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THE RELATIONSHIP OF NT PRO BNP AND ECHOCARDIOGRAPHIC FEATURES OF RIGHT VENTRICLE DISFUNCTION WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AT HAJI ADAM MALIK GENERAL HOSPITAL MEDAN

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Abstract

Background: Cardiovascular complications caused by Chronic Obstructive Pulmonary Disease (COPD) will affect structure and function of heart's normal anatomy. This study aims to determine the relationship between the abnormality of NT Pro BNP levels and echocardiographic features of right ventricular (RV) dysfunction in COPD.

Method: A cross-sectional study to assess the association between the abnormality of NT Pro BNP levels and echocardiographic features of right ventricular dysfunction in COPD in the outpatient unit of the Integrated Heart Center H. Adam Malik Hospital Medan. COPD patients were grouped based on GOLD criteria from spirometry examination into severe COPD (GOLD III) and very severe COPD (GOLD IV). Subjects then performed NT pro BNP and echocardiography examination to assess pathological changes in cardiac.

Result: NT Pro BNP was higher in GOLD IV. Cut off value of NT Pro BNP > 172 pg/nl is the initial parameter of right ventricular dysfunction. Pulmonary hypertension was found in 93% of cases. The most common cardiac pathological findings were RV hypertrophy (71%), RV dysfunction (86.7%) and pulmonary regurgitation (87.5%). Pathological findings on echocardiography were more common in the GOLD IV group. COPD severity was associated with NT Pro BNP abnormalities ($p < 0.001$) and associated with pathologic echocardiographic findings ($p < 0.001$).

Conclusion: Severe COPD is associated with increased NT pro-BNP abnormalities and pathological findings on echocardiography. Echocardiography facilitates early detection of cardiovascular complications in patients with severe and very severe COPD (GOLD III and IV).

Introduction

The heart and lungs are two organs that are interconnected, so that if there is a pathological condition in one of them it will interfere with the function of the other. One of the most common lung diseases we encounter is COPD.[1] A report from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) states that in 2010 as many as 384 million people or around 11.7% of the world's population were COPD sufferers with a death rate up to three million people each year.[1] Data from the Indonesian Lung Doctors Association in 2015, at least 4.5 - 5.5% of Indonesia's population is suffering from COPD, and could increase to 7.2% in rural areas.[2]

Chronic inflammation that occurs in COPD does not only cause disturbances in the respiratory system, but also has a significant systemic impact as a sign that there is a comorbid condition in the sufferer. Some of the COPD comorbid that are often encountered include cardiovascular disease, metabolic syndrome, osteoporosis, lung cancer and muscle dysfunction.[2] Natriuretic peptide is a biomarker that is widely used to diagnose heart failure. N-Terminal pro Brain Natriuretic Peptide (NT-pro BNP), which is one type of natriuretic peptide, is a polypeptide produced by the ventricular myocardium due to stress on the heart wall.[3,4]

All of the complications to the heart caused by COPD as mentioned above will change the function and anatomical shape of the heart. Echocardiography is a non-invasive examination procedure that can be used to evaluate changes in the heart, both functionally and anatomically. Apart from being safer and more comfortable for the patient, this examination has good sensitivity and specificity, so that this examination can be used in COPD patients both for screening, diagnosis and evaluation of cardiovascular complications.[5]

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From several studies it was found that serum NT-pro BNP concentrations were associated with an increase in end-diastolic pressure which was strongly associated with shortness of breath in heart failure and correlated with the prognosis of left ventricular dysfunction. This study wanted to assess the relationship between the abnormality of NT Pro BNP levels and echocardiographic features of RV dysfunction with the severity of COPD which indicates changes in the structure and function of the heart.

