Original Article

Severity of Obstruction Associated with Pulmonary Hypertension in COPD Patients at Arifin Achmad General Hospital: What Factors Influence?

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Abstract

Background: Pulmonary hypertension can occur in stable chronic obstructive pulmonary disease (COPD) patients despite its unknown etiology or as a complication associated with other processes. Pulmonary hypertension was divided into five broad categories, including processes with common pathogenic mechanisms. The true incidence of pulmonary hypertension in COPD is unknown, as no systematically performed screening method can be widely used in COPD patients, while the mortality rate or complications from COPD are still very high.

Method: This study method was a cross-sectional study. This study was conducted on stable COPD patients who came to the pulmonary department at Arifin Achmad General Hospital to assess its association with the risk of pulmonary hypertension.

Results: This study involved 77 research subjects with the highest age <65 years (64.9%) with male gender (84.4%), airflow limitation degree GOLD II (moderate) (50.6%), severe Brinkman Index (76.6%), comorbid hypertension (7.8%), Asymmetric Dimethylarginine (ADMA)0 inflammatory marker including low-risk category (77.9%) and mild echocardiographic interpretation (75.3%). The Association of COPD severity was significant to the risk of pulmonary hypertension, the degree of airflow limitation (P=0.0001) and echocardiography interpretation (P=0.0001). At the same time, there was no significant association with ADMA levels (P=0.239). The Brinkman Index of smokers (P=0.006) was an important risk factor for pulmonary hypertension.

Conclusion: There was an association between COPD severity, echocardiographic interpretation and smoking status based on the Brinkman Index and the risk of pulmonary hypertension.

Keywords: COPD, ejection fraction, pulmonary hypertension, tricuspid regurgitation

INTRODUCTION

Pulmonary hypertension (PH) is a functional disorder that occurs clinically. It is caused by pulmonary artery vascular disorders of unknown etiology. Pulmonary hypertension may also occur as a complication associated with other

processes.[1]

The classification of PH consists of five broad categories that include processes with common pathogenic mechanisms. Pulmonary hypertension due to pulmonary disease or hypoxia is group 3 of the PH classification. This third classification is the most common PH, with chronic obstructive pulmonary disease (COPD) being the most common cause.[1]

The prevalence of pulmonary hypertension in COPD patients varies depending on the diagnostic criteria used and the severity of COPD. According to a study by Thabut et al, pulmonary hypertension is found in approximately 30-50% of patients with advanced COPD.[1]

Another study by Chaouat et al reported that about 90% of COPD patients with chronic respiratory failure showed signs of mild to moderate pulmonary hypertension. In addition, a meta-analysis by Oswald-Mammosser et al. showed that mean pulmonary artery pressure (mean PAP) in COPD patients was in the range of 20-35 mmHg, with a significant proportion having mild pulmonary hypertension.[2]

Several factors have been identified as major contributors to the occurrence of pulmonary hypertension in COPD patients. The most dominant factor is chronic hypoxia, leading to pulmonary artery vasoconstriction and vascular remodeling.[3]

In addition, capillary loss due to alveolar destruction (as in emphysema), pulmonary hyperinflation and increased intrathoracic pressure also contribute to increased pressure in the pulmonary artery. Additional factors such as systemic inflammation, imbalance of vasodilators and vasoconstrictors (e.g., decreased nitric oxide (NO) and increased endothelin-1), and comorbidities such as sleep apnea or chronic pulmonary thromboembolism also aggravate the condition.[3]

Research on Asymmetric Dimethylarginine (ADMA) as a biomarker of pulmonary hypertension in patients with COPD is limited, especially in the context of the Indonesian population. However, several international studies have shown that elevated ADMA levels are associated with endothelial dysfunction and may contribute to the development of pulmonary hypertension.[4]

