Original Article

Prevalence of Pulmonary Hypertension in Indonesian Patients with Stable Chronic Obstructive Pulmonary Disease

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Abstract

Background: Pulmonary hypertension (HT) is a common comorbidity and implicated in the cardiac-related mortality in chronic obstructive pulmonary disease (COPD) patients. Echocardiography provides accurate and rapid information to detect pulmonary HT. The prevalence of HT among Indonesian patients with COPD, however, remains unclear. The aim of this study is to elucidate the prevalence of pulmonary HT based on echocardiography findings in stable COPD Indonesian patients at the Persahabatan Hospital, Jakarta, Indonesia. **Methods:** This is a cross-sectional study among stable COPD patients who visit COPD Outpatient Clinics in Persahabatan Hospital, Jakarta, Indonesia, from January to June 2017. Medical history interview, physical examination, spirometry, and echocardiography were performed to all participants who meet the criteria. **Results:** A total of seventy subjects with COPD performed echocardiography with a mean age of 65.68 ± 7.65 years old. Most of subjects were men (95.7%). There were 30% participants with pulmonary HT and 8.6% participants with right ventricle dilatation. Statistical analysis revealed a significant association between pulmonary HT and forced expiratory volume in 1 s (FEV1) <30% and body mass index (BMI). **Conclusion:** Pulmonary HT is frequent in Indonesian patients with COPD and is associated with severe airway obstruction as well as reduced BMI; therefore, pulmonary HT should be well managed in a holistic manner to prevent the deteriorating conditions.

Keywords: Cardiovascular, echocardiography, spirometry

Introduction

Chronic obstructive pulmonary disease (COPD) is a fourth common cause of mortality and is a major cause of disability worldwide.[1] The most common cause of mortality among COPD patients is due to the abnormalities of cardiovascular system.[2] Accumulation evidence suggests that cardiovascular disease is a major complication in COPD.[3] Long-term reduced intra-alveolar oxygen pressure also implicated in the pulmonary circulation with the consequences such as pulmonary hypertension (HT). Various studies showed a variable prevalence of pulmonary HT in patients with COPD, from 25% to 90%.[4]

Systemic inflammation that occurred in COPD could also indirectly increase the risk cardiovascular disease. Changes of pathophysiology in COPD played a direct role in the cardiac function. Moreover, emphysema and lung hyperinflation could disturb the left ventricular filling and therefore reduced the cardiac output and resulted in HT and right cardiac failure.[5,6] Increased vascular pressure in pulmonary arteries, endothelial dysfunction, accompanied by alveolar hypoxia-induced pulmonary vascular cells' proliferation was common in individuals with mild-moderate COPD. Furthermore, early changes in the structure and function of right ventricle could lead to reduced left ventricular function.[7-9]

The current study reveals the prevalence of pulmonary HT based on echocardiography and identified the associated factors related to pulmonary HT in Indonesian patients with COPD.

Methods

This is a cross-sectional survey conducted in the COPD outpatient clinic at the Persahabatan Hospital, Jakarta,

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Indonesia, from January 2017 to July 2017. The study received ethical approval from the Institutional Review Board of Faculty of Medicine Universitas Indonesia (Ethical Clearance No. 933/UN2.FI/ETIK/2016 with Protocol No. 16-10-400). The inclusion criteria were stable mild-to-severe COPD patients and willing to participate by signing the written informed consent. The exclusion criteria were patients with poor echocardiography window in the examination, acute coronary syndrome, and patients with destroyed lung.

The samples were recruited by a consecutive sampling. After medical history was obtained, patients were undergone physical examination and spirometry using Spirobank II (Medical International Research, Rome, Italy) and confirmed the diagnosis of stable mild-to-moderate COPD. Echocardiography examination was performed using Philips Ultrasound HD 15 (Philips, Bothell, WA, USA).

Statistical analysis was performed in the obtained data using the Statistical Package for the Social Sciences (SPSS) software program version 20 (IBM Corp, Armonk, NY, USA). $P < 0.05$ was considered to be statistically significant.