Methods

This was a cross-sectional study to assess the association of NT Pro-BNP and echocardiographic features of RV dysfunction with the severity of COPD. COPD patients were grouped into 2 groups based on their severity: GOLD III and GOLD IV. This research was conducted on COPD patients who were seeking outpatient treatment at the Outpatient Installation of the Haji Adam Malik Hospital in Medan from August 2019 to April 2020 with consecutive sampling up to a total sample size of 38 people. Inclusion criteria were male and female patients age >30 years who have been diagnosed with COPD from the outpatient polyclinic of the Department of Pulmonology and Respiration Medicine of H. Adam Malik Hospital, have undergone a spirometry examination, willing to participate in the study by signing informed consent. Exclusion criteria were patients with other pulmonary disorders other than COPD who have been diagnosed previously, patients with other heart defects (coronary artery disease, significant heart valve disorders and congenital heart problems) who have been previously diagnosed. The researcher asked for ethical clearance to the Permanent Committee for Research Ethics Evaluation, Faculty of Medicine, University of North Sumatra.

Researchers reviewed the patient's medical records, ECG, chest X-ray, and spirometry to confirm the diagnosis of the disease and its severity, then performed NT Pro-BNP examination and echocardiography in the left lateral decubitus position using a GE Vivid S6 echocardiography device with a 3 frequency heart probe sector 2 MHz in the echocardiography laboratory of the Integrated Heart Center of the Haji Adam Malik Hospital Medan by residents who work in the echocardiography stage under the supervision of an echocardiography supervisor. The parasternal long axis view was taken and then the left ventricular ejection fraction was measured using the Teicholdz method, assessing left ventricular hypertrophy and right ventricular hypertrophy using the M mode technique. Parasternal short axis view was taken and evaluated for the presence or absence of abnormal interventricular septal wall motion using 2-dimensional techniques. The apical 4 chamber view was taken, and then measured the TAPSE of the right ventricle using the M mode technique, measuring the basal diameter of the right ventricle, the major axis and minor axis of the right ventricle in 2 dimensions and evaluating tricuspid regurgitation using color and continuous wave Doppler. Left ventricular diastolic function was measured using the ratio of the E and A waves of the pulse wave Doppler. Subcostal view was taken and RAP measurement of the inferior vena cava using M mode.

Data analysis including cut off point values for numerical data obtained through the receiving operator curve (ROC). Comparison between the two groups on the numerical independent variable and the dependent variable numerically using a linear regression test. Multivariate analysis of numerical independent variables with numerical dependent variables was tested by linear regression test. The variable is considered significant if the p value <0.05.

Results

Research Characteristics

Of the total 38 people with COPD, 14 GOLD III and 24 GOLD IV people, 36 (94.7%) were men, with a history of smoking in 35 people (92.1%).

Table 1. Baseline demographics of study subjects comparing smoking history, hemodynamics, spirometry and echocardiographic examination results in each of the GOLD groups.

Variable	Normal range	GOLD III N = 14 n(%)	GOLD IV N = 24 n(%)	p value
Gender	-			
- Men		13 (36,1)	23 (63,9)	1,000
- Women		1 (50)	1 (50	1,000
Age (Years)	-	67,8±11,1	61,2±7,3	0,03

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Body weight (Kg)	-	62,2±12,1	60,6±15,2	0,741
height (cm)	-	159,7±3,9	160,6±8,2	0,675
Systolic blood pressure (mmHg)	100-130	127,4±18,1	122,5±12,2	0,324
Diastolic blood pressure (mmHg)	60-90	77,7±11,2	77,5±7,4	0,944
Heart rate (times/minute)	60-100	70,9±11,5	82,0±10,5	0,005
FEV_1 (%)	80-120	38,0±6,6	21,0±5,8	0,000
FVC (%)	≥70	54,3±8,7	31,1±10,2	0,000
FEV_1 / FVC	70-85	58,0±13,0	53,5±18,3	0,417
Duration of smoking				
< 20 years	-	2 (66,7)	1 (33,3)	0,132
>20 years		12 (34,3)	23 (65,7)	0,132
Types of cigarette				
Filter	-	5 (41,7)	7 (58,3)	1,000
Kretek		8 (32,0)	17 (68,0)	1,000
Number of cigarette/day				
< 1 pack	-	2 (100,0)	0 (0)	0,129
1 -2 packs		9 (36,0)	16 (64,0)	0,129
> 2 packs		3 (27,3)	8 (72,7)	0,268
NT-Pro BNP		129,5±36,6	343,3±340,0	0,006