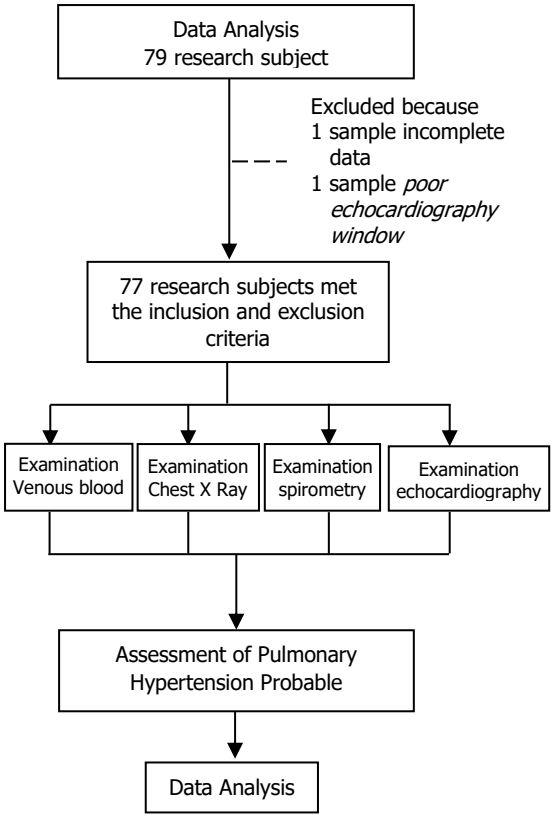
Asymmetric Dimethylarginine is an endogenous inhibitor of NO synthesis, which plays an important role in pulmonary vascular vasodilation. Increased levels of ADMA may lead to decreased NO production, which in turn causes vasoconstriction and vascular remodeling, two key mechanisms in the pathogenesis of pulmonary hypertension.[4]

In the context of COPD, frequent chronic hypoxia may increase ADMA production, thereby exacerbating endothelial dysfunction and accelerating the development of pulmonary hypertension. Nonetheless, more studies are needed to confirm the role of ADMA as a diagnostic or prognostic biomarker in COPD-related pulmonary hypertension.[5]

The aim research was to analyze the severity of COPD with probable pulmonary hypertension and its influencing factors at Arifin Achmad General Hospital.

METHOD

This study was a descriptive-analytic study using a cross-sectional research design. The study was conducted at Arifin Achmad Regional General Hospital from January 2023 to March 2023. The population of this study was stable COPD patients (mild to severe according to GOLD) who came to Arifin Achmad General Hospital and met the inclusion and exclusion criteria.



Inclusion criteria consisted of patients with mild to severe stable COPD, both male and female, who came to the pulmonary clinic or who were admitted to Arifin Achmad General Hospital, aged 18 to 85 years, and willing to voluntarily participate in all stages of the study by giving written consent and signing an informed consent form. Exclusion criteria consisted of patients with poor echocardiography windows on examination, patients with acute coronary syndrome, patients diagnosed with moderate to severe mitral stenosis, and patients with lung parenchyma and pleura abnormalities from the results of thoracic photographs.

Data were collected after screening the subjects according to the inclusion and exclusion criteria. In this study, a total sample size of 79 subjects was obtained. A total of 2 subjects were excluded because one sample had incomplete patient data, and another had a poor echocardiography window. The total sample was 77 people. Statistical analysis application used SPSS version 25.

The analysis of this study was divided into univariate and bivariate. The univariate analysis consisted of the characteristics of the study subjects and the Tricuspid Regurgitation description of the study subjects. In contrast, the bivariate analysis consisted of the association between COPD severity (airflow limitation, ADMA inflammatory marker, and Tricuspid Regurgitation degree) to probable pulmonary hypertension and the association between risk factors to probable pulmonary hypertension. The value of $P<0.05$ indicates a statistically significant.

Spirometry using the CHEST^{R} brand and echocardiography using the Hilips Healthcare brand EPIQ^{R} 7. The measurement of ADMA levels in this study was performed using venous blood samples. Asymmetric Dimethylarginine is

often categorized into three concentration levels—low, moderate, and high—based on plasma concentration values. These categories are typically used in the context of clinical research or diagnosis to assess cardiovascular risk or endothelial dysfunction.

A volume of 5 ml of peripheral venous blood was drawn from each subject, collected in a plain vacutainer tube, and allowed to clot at room temperature. The samples were then centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum was stored at -20°C until analysis.