Results

This study involved seventy stable COPD patients with complete echocardiography data and fulfilled the inclusion criteria. The demography characteristics of participants, including gender, age, level of education, smoking status, body mass index (BMI), COPD severity, COPD group according to Global Initiative for Chronic Obstructive Lung Disease (GOLD), history of exacerbations, COPD assessment test (CAT) score, level of breathlessness assessed by modified Medical Research Council (mMRC), the use of inhaled corticosteroid (ICS), and history of HT as well as diabetes mellitus (DM), are described in Table 1.

First, we look for the pulmonary HT by echocardiography examination in COPD patients [Table 2]. Using the tricuspid annular plane systolic excursion (TAPSE) assessment, the right ventricle contractility was reduced in 8 (11.4%) patients, and this represents the prevalence of right ventricle failure. Based on the mean pulmonary arterial pressure (MPAP) assessment, there were 14 patients (20%) with mild degree pulmonary HT, followed by moderate degree and severe degree as much as 3 (4.3%) patients and 4 (5.7%) patients, respectively.

Next, we assessed the relationship between pulmonary HT and various variables of the COPD participants as shown in Table 3. We found a significant relationship between BMI and pulmonary HT ($P = 0.027$). However, there was no significant relationship between gender, age, smoking status, education, history of exacerbation, the use of ICS, duration of COPD, comorbidities such as HT and DM, and mean forced expiratory volume in 1 s (FEV1) percentage prediction. To note, there was a tendency that patients who suffer from pulmonary HT had a lower FEV1/FVC, although it did not reach the statistical threshold. In this study, we also observed a significant

Table 1: Subject demographic characteristics

Subject characteristics	*n* (%)
Gender	
Male	67 (95.7)
Female	3 (4.3)
Age (years old)	
<65	34 (48.6)
≥65	36 (51.4)
Smoking status	
Former smoker	64 (91.4)
Nonsmoker	6 (8.6)
Brinkman Index	
Mild	7 (10)
Moderate	21 (30)
Severe	36 (51.4)
Education	
Low	20 (28.6)
High	50 (71.4)
Body mass index	
Underweight	19 (27.1)
Normal	22 (31.4)
Overweight	14 (20)
Obese	15 (21.4)
Severity of COPD	
GOLD 1	7 (10)
GOLD 2	23 (32.9)
GOLD 3	29 (41.4)
GOLD 4	11 (15.7)
COPD group	
A	9 (12.9)
B	10 (14.3)
C	5 (7.1)
D	46 (65.7)
History of exacerbation	
Exacerbation	51 (72.9)
No exacerbation	19 (27.1)
CAT score	
<10	15 (21.4)
≥10	55 (78.6)
mMRC	
0-1	21 (30)
≥2	56 (80)
The use of ICS	
Yes	48 (68.6)
No	22 (31.4)
Duration of COPD diagnosis (years)	
<2	34 (48.6)
≥2	36 (51.4)
Hypertension	
Yes	14 (20)
No	56 (80)
Diabetes mellitus	
Yes	5 (7.1)
No	65 (92.9)

CAT: COPD assessment test, COPD: Chronic obstructive pulmonary disease, GOLD: Global Initiative for Chronic Obstructive Lung Disease, ICS: Inhaled corticosteroid, mMRC: Modified Medical Research Council

Table 2: Pulmonary hypertension in chronic obstructive pulmonary disease patients based on echocardiography

Echocardiography results	*n* (%)
Right ventricle contractility (TAPSE)	
Normal	62 (88.6)
Reduced	8 (11.4)
MPAP	
Normal	49 (70)
Mild PH	14 (20)
Moderate PH	3 (4.3)
Severe PH	4 (5.7)

TAPSE: Tricuspid annular plane systolic excursion: MPAP: Mean pulmonary arterial pressure: PH: Pulmonary hypertension

relationship between pulmonary HT and FEV1 <30% predicted which represent GOLD Grade 4 patients ($P = 0.008$).