The mean FEV1 in the GOLD III group was 38.0 ± 6.6% and that in the GOLD IV group was 21.0 ± 5.8%. The mean FVC in the GOLD III group was 54.3 ± 8.7% and in the GOLD IV group was 31.1 ± 10.2%. The mean FEV1 / FVC ratio in the GOLD III group was 58.0 ± 13.0 and in the GOLD IV group was 53.5 ± 18.3. NT Pro BNP in the table above, obtained significant results based on statistics. The mean levels of NT-pro BNP in the GOLD III group were 129.5 ± 36.6 and in the GOLD IV group were 343.3 ± 340.0

Table 2. Demographic Data of Subjects Based on Right Heart Echocardiography

Variable	Normal range	GOLD III N = 14	GOLD IV N = 24	p value
Right atrial dilatation (N, %)	-	5 (21,7)	18 (78,3)	0,017
Right atrial mayor axis (mm)	34-52	44,5±5,43	48,0±6,3	0,749
Right atrial minor axis (mm)	26-44	38,7±7,1	43,4±5,5	0,537
Right ventricle dilatation (N, %)	-	3 (14,3)	18 (85,7)	0,001
Right ventricle linier dimension (mm)	24-41	38,7±3,8	42,6±5,1	0,465
Right ventricle dimension (N, %)	-	2 (13.3)	13 (86.7)	0,015
TAPSE (mm)	16-30	18,9±2,3	17,4±3,4	0,040
Tricuspid regurgitation (N, %)	-	5 (21,7)	18 (78,3)	0,170
Mild		5 (38,5)	8 (61,5)	
Moderate		0 (0)	7 (100,0)	
Severe		0 (0)	3 (100,0)	
Tricuspid regurgitation peak velocity (m/s)	1.9-2.5	1.7±0,5	2,4±0,6	0,427
Tricuspid regurgitation peak gradient (mmHg)	< 30	19,2±7,9	29,0±8,7	0,716
E/A		0,8±0,2	0,8±0,3	0,644

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LV D Shape		3 (25,0)	9 (75,0)	0,480
IVS Paradox		2 (13,3)	13 (86,7)	0,010
Left ventricular diastolic dysfunction		12 (36,4)	21 (63,6)	1,000
Right ventricular hypertrophy (N, %)	-	9 (29,0)	22 (71,0)	0,080
Left ventricular hypertrophy (N, %)		3 (30,0)	7 (70,0)	0,710
Reduced-EF		0 (0)	2 (100)	0,520
Right ventricle thickness (mm)	2-5	6,0±0,8	6,3±0,9	0,475
Left Ventricular Mass Index		100±32,0	98,9±34,0	0,967
Left Ventricular Systolic Function		60±6,8	60,0±6,3	0,871
Pulmonary regurgitation (N, %) mild moderate	-	3 (14,3) 2 (13,3) 1 (16,7)	18 (85,7) 13 (86,7) 5 (83,3)	0,001
Pulmonary Pressure half time (msec)	-	560±78,3	476,5±94,5	0,290
RAP (mmHg)	3-15	5.1±2,6	8,3±3,1	0,281
PASP (mmHg)	18-25	26,4±5,1	37,0±9,8	0,008
MPAP (mmHg)	12-16	28,8±4,0	31,2±4,3	0,512
Pulmonary Hypertension (N, %)	-	1 (6,7)	14 (93,3)	0,002

On the right heart echocardiography examination (Table 2), there were significant changes in heart pathology based on the severity of COPD (p value <0.05), right atrial dilatation (p = 0.017), right ventricular dilatation (p= 0.001), right ventricular dysfunction. (p = 0.015), Interventricular Septum paradox (IVS) (p = 0.01), pulmonary regurgitation (p = 0.001), pulmonary hypertension (p = 0.002), mean TAPSE value (p = 0.04) and mean PASP value (p = 0.008).

Relationship of NT Pro BNP Abnormalities to the Severity of COPD

Bivariate analysis of NT-pro BNP levels with COPD severity was carried out. The mean levels of NT-pro BNP in the study were 130.86 ± 36.82 in the GOLD III group and 236.5 (164-1489) in the GOLD IV group. There were differences in the mean levels of NT-pro BNP in the GOLD III and GOLD IV groups which were statistically significant (p <0.001).