The quantification of serum ADMA levels was carried out using the enzyme-linked immunosorbent assay (ELISA) method, following the manufacturer's instructions, CUSABIO®. The ELISA kit used was specific for human ADMA and had a detection range of approximately 0.05–10 µmol/L. This study is approved by the ethical committee of Arifin Achmad General Hospital, with research ethics code number B/005/UN19.5.1.1.8/UEPKK/2023.

RESULT

The characteristics of COPD patients in this study are shown in Table 1. This study found that most age of COPD patients was <65 years old, as many as 50 people (64.9%), the severity of COPD was predominantly GOLD II (moderate) 39 people (50.6%), the degree of smoking (index Brinkman (IB)) was heavy 59 people (76.6%), the most comorbid hypertension 7 people (9.1%), the most ADMA levels included low risk 60 people (77.9%).

In this study, the frequency of interpretation of tricuspid regurgitation (TR) in COPD was mostly mild 58 subjects (75.3%), followed by moderate 14 subjects (18.2%) and severe 5 subjects (6.5%). Echocardiographic interpretation consists of the appearance of the right ventricle, right atrium, pulmonary artery, and superior vena cava.

Table 1. Characteristics of research subjects

Variable	n (%)
Age	
<65 years	50 (64.9%)
≥65 years old	27 (35.1%)
Gender	
Male	65 (84.4%)
Female	12 (15.6%)
Severity of COPD	
GOLD I (mild)	2 (2.6%)
GOLD II (moderate)	39 (50.6%)
GOLD III (severe)	32 (41.6%)
GOLD IV (very severe)	4 (5.2%)
Smoker's Brinkman Index	
Mild BI	2 (2.6%)
Moderate BI	16 (20.8%)
Severe BI	59 (76.6%)
Comorbidities	
Diabetes Mellitus	3 (3.9%)
Hypertension	7 (9.1%)
No comorbidities	67 (87.0%)
Inflammation marker (ADMA)	
Low risk	60 (77.9%)
Moderate risk	11 (14.3%)
High risk	6 (7.8%)
Normal	0 (0.0%)

The association between the severity of COPD based on airflow limitation (GOLD criteria) with probable pulmonary hypertension seen from the results of echocardiography was shown in Table 2. In GOLD I (mild), all had mild risk, as many as 2 people (100.0%). GOLD II (moderate)

most had a mild risk of 25 people (64.1%). In contrast to GOLD I and GOLD II, the most moderate risk in GOLD III (severe) was 23 people (71.9%).

Global Initiative for Chronic Obstructive Lung Disease IV (very severe) had a severe risk for probable pulmonary hypertension in as many as 4 people (100.0%). There is a significant Association between the severity of COPD based on GOLD with probable pulmonary hypertension, with P<0.05.

Asymmetric Dimethylarginine levels from the low-risk category to the highest probable pulmonary hypertension moderate risk were found in 30 people (50.0%). Asymmetric Dimethylarginine levels were found in 60 people at low risk, 11 at moderate risk, and 6 at high risk. There was no significant Association between ADMA levels and probable pulmonary hypertension, where the P>0.05 could be seen in Table 2.

The association between COPD risk factors to probable pulmonary hypertension was shown in Table 2. For patients below 65 years old, there was no difference between the mild and moderate risk of probable pulmonary hypertension, namely 20 people (40.0%), with P=0.267.

Table 2. Association between the severity of COPD based on airflow limitation (GOLD criteria), Inflammatory Marker ADMA and Inflammatory Marker ADMA with probable pulmonary hypertension seen from the results of echocardiography

