.6%)	<0.0001
RV dilatation	0	11 (24.4%)	51 (78.5%)	62 (49.6%)	<0.0001
RVH	0	8 (17.8%)	33 (50.8%)	41 (32.8%)	<0.0001
RV dysfunction	0	0	19 (29.2%)	19 (15.2%)	<0.0001
LVH	0	1 (2.2%)	5 (7.7%)	6 (4.8%)	0.272
LVSD	0	2 (4.4%)	17 (26.1%)	19 (15.2%)	0.001
LVDD	0	8 (17.8%)	37 (56.9%)	45 (36%)	<0.0001
IVS motion abnormality	0	3 (6.7%)	22 (33.8%)	25 (20%)	0.001
PAH	5 (33.4%)	18 (40%)	49 (75.4%)	72 (57.6%)	0.001
Cor-pulmonale	2 (13.3%)	12 (26.7%)	35 (53.8%)	49 (39.2%)	0.001
Normal	10 (66.6%)	14 (31.1%)	0	24 (19.2%)	<0.0001

RA- right atrium, RV- right ventricle, RVH- right ventricular hypertrophy, LVH- left ventricular hypertrophy, LVSD- left ventricular systolic dysfunction, LVDD- left ventricular diastolic dysfunction, IVS- interventricular septum, PAH- pulmonary artery hypertension.

Discussion

In our study, breathlessness followed by cough with sputum were most common presenting symptoms. Breathlessness is the symptom that most commonly pursue the patient to seek the medical attention. However, patients often date the onset of their illness to an acute exacerbation of productive cough, which leaves them with a degree of chronic breathlessness. Among various signs, tachypnea was present in 73% patients while RHC tenderness was present in 4% patients. In our study, 80% patients had chest X-ray evidence of emphysema. Findings of our study are in congruence with study by Krishnan et al. [18] and Suma et al. [19].

Among ECG findings, 47.2% of the patients in our study had right axis deviation. The incidence of right axis deviation varies widely among various studies depending upon the criteria used. In a study by Banker et al. [20] in patients with COPD, classical RVH is less commonly observed in ECG than expected. According to them, when the classical pattern of RVH is not present then, the features suggesting RVH are the combination of RAD, R/S ratio in lead V1 >1, Dominant 'R' in aVR, abnormal ST – T changes, and 'p' pulmonale. Other less commonly observed ECG changes in their study were RBBB, low voltage QRS, SI SII SIII, and arrhythmia. In our study also, 53.2% patients had ECG features of RVH while 20% patients had normal ECG. In remaining 26.8% patients, surrogate criteria were used to diagnose RVH. According to Banker et al. [20], poor 'r' wave progression and low voltage ECG complexes are the commonest ECG changes suggestive of RVH. In our study, on correlating the ECG findings with duration of symptoms, the incidence of 'p' pulmonale, right axis deviation, RVH and incomplete RBBB increased with increasing duration of the disease. However, statistically significance difference was found only with right axis deviation (p=0.03).

In the analysis of Echo findings, our study showed 57.6% patients with evidence of PAH comprised by RA/ RV dilatation, RV hypertrophy, evidence of RV dysfunction, or inter ventricular septum motion abnormality. Similar incidences were found in

previous study [21]. In our study, echocardiographic signs of PAH correlated significantly with the severity of the COPD ($p< 0.05$). Other studies correlating the ECHO findings with severity of the disease have also made similar observations, and also have given different explanations for their observation [20].

Pulmonary artery hypertension and right ventricular dysfunction are the main established complications described in many studies. Our study has added a little more strength to previous studies. In our study, we also found increased incidence of changes of PAH and COR-P in patients with COPD. This is because cigarette smoking and other exposure factors lead to inflammatory changes in the lung that lead to disruption of the pulmonary vascular endothelium and changes of chronic bronchitis and emphysema leads to chronic hypoxia that results into pulmonary artery remodeling and vasoconstriction. The other mechanism leading to the damage is the change in balance of intrinsic pulmonary vasodi-lators such as prostacyclins, endothelial nitric oxide and constrictors such as endothelin 1. Along with these factors, changes in respiratory mechanics and increase in blood viscosity lead to PAH. Long standing PAH eventually result in increased right ventricular afterload and increase in RV work. All these result in right ventricular hypertrophy and dilatation giving a clinical presentation of the right heart failure [21].

There are no exact data of PAH prevalence in COPD. Studies have reported 20–90% incidence of elevated PAP when measured by right heart catheterization. Our study revealed 48% incidence of PAH. Further, studies have reported increasing severity of PAH with increase in severity of airflow obstruction [22]. Kessler et al. [23] and Oswald-Mammosser et al. [24] in their study have shown an abnormal increase in mean PAP in COPD of 0.4-0.6 mmHg per year. These studies illustrate that PAH in COPD progresses slowly and occur in mild as well as severe forms of disease. Several studies have demonstrated the positive association between the severities of PAH in COPD and poor prognosis [25]. COR-P was present in 32% of patients in our study. This is comparable to previous study [21,26].

In our study, LVDD was present in 58% of patients as compared to 47.5% seen in study by Gupta et al [22]. LVDD in COPD patients could be due to chronic hypoxemia leading to changes in myocardial relaxation, distension, and lung hyperinflation and also due to ventricular interdependence.

Limitations

Smaller size of study population is main limitation of our study. Other is lack of right heart catheterization which is still gold standard for PAP.