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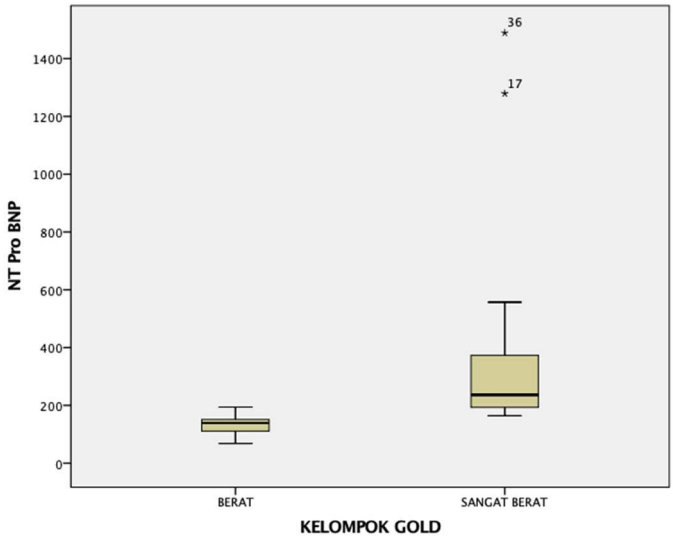

Figure 1. Bivariate analysis of NT-pro BNP levels with COPD severity

Table 3. Bivariate analysis of degree and correlation of NT-pro BNP levels with the COPD severity

NT-Pro BNP	COPD Severity		p value	Correlation coefficient * (*r*)	p value
(N, %)	Severe N = 14	Very Severe N = 24			
Value NT-Pro BNP	130,86 ±36,82	236,5 (164-1489)	< 0.001	0,652	<0,000

*The correlation coefficient is obtained from the results of the Spearman correlation test

The NT-pro BNP level was significantly correlated with the severity of COPD. The correlation coefficient is 0.652 with the strength of a strong relationship and the direction of the relationship is parallel or has a significant positive correlation (p value <0.000). This study also conducted a search for a new cut-off point for NT-Pro BNP levels as a biomarker for an increase in right heart pressure which is expected to be used as a reference that the right heart has experienced changes due to the severity of COPD. The search was carried out using the ROC method and the cutoff point that had the best sensitivity was taken while maintaining the good specificity value.

Table 4 ROC curve for NT-Pro BNP levels and COPD severity

Variable	Cut-off	Sensitivity (%)	1-Spesificity (%)	AUC	p value
NT-pro BNP	172,00	75	7,1	89,0%	<0.000

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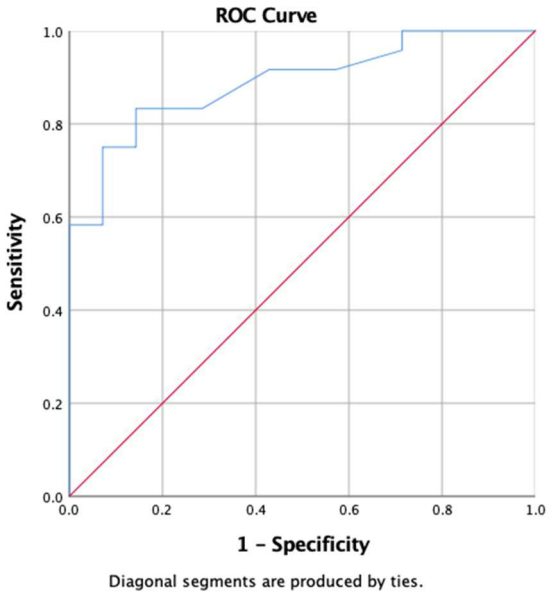

Figure 2. ROC curve for NT-Pro BNP levels and COPD severity

NT-pro BNP is an independent predictor of short-term prognosis in exacerbation of COPD. The NT-pro BNP threshold for assessing the severity of COPD between the GOLD III and GOLD IV groups was 172.0 pg / ml.