Variable	Probable Pulmonary Hypertension			P
	Mild Risk	Moderate Risk	Severe Risk	
Severity of COPD based on spirometry				
GOLD I (mild)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0.0001[b]
GOLD II (moderate)	25 (64.1%)	14 (35.9%)	0 (0.0%)	
GOLD III (severe)	0 (0.0%)	23 (71.9%)	9 (28.1%)	
GOLD IV (very severe)	0 (0.0%)	0 (0.0%)	4 (100.0%)	
ADMA Inflammatory Markers				
Low risk	22 (36.7%)	30 (50.0%)	8 (13.3%)	0.239[b]
Moderate Risk	4 (36.4%)	3 (27.3%)	4 (36.4%)	
High Risk	1 (16.7%)	3 (50.0%)	2 (33.3%)	
Age				
<65 years	20 (40.0%)	20 (40.0%)	10 (20.0%)	0.267[a]
≥65 years old	7 (25.9%)	16 (59.3%)	4 (14.8%)	
Gender				
Male	23 (35.4%)	33 (50.8%)	9 (13.8%)	0.240[b]
Female	4 (33.3%)	3 (25.0%)	5 (41.7%)	
Brinkman index (BI) Smokers				
Mild BI	2 (100.0%)	0 (0.0%)	0 (0.0%)	0.006[a]
Moderate BI	10 (62.5%)	4 (25.0%)	2 (12.5%)	
Severe BI	15 (25.4%)	32 (54.2%)	12 (20.3%)	
Comorbidities				
Diabetes Mellitus	1 (33.3%)	2 (66.7%)	0 (0.0%)	0.126[b]
Hypertension	0 (0.0%)	4 (57.1%)	3 (42.9%)	
No comorbidities	26 (38.8%)	30 (44.8%)	11 (16.4%)	

Note: [a]Chi-square test; [b]Uji Fisher Test

Table 3. Association of Inflammatory Marker ADMA with COPD Severity

Degree of ADMA	COPD Severity				P
	GOLD I (Mild)	GOLD II (Moderate)	GOLD III (Severe)	GOLD IV (Very severe)	
Low risk	2 (3.3%)	32 (53.3%)	24 (40.0%)	2 (3.3%)	
Moderate risk	0 (0.0%)	5 (45.5%)	5 (45.5%)	1 (9.1%)	0.373*
High risk	0 (0.0%)	2 (33.3%)	3 (50.0%)	1 (16.7%)	

Note: *Uji Fisher Test

At the age of ≥65, the highest probable pulmonary hypertension at moderate risk was 16 people (59.3%). Male have the highest risk for pulmonary hypertension, namely moderate risk, 33 people (50.8%), and female, the severe risk, is the highest risk for probable pulmonary hypertension, 5 people (41.7%).

Based on smoking status, Brinkman index (BI), mild BI and moderate BI had the highest risk of probable pulmonary hypertension (100.0% and 62.5%). The most severe BI had a moderate risk of 32 people (54.2%). The most common comorbidities in this study were hypertension, with 4 participants having moderate risk for PH (57.1%), followed by type II DM, with 2 participants in moderate risk for PH (66.7%). There was a significant Association between BI smokers and the incidence of probable pulmonary hypertension in COPD patients, with P<0.05.

The association between ADMA and the severity of COPD is presented in Table 3. In the low-risk ADMA category, there were 32 people (53.3%) in GOLD II. Moderate risk ADMA was found in GOLD II and GOLD III (5 people; each 45.5%). The high-risk ADMA category was found in GOLD III in as many as 3 people (50.0%). There was no significant association between the degree of ADMA and the severity of COPD, with P=0.373.

DISCUSSION

Chronic obstructive pulmonary disease is a preventable and treatable lung disease characterized by persistent and generally progressive airflow limitation, airway and/or alveoli abnormalities due to harmful gases or particles, influenced by host factors and abnormal lung development, exacerbations and comorbidities contribute to the severity of the disease. Chronic obstructive pulmonary disease patients with age <65 years old in this study had a greater proportion than ≥65 years old. This result aligns with Muzlifa et al's and Nugraha's research, where most were <65 years old.[6,7]

Different results were found in The Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO), which estimated that the prevalence of COPD increased gradually with age, with the highest being >60 years old. The prevalence of COPD is two to three times higher in people over 60 years old compared to younger age groups. COPD has been considered a condition of accelerated lung aging.[3,8]

The most common gender in this study was male. These results align with

Hariyanti's research, where the highest proportion of COPD sufferers was male.[9] Tabar's research also obtained the same results, mostly in males.[10] The prevalence of males suffering from COPD is three times higher than females in Indonesia.[8]