GOLD 2017 classified COPD based on the history of exacerbation and symptoms. Based on exacerbation, COPD is classified into patients without exacerbation that leads to hospital (a and B) and those with exacerbation that leads to hospital (c and d). As for symptoms-based classification, patients, who had symptoms with CAT score <10 and/or mMRC 0–1, are classified as A–C, whereas symptomatic patients are classified as B–D. We then analyzed the relationship between pulmonary HT and these two COPD classifications. In the statistical analysis, pulmonary HT was not significantly related with both symptom-based and exacerbation-based COPD classifications [Table 4].

Finally, we evaluated the cardiac function as a predictor for COPD exacerbation. As shown in Figure 1, this study found median TAPSE 1.9 (0.38–3.14) was significantly related with one or more exacerbation ($P = 0.009$).

Discussion

Pulmonary HT is a serious complication of COPD and represents a preliminary event, leading to right heart failure and eventually, mortality. The current study identified a prevalence of pulmonary HT among Indonesian patients with stable COPD was 30%. This finding is different with the previous study conducted by Kusmana *et al*. at the Persahabatan Hospital who found the prevalence of pulmonary HT was 86%.[10] The diagnostic methods that is being used were MPAP measurement. The different results were caused by different diagnostic methods. If we use the pulmonary HT probability methods based on the newest pulmonary HT guideline, which is the tricuspid regurgitant parameter, we will obtain 58.6% of COPD patients had the probability of pulmonary HT. There has been no study that used the pulmonary HT probability and the relationship with COPD. Prevalence of pulmonary HT was variably reported from 25% to 90% in several studies. The definitive prevalence of pulmonary HT is using the right ventricle catheterization. This procedure is difficult to perform because catheterization is an invasive procedure and carries a high risk of adverse event. It is difficult to know the exact prevalence of pulmonary HT because of lacking of large-scale right cardiac catheterization in COPD patients.[2]

One of the most important clinical impacts of the prevalence rate of pulmonary HT among Indonesian COPD patients is the overall future prognosis of COPD. Despite adequate treatment, COPD patients will have a gradual deteriorating lung function,

Table 3: The relationship between risk factors and pulmonary hypertension

Subject characteristics	Pulmonary hypertension		*P*
	Yes, *n* (%)	No, *n* (%)	
Gender			
Male	21 (31.3)	46 (68.7)	0.549[a]
Female	0 (0)	3 (100)	
Age (years old)			
<65	12 (35.3)	22 (64.7)	0.348[b]
≥65	9 (25)	27 (75)	
History of smoking			
Former smoker	21 (32.8)	43 (67.2)	0.168[a]
Non smoker	0 (0)	6 (100)	
Education			
Low	9 (45)	11 (55)	0.083[b]
High	12 (24)	38 (76)	
History of exacerbation			
Exacerbation	17 (33.3)	34 (66.7)	0.319[b]
No exacerbation	4 (21.1)	15 (78.9)	
The use of ICS			
Yes	15 (31.2)	33 (68.8)	0.736[b]
No	6 (27.3)	16 (72.7)	
Duration of COPD (years)			
<2	12 (35.3)	22 (64.7)	0.348[b]
≥2	9 (25)	27 (75)	
CAT score			
<10	3 (20)	12 (80)	0.340[b]
≥10	18 (32.7)	37 (67.3)	
mMRC			
0-1	3 (14.3)	18 (85.7)	0.06[b]
≥2	18 (36.7)	31 (63.3)	
Hypertension			
Yes	2 (14.3)	12 (85.7)	0.151[b]
No	19 (33.9)	37 (66.1)	
Diabetes mellitus			
Yes	0 (0)	5 (100)	0.313[a]
No	21 (32.3)	44 (67.7)	
Mean BMI (SD) (kg/m^3)	20.11 (3.97)	22.73 (5.31)	0.027[c]
Mean FEV1% predicted (SD)	45.48 (18.96)	51.7 (20.10)	0.224[c]
FEV_1% predicted			
≥30%	14 (23.7)	45 (76.3)	0.008[b]
<30%	7 (63.6)	4 (36.4)	
Mean FEV_1/FVC (SD)	49.45 (12.30)	54.98 (10.09)	0.079[c]