Relationship of Abnormality of Echocardiographic Pathological Findings to the Severity of COPD

Severity of COPD and echocardiographic findings was performed using the independent t-test statistical test if the data were numerical and using the chi-square statistical test if the data were categorical. There were significant mean differences in echocardiographic parameters of RA minor axis (p = 0.026), linear dimensions of the right ventricle (p = 0.007), TR Peak Velocity (p = 0.001) , TR Peak Gradient (p = 0.001), PR PHT (p = 0.005), RA Pressure (p = 0.006), PASP (p = 0.000), MPAP (p = 0.042) which were greater in GOLD IV than in GOLD III.

Table 5. Spectrum of COPD severity with the measurement of cardiac anatomical and physiological functions through echocardiography

Echocardiographic Pathological Changes (N, %)	COPD Severity		p value
	Mean Difference	Standard Error Difference	
RA Mayor Axis	-3,417	2,016	0,088
RA Minor Axis	-3,417	1,938	0,026
Linear Dimension Right Ventricle	-4,268	1,490	0,007
TAPSE	1,339	0,937	0,162
TR Peak Velocity	-6,71	1,762	0,001
TR Peak Gradient	-10,327	2,720	0,001
RV Wall Thickness	-0,220	0,2950	0,461
LV Mass Index	-0,202	11,022	0,985
LV Systolic function	0,655	2,348	0,783
PR PHT	86,500	28,885	0,005

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RA Pressure	-2,750	0,938	0,006
PASP	-10,988	2,836	0,000
MPAP	02,923	1,375	0,042

Discussion

Study subject was 38 people consisting of 14 people (37%) for the GOLD III group and 24 people (63%) for the GOLD IV group. The current theory states that male gender and older age are one of several risk factors for increasing the severity of COPD. This is in line with the results of a study where this study showed that the proportion of men in the GOLD IV group (63.9%) was greater than the proportion of men in the GOLD III group (36.1%). Both GOLD III and GOLD IV are subjects with age > 60 years, which indicates that old age is a risk factor for increasing the severity of COPD.

There is no doubt that the longer exposure to cigarette smoke, the heavier the COPD severity will be suffered. [6,7] From the smoking history, in this study it can be observed that many GOLD IV patients have a history of smoking more than 20 years (65.7%) with the number of cigarette consumption of 1 to 2 packs per day (64%).

From the results of echocardiography examination, in this study there were significant cardiac pathological findings based on the severity of COPD (p value <0.05), such as right atrial dilatation (p = 0.017), right ventricular dilatation (p = 0.001), right ventricular dysfunction (p = 0.015), paradoxical interventricular septum (IVS) (p = 0.01), pulmonary regurgitation (p = 0.001), pulmonary hypertension (p = 0.002), mean TAPSE value (p = 0.04) and mean PASP value (p = 0.008). This is in line with a study conducted by Jatav VS, et al., 2017 where all echocardiographic findings of right ventricular dysfunction such as PAH, cor pulmonal, RA / RV dilatation, RVH and RVSD were linearly correlated significantly with the severity of COPD (p <0, 05). Similar results were obtained by Jatav et al (2017) who conducted a study of 100 COPD patients consisting of 28 GOLD I/II and 73 GOLD III/IV people where the enlargement of the right atrium and ventricle was 43%, right ventricular dysfunction was 14%, and pulmonary hypertension by 44%.[7] Meanwhile, from a study conducted by Venkateswara Rao et al in 2016 on 62 COPD patients consisting of 23 GOLD II and 39 GOLD III/IV patients, pathological echocardiography was found in right atrial enlargement (48.38%), right ventricular enlargement (46.77%), abnormal motion of the interventricular septum (17.74%), and pulmonary hypertension (56.45%).[8] The greater difference in numbers in the study conducted by Jatav and Venkateswara was due to the greater number of subjects with GOLD III/IV degrees compared to this study.