This is due to the habit of smoking more among males. The prevalence of COPD increases with smoking status, and only 4% showed the presence of other risk factors, such as passive smoking or occupational exposure factors.[3] Riskesdas data in 2018 showed that the prevalence of smokers in Indonesia was 16 times higher in males (65.8%).[2]

Chronic obstructive pulmonary disease patients, based on GOLD criteria in this study, were mostly in the GOLD II group. These results align with Marco's research in Spain, where most COPD patients were in the GOLD II population.[3] In contrast to Salawati's research, the classification of COPD patients was mostly in the GOLD III group.[11] The severity of COPD is associated with increased mortality and hospitalization.[12] However, the development of the severity of COPD disease in the early stages has no significant difference in health status.[4]

Husnah's research found an association between the severity of COPD and malnutrition in COPD patients and was associated with an increased risk and frequency of acute exacerbations.[13] The higher the severity of COPD, the higher the metabolism. The type of metabolism referred to is increased energy metabolism (hypermetabolism), specifically due to the increased work of breathing in patients with COPD, particularly in moderate to severe stages (GOLD II and above).[10]

Due to the increased energy expenditure associated with labored breathing, individuals with COPD often experience insufficient caloric and protein intake, leading to compromised nutritional status. The increase in energy needs due to increased work of the respiratory musculature, due to chronic hypoxemia causes hypermetabolism.[14] This study was mostly GOLD II because stable COPD dominated the study sample.

Smoking status in this study was mostly in the heavy BI group. These results align with Nugraha's and Salawati's research, where most were heavy BI.[7,11] In contrast to the study by Muzlifa et al, most COPD with moderate BI (46.7%).[6] The moderate and heavy smokers group had 8 times higher risk of experiencing COPD compared to the light smokers group.[7]

The association between smoking and COPD depends on the dose/number of cigarettes and the airway response, where the risk of COPD increases with the number of cigarettes smoked daily and the longer the smoking habit.[15] Bronchoalveolar fluid samples from COPD smokers show that smoking contributes significantly to morbidity and mortality, with an increase in the number of macrophages and neutrophils in smokers compared to non-smokers.[8]

The most common comorbidity in this study was hypertension. This is similar to the study by Imaizumi et al shows that hypertension is the most prevalent comorbid in COPD patients.[8] COPD causes

the thickening of the airways and stiffness of blood vessels, thus reducing the amount of oxygen entering the lungs. This can cause the arteries around the lungs to narrow and risk of hypertension. Vascular stiffness may also result in increased sympathetic nerve activity. Air pollution can also be a risk for decreased arterial blood vessel development and morning hypertension, both of which can worsen atherosclerosis.[3]

The most common ADMA inflammatory markers in this study were in the low-risk group. ADMA levels will increase along with the severity of COPD. The study by Parmaksiz et al found that the average ADMA level was 0.11 µmol/L in GOLD I, 0.18 µmol/L in GOLD II, 0.19 µmol/L in GOLD III, and 0.23 µmol/L in GOLD IV.[4] Oxidative stress in COPD can increase the activity of arginine methylation enzymes that produce inhibitors of ADMA.[3]

Increased ADMA concentrations are associated with increased pulmonary artery pressure (PAP) measurements in COPD patients.[3] The low-risk group was the most common because the study sample was also predominantly in the GOLD II (moderate) population, so the risk for endothelial dysfunction was also not too high.

There is no data on the distribution of tricuspid regurgitation in COPD patients. These results align with found that almost 50% of COPD patients had varying degrees of tricuspid valve disorders.[6] Increasing degrees of COPD and lung hyperinflation have also been associated with worsening tricuspid regurgitation (TR) severity.[16] Severe and very severe COPD patients have been shown to have structural changes in the right heart, which can ultimately lead to the development of pulmonary hypertension.[17]