Statistical analysis: [a]Fischer exact test, [b]Chi-square test, [c]Unpaired *t*-test. BMI: Body mass index, CAT: COPD assessment test, COPD: Chronic obstructive pulmonary disease, FEV1: Forced expiratory volume in 1 s, FVC: Forced vital capacity, GOLD: Global Initiative for Chronic Obstructive Lung Disease, ICS: Inhaled corticosteroid, mMRC: Modified Medical Research Council, SD: Standard deviation

Table 4: Relationship between pulmonary hypertension and chronic obstructive pulmonary disease classifications

COPD classifications	Pulmonary hypertension		*P*
	Yes, *n* (%)	No, *n* (%)	
Exacerbation-based COPD class			
A-B	4 (20)	16 (80)	0.248
C-D	17 (34)	33 (66)	
Symptom-based COPD class			
A-C	3 (20)	11 (78.6)	0.434
B-D	18 (32.1)	38 (67.9)	

P values were calculated using Chi-square test. COPD: Chronic obstructive pulmonary disease

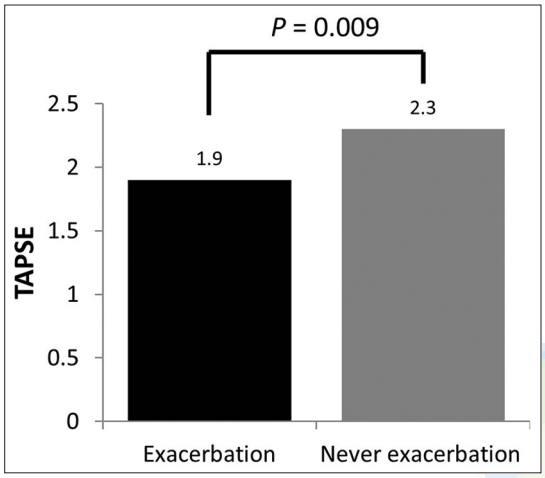

Figure 1: The relationship between tricuspid annular plane systolic excursion and history of exacerbation

and this may implicate in the chronic alveolar hypoxia and cause further vasoconstriction in the pulmonary circulation. Eventually, pulmonary HT will become more prevalent. If left untreated, pulmonary HT will contribute to the increased cardiac-associated mortality among Indonesian population.

The prevalence of pulmonary HT reported by Gupta *et al*. was 42.5%.[2] If participants were grouped as FEV <30% predicted and ≥30% predicted, there was significant relationship between severe COPD (FEV <30% predicted) and pulmonary HT. Pulmonary HT was observed in 63.4% of patients with very severe COPD (GOLD 4). The study by Gupta *et al*. also showed the prevalence of pulmonary HT in a very severe COPD patients was 83.3%.[2]

Mean of BMI among pulmonary hypertensive patients was 20.11 ± 3.97 kg/m^2 and this is lower compared to participants without pulmonary HT, 22.73 ± 5.31 kg/m^2. The statistical analysis showed a significant relationship between BMI and pulmonary HT. Study by Hurdman *et al*. found COPD patients with pulmonary HT had a mean BMI 28 ± 8 kg/m^2 and those with severe pulmonary HT had mean BMI 27 ± 6 kg/m^2; however, BMI did not contribute to the survival of COPD patients.[11] Study by Yamauchi *et al*. revealed COPD patients with low BMI had an increased risk of mortality compared to normal BMI.[12] These evidences suggest that BMI is an important factors that played role in the prevalence of pulmonary HT among COPD patients.

The study limitation is the small number of patients involved in the study, 70 stable COPD patients. The study that involves multicenter subjects will be helpful in identifying the factors that are implicated in the increasing prevalence of pulmonary HT among COPD patients. Another limitation is that characteristic of cross-sectional study design which, captured the multiple variables in one time and therefore, limits the ability to establish the cause-effect association.

Conclusion

Taken together, the prevalence rate of pulmonary HT is high in patients with clinically stable COPD and is related significantly with reduced BMI as well as severe airway obstruction. This prevalence rate is quite smaller as compared to study in other regions such as study in a state in India. The current findings pointed an important issue in identifying pulmonary HT as early as possible in a multidisciplinary fashion to address the complex condition suffered by COPD patients.

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Conflicts of interest

There are no conflicts of interest.

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