Although the incidence of pulmonary hypertension was only 17% (15 people) in this study, signs of volume overload in the right ventricle were common. This can be seen from the mean values of anatomical measurements and physiological functions through echocardiography. In this study, it was found that the major axis and minor axis of the right ventricle were still within normal ranges, but with the increasing severity of COPD, the value of this measurement also increased. The linear dimensions of the right ventricle were also within the normal range, except for the GOLD IV group of subjects who had left the normal range. In accordance with the theory put forward by Falk et al (2008), this phenomenon occurs due to the compensation of the heart against increased pulmonary vascular pressure due to vascular remodeling in COPD, so that the right ventricle must increase its contractility to deplete the volume of blood in it. The thickness of the right ventricle has increased, starting from the COPD group with GOLD III and increasing according to the increasing degree of disease severity.[11] This finding is consistent with the statement of Vork-Noordegraaf et al (2005) who in their study succeeded in drawing the conclusion that the initial sign of increased right ventricular pressure from echocardiography was right ventricular hypertrophy without the presence of right or left ventricular failure.[10]

The mean left ventricular mass index was still within the normal range for each GOLD group. In the assessment of the physiological function of the heart, the mean measurement right ventricular contractility value is still within the normal range, but the increasing the severity of COPD, the lower the value. This is consistent with the decreased compensatory ability of the heart to the increase in right ventricular pressure due to worsening COPD.[9]

In the pressure measurement of RAP, PASP and MPAP, it can be seen that the heavier the severity of COPD, the higher the pressure value, where the highest average pressure value is in GOLD IV group. The study conducted by Jatav et al. and El Wahsh et al. also demonstrated a positive correlation between increased severity of COPD

and increased systolic pulmonary artery pressure in 44% and 55.6% of patients, respectively. This is in line with the increasing velocity of tricuspid regurgitation which is getting worse with the increasing degree of disease severity.[7,11] Previous studies conducted by Yasser Moustfa, et al (2019) also showed a positive correlation between the severity of obstruction in COPD and tricuspid regurgitation.[12] According to the researchers' observations, this may be due to the proportion of COPD subjects in the GOLD III and IV groups more than the proportion of subjects with GOLD I and II in the two previous studies. However, despite this, the incidence of left ventricular hypertrophy and impaired left ventricular diastolic function was still higher in the severe COPD group (GOLD III and IV) in both studies.

Another study by Lang, et al. and Chi et al. showed that there was an increase in NT-pro BNP levels in COPD patients compared to control patients. NT-pro BNP can describe the presence of right ventricular dysfunction due to COPD. RV function has an important role in the development of clinical symptoms and prognosis of COPD patients. So far, RV function can be assessed based on echocardiographic variables, namely Tricuspid annular plane systolic excursion (TAPSE) although RV strain was found to be better in quantifying RV function.[13,14] In this study, there was a significant difference in the mean TAPSE value ($p = 0.04$) between COPD GOLD III and IV. This suggests that there is an impact of increasing the severity of COPD on RV dysfunction. RV dysfunction in COPD begins with pulmonary hypertension, which will increase RV afterload resulting in RV dysfunction. Assessment of RV dysfunction is difficult and not routine because of the complex anatomy and high dependency burden.

Study conducted by Lamia Ouanes-Besbes, et al showed that NT-pro BNP was accurately correlated with changes in morphology and changes in RV function, RV/LV ratio ($R2 = 0.22$; p value = 0.02), PAPs ($R2 = 0.37$; p value = 0.001) and RV diameter ($R = 0.24$; p value = 0.01).[15] Study by Sharif et al. demonstrated that BNP correlates with pathological conditions that cause chronic overloading of the right ventricle as in pulmonary hypertension. BNP correlated with right ventricular remodeling as well as the severity of pulmonary hypertension.[16] NT-pro BNP is known to result from ventricular stretching in the presence of COPD exacerbation. This was found in a study conducted by Farnoosh et al. in 2018, where there was a significant relationship between the mean serum levels of NT-pro BNP and the severity of acute COPD exacerbations with $p = 0.009$.[17] A study by Pasha, et al. Showed that NT-pro BNP levels were strongly correlated with RVEF in Pulmonary Embolism (PE) patients. The study showed that RVEF was significantly lower in patients with PE than in patients without PE ($45.2\% \pm 12$ vs. $50.5\% \pm 10$; $p < 0.001$).[18]