This study population consisted mostly of mild TR because stable COPD dominated the COPD sample with GOLD II (moderate), so the picture of tricuspid regurgitation was mostly in the mid-TR condition. Tricuspid regurgitation is associated with lower survival, regardless of left ventricular ejection fraction (LVEF) or pulmonary hypertension. Several studies have confirmed a close association between pulmonary artery pressure estimated by tricuspid regurgitation in COPD patients.[17]

This study found that the most common severity of COPD (GOLD criteria) was in GOLD II, and the higher the severity of COPD, the greater the risk of pulmonary hypertension. Moderate risk of pulmonary hypertension is the most apparent in GOLD III and IV. All patients in these groups have a high risk for the incidence of pulmonary hypertension. The severity of COPD is directly proportional to the incidence of pulmonary hypertension; the largest percentage of patients with pulmonary hypertension was in GOLD IV, followed by GOLD III. Severe pulmonary hypertension only occurs in severe or very severe COPD.[17]

The overall incidence of pulmonary hypertension in COPD, and this rate was directly proportional to the severity of COPD. In contrast to this study, although

Aguirre-Franco's study found the highest frequency of COPD degree was the very severe category, both found a significant Association between the severity of COPD and the incidence of pulmonary hypertension.[17] These results align with the theory that pulmonary hypertension occurs along with the severity of COPD. The higher the severity of COPD, the higher the probable pulmonary hypertension caused by chronic hypoxemia.

The main pathophysiological cause of pulmonary hypertension is chronic alveolar hypoxia. Chronic hypoxia and hypoxemia, systemic inflammation, atherosclerosis, and pulmonary artery endothelial dysfunction lead to increased pressure in the pulmonary artery, therefore triggering pulmonary hypertension.[17]

Pulmonary hypertension is a significant risk factor for hospitalization and is associated with shorter life expectancy. Residential location also affects the incidence of pulmonary hypertension. There is a higher risk of developing pulmonary hypertension in COPD patients who live in the highlands compared to the lowlands, despite having the same severity of COPD based on the same GOLD criteria.[17]

This study identified three categories of risk based on Asymmetric Dimethylarginine (ADMA) levels: low, moderate, and high risk. Both the low-risk and high-risk ADMA groups were most commonly associated with a moderate risk of developing pulmonary hypertension. Interestingly, the moderate-risk ADMA group showed a more variable distribution, with equal proportions (36.4%) experiencing either mild or severe risk of probable pulmonary hypertension.

These results align with Aguirre-Franco's research, where higher ADMA levels (high risk) in COPD patients are significantly associated with the incidence of pulmonary hypertension.[17] There is not much research data regarding the Association between ADMA levels and the incidence of pulmonary hypertension. However, ADMA has emerged as a risk marker for many conditions related to pulmonary hypertension.[4]

Asymmetric dimethylarginine is an endogenous competitive inhibitor of nitric oxide (NO) synthase. L-Arginine metabolism, including NO synthesis pathways and arginase, is important in maintaining airway function.s[18] The lungs produce significant amounts of ADMA. ADMA levels are associated with the severity of vascular endothelial damage. A study shows that AMDA levels are associated with the incidence and severity of asthma and cystic fibrosis. Parmaksız's study found that ADMA levels were proportional to the severity of COPD based on GOLD criteria. The higher the severity of COPD, the higher the ADMA levels. FEV1 tends to decrease as ADMA concentration increases.[4]

The degree of ADMA levels of this study was mainly dominated by GOLD II in the low-risk group, GOLD II and GOLD III in the moderate-risk group, and GOLD III in the high-risk group. There was no significant association between the degree

of ADMA and the severity of COPD. These results align with a study by Ozkarafakili, where the degree of ADMA is proportional to the severity of COPD; the higher the ADMA levels, the higher the severity of COPD.[19]

The same thing is also found in a study by Zinellu, where increasing ADMA levels and the ADMA/arginine ratio (mainly due to reduced arginine concentration) are directly proportional to the severity of COPD.[20] In theory, ADMA in the COPD airway causes a functionally relevant shift of l-Arginine breakdown by NO synthase.[18] This study was mostly at low risk because the study sample was dominated by GOLD II COPD (moderate degree).