Conclusion

The study shows significant prevalence of cardiac co-morbidities such as PAH, COR-P, LVDD in COPD patients and the severity of complications increases with increase in severity of COPD. Hence, cardiac screening should be done early in disease in all COPD patients irrespective of its severity to identify the patients who are likely to suffer increase morbidity and mortality.

Conflicts of interest: Nil

Sources of funding for the work: Nil

References

1. Kaushal M, Shah PS, Shah AD, Francis SA, Patel NV, Kothari KK. Chronic obstructive pulmonary disease and cardiac comorbidities: A cross-sectional study. Lung India. 2016;33(4):404–409.
2. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: Current burden and future projections. Eur Respir J. 2006;27:397–412.
3. Salvi S, Agrawal A. India needs a national COPD prevention and control programme. J Assoc Physicians India. 2012;60:5–7.
4. Global Initiative for Chronic Obstructive Lung Disease: Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2016.
5. Rutten FH, Moons KG, Cramer MJ, Grobbee DE, Zuithoff NP, Lammers JW, et al. Recognising heart failure in elderly patients with stable chronic obstructive pulmonary disease in primary care: Cross sectional diagnostic study. BMJ. 2005;331:1379.
6. Rutten FH, Cramer MJ, Lammers JW, Grobbee DE, Hoes AW. Heart failure and chronic obstructive pulmonary disease: An ignored combination? Eur J Heart Fail. 2006;8:706–11.
7. Sin DD, Man SF. Chronic Obstructive Pulmonary Disease as a Risk Factor for Cardiovascular Morbidity and Mortality, Proceedings of the American Thoracic Society, Symposium: Chronic ob-structive

pulmonary disease: A disorder of the cardiovascular and respiratory systems. 2005;2:8–11.

8. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: Role of comorbidities. Eur Respir J. 2006;28:1245–57.
9. Kitzman DW, Little WC, Brubaker PH, Anderson RT, Hundley WG, Marburger CT, et al. Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure. JAMA. 2002;288:2144–50.
10. Boussuges A, Pinet C, Molenat F, Burnet H, Ambrosi P, Badier M, 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(2 Pt 1):670–5.
11. Bhattacharyya P, Roy Chowdhury S, Nag S, Sarkar D, Ghosh G, Bardhan S, et al. Diastolic dysfunction in advanced COPD patients: Early results of an observational study. Respirology. 2004;9:A98.
12. Rappaport E. Cor pulmonale. In: Murray JJ, Nadel JA, Mason RM, Boushey H, editors. Textbook of Respiratory Medicine. 4th ed. Philadelphia: W.B. Saunders; 2000.pp.1631–48.
13. Chemla D, Castelain V, Humbert M, Hébert JL, Simonneau G, Lecarpentier Y, et al. New formula for predicting mean pulmonary artery pressure using systolic pulmonary artery pressure. Chest. 2004;126:1313–7.
14. Weitzenblum E, Chaouat A. Cor pulmonale. Chron Respir Dis. 2009;6:177–85.
15. Daniels LB, Krummen DE, Blanchard DG. Echocardiography in pulmonary vascular disease. Cardiol Clin. 2004;22:383–99, vi.
16. Yock PG, Popp RL. Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation. 1984;70:657–62.
17. Tramarin R, Torbicki A, Marchandise B, Laaban JP, Morpurgo M. Doppler echocardiographic evaluation of pulmonary artery pressure in chronic obstructive pulmonary disease. A European multicentre study. Working Group on Noninvasive Evaluation of Pulmonary Artery Pressure. European Office of the World Health Organization, Copenhagen. Eur Heart J. 1991;12:103–11.
18. Radha Krishnan D, Srihari B. A study on the severity of right ventricular dysfunction in correlation with the severity of Lung dysfunction in Chronic Obstructive Pulmonary Disease patients – COPD. The Ame J Sci & Med Res. 2015;1:112-119.
19. Suma K. R, Srinath S, Praveen. Electrocardiographic and Echocardiographic changes in chronic obstructive pulmonary disease (COPD) of different grades of severity. J Evol Med Dent Sci. 2015;4(30): 5093- 101.
20. Banker H, Verma A. Electrocardiographic changes in COPD. NHL Journal of Medical Sciences. 2013; 2(2):55-58.
21. Falk JA, Kadiev S, Criner GJ, Scharf SM, Minai OA, Diaz P. Cardiac Disease in Chronic Obstructive Pulmonary Disease. Proc Am Thorac Soc. 2008;5(4): 543–548.
22. Gupta NK, Agrawal RK, Srivastav AB, Ved ML. Echocardiographic evaluation of heart in chronic obstructive pulmonary disease patient and its co-relation with the severity of disease. Lung India. 2011;28:105–9.
23. Kessler R, Faller M, Weitzenblum E, Chaouat A, Aykut A, Ducoloné A, et al. "Natural history" of pulmonary hypertension in a series of 131 patients with chronic obstructive lung disease. Am J Respir Crit Care Med. 2001;164:219–24.
24. Oswald-Mammosser M, Weitzenblum E, Quoix E, Moser G, Chaouat A, Charpentier C, et al. Prognostic factors in COPD patients receiving long-term oxygen therapy. Importance of pulmonary artery pressure. Chest. 1995;107:1193–8.
25. Higham MA, Dawson D, Joshi J, Nihoyannopoulos P, Morrell NW. Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. Eur Respir J. 2001;17:350–5.
26. Thabut G, Dauriat G, Stern JB, Logeart D, Lévy A, Marrash-Chahla R, et al. Pulmonary hemodynamics in advanced COPD candidates for lung volume reduction surgery or lung transplantation. Chest. 2005;127:1531–6.