A cohort study conducted by Labaki et al also found that higher levels of NT-pro BNP were associated with increased COPD exacerbations within 1 year of follow-up. Myocardial strains and hypoxia caused by exacerbation of COPD and increasing severity of COPD will increase blood levels of NT-pro BNP.[19] There are several mechanisms that may cause impaired right ventricular function in COPD patients. First, the presence of chronic hypoxemia causes disruption of intracellular calcium transport which in turn results in abnormalities in myocardial relaxation. Second, the presence of pulmonary hypertension with chronic right ventricular hypertrophy in COPD was followed by right ventricular dilatation. As a result, during the initial diastolic period, the inter-ventricular septum will push the left ventricular cavity so that the left ventricle loses its circular configuration.[20] It also depends on the difference in trans-septal pressure gradient. Third, the presence of emphysema and pulmonary hyperinflation in COPD is associated with failure of the left ventricular filling phase. An increase in intra-thoracic pressure will decrease the preload of both ventricles and increase left ventricular afterload (Barr et al, 2010).[21]

Furthermore, Huang et al (2015) explained that the presence of atherosclerotic plaques that are getting worse due to smoking and the aging process in COPD patients will cause myocardial ischemia and ultimately lead to left ventricular diastolic disorders in COPD.[22] A study by Akpinar, et al. showed that NT-pro BNP was a variable that significantly increased in exacerbation of COPD conditions (p value <0.001). The study showed that the limit value of NT-pro BNP levels in predicting the occurrence of acute exacerbation of COPD was 303.5 pg/ml (63.9% sensitivity and 72% specificity) with an area under the ROC curve of 0.711 (95% CI: 0.602–0.820), p value = 0.001).[23]

The frequency of pulmonary hypertension in COPD varies in different study findings. Frexia et al. reported that 19% of COPD patients had pulmonary hypertension while the study by Gupta et al. reported that 63% of COPD patients had pulmonary hypertension.[5,24] Several studies have shown a positive correlation between increased levels of NT-pro BNP and pulmonary artery pressure. A study by Chi, et al. showed a positive correlation between PAP and NT pro BNP levels in COPD patients. In this study, we found that the NT-pro BNP level was significantly

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increased (p <0.001) based on the severity of COPD with a mean value of 236.5 (164-1489).[14] Based on the analysis of the ROC curve in this study, the threshold value levels of NT-pro BNP based on the severity of COPD was 172 pg/ml. This threshold value has a sensitivity of 75% and a specificity of 92.1% (p value <0.001), with a false-positive value of 7.1%. An increase in NT-pro BNP levels with a threshold value of 172 pg/ml can be used as a supporting biomarker in determining the classification of COPD based on the degree of severity.

The study limitations were number of samples in this study is relatively small and this study was only conducted in one health center, and only carried out measurements at one time in assessing cardiac pathological changes through echocardiography in COPD patients, so it is not known exactly when cardiac pathological changes began to occur. This research needs to be continued by involving a larger number of samples and carried out in more than one place. In future studies it is preferable to do a prospective cohort design, involving more than one diagnostic modality such as electrocardiography, chest X-ray and if necessary right heart catheterization as the gold standard in diagnosing pulmonary hypertension.

Conclusion

There is a relationship between the severity of COPD with the findings of NT Pro BNP abnormalities with pathological findings on echocardiography (right atrial dilatation, right ventricular dilatation, right ventricular dysfunction, paradoxical Interventricular Septum (IVS), pulmonary regurgitation, pulmonary hypertension, mean TAPSE and the mean value of PASP). Echocardiographic pathologic findings are more common in patients with very severe COPD (GOLD IV). There is a strong and significant positive correlation between NT-pro BNP levels and the severity of COPD and there is a significant difference in the mean NT-pro BNP levels based on the severity of COPD. The increase in NT-pro BNP levels with a threshold value of 172 pg/ml can be used as a supporting biomarker in determining the diagnosis of COPD classification based on the degree of severity with a sensitivity of 75% and a specificity of 92.1%.

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