This study found that age <65 years had the highest risk of pulmonary hypertension, namely mild and moderate risk, while at age ≥65 years, the most prevalent for pulmonary hypertension was the moderate risk group. There is no significant association between age and the risk of pulmonary hypertension. This result is different from the study that found an increase in the prevalence of up to 10 times at the age of ≥65 years. The prevalence of pulmonary hypertension increases with age. Other studies also found the prevalence of pulmonary hypertension in COPD at a median age of 68.1 years.[21]

Even higher mean age in stable COPD subjects with pulmonary hypertension of 71.1±11.8 years compared to COPD without pulmonary hypertension of 63.7±10.2 years.[22] The different results in this study were because the sample was dominated by age <65 years.

In this study, males were most commonly associated with a moderate risk of developing pulmonary hypertension, whereas females had the highest risk in the severe category. There is no significant association between gender and the risk of pulmonary hypertension. This result aligns with a study by Mohammed that the incidence of pulmonary hypertension is unrelated to gender.[22]

Basak et al found that 95% of male subjects had stable COPD and impaired cardiac function.[23] This result also aligns where female gender is a probable pulmonary hypertension factor, even though females with this condition can survive better than males.[20] This is because females with pulmonary hypertension or those associated with connective tissue have higher cardiac output and lower pulmonary vascular resistance.[24]

The Brinkman index of COPD in this study was statistically associated with probable pulmonary hypertension, where mild BI and moderate BI had a low risk for pulmonary hypertension, while severe BI had the highest at moderate risk. There is no research data regarding the Brinkman index on probable pulmonary hypertension.

The study by Mohammed found that 30.8% of smokers had pulmonary hypertension, but not statistically significant.[22] Smoking causes an acute increase in blood pressure and heart rate. Smoking is also a major contributor to the

development of COPD, chronic bronchitis, and emphysema, which are diseases correlated with secondary pulmonary hypertension.[8]

Chronic obstructive pulmonary disease and cardiovascular disorders have been recognized as shared risk factors for smoking. Cigarette smoke has increased the risk of atherosclerosis and the systemic inflammatory response. The inflammatory state in COPD occurs due to the adhesion of leukocytes and other molecules to the endothelium, damaging the endothelial wall and forming atherosclerotic plaques.[8]

Cigarette smoke is associated with pulmonary hypertension in humans and animal models. Although the etiology of pulmonary hypertension in smokers is not understood, some studies suspect a role in inducible nitric oxide synthesis (iNOS) and oxidative vascular damage in inducing oxidative stress.[8]

Among the comorbidities identified in COPD patients—namely diabetes mellitus, hypertension, and hypertensive heart disease—hypertension was the most common. It was also the only comorbidity significantly associated with a high risk of developing pulmonary hypertension. In contrast, diabetes mellitus and hypertensive heart disease were not associated with an increased risk.[8]

Cardiovascular disease, hypertension and COPD are correlated with each other, and it is difficult to adjust the risk factor of smoking as the cause of one of the above conditions.[8] Hypertension, as a risk factor for cardiovascular disorders, will also adversely affect the prognosis and mortality in COPD. Possible Association mechanisms between COPD and hypertension are systemic inflammatory conditions, chronic hypoxia, and hypercapnia due to airway obstruction, causing increased intrathoracic pressure.[25]

The limitation of this study was that the sample was dominated by moderate severity of COPD, so a larger and heterogeneous sample was needed to assess the degree of risk of pulmonary hypertension. Additionally, this study design is cross-sectional and the data of this study were retrieved from medical records. It is suggested to conduct a cohort study design to establish the association between COPD and pulmonary hypertension.

CONCLUSION

These findings indicate that pulmonary hypertension in COPD is strongly correlated with the degree of airflow obstruction, which is likely mediated by chronic hypoxia, pulmonary vascular remodeling, and systemic inflammatory response.

Although ADMA is known to be an endogenous inhibitor of nitric oxide synthase that may affect endothelial function, the results of this study suggest that the role of ADMA as a biomarker of pulmonary hypertension in COPD has not been significantly proven, so further studies with more heterogeneous samples and longitudinal designs are needed for evaluation of causal relationships.

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