Acta Cardiologia Indonesiana

pISSN:2460-5700
eISSN:2579-4345

Web page: jurnal.ugm.ac.id/v3/jaci

Relationship Between Degree of Disease and Pathological Findings of Echocardiography in Patient with Chronic Obstructive Pulmonary Disease

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Keywords:
COPD;
echocardiography;
severity

Manuscript submitted: February 15, 2019
Revised and accepted: November 19, 2019

ABSTRACT

Background: Cardiovascular complications caused by COPD will change the normal function and shape of the heart's anatomy. The purpose of this study was to determine whether there was relationship between the degree of severity of COPD and cardiac pathology abnormalities through echocardiography.

Methods: A cross-sectional analysis was conducted on 88 COPD patients at outpatients cardiology clinic Haji Adam Malik General Hospital Medan from October 2018 to December 2018. COPD patients were grouped in 4 groups based on GOLD criteria from spirometry examination, then grouped into 2 large groups, group of patients with mild to moderate COPD (GOLD I - II) and patients with severe COPD (GOLD III - IV). Then all patients underwent echocardiography examination to determine changes in the heart.

Results: Pulmonary hypertension was found in 17% of cases. The most common heart pathology disorders were right ventricular hypertrophy (64.8%), left ventricular diastolic dysfunction (52.3%) and tricuspid regurgitation (35.2%). Echocardiographic abnormalities were most commonly found in groups with severe COPD (GOLD III – IV). The severity of COPD was associated with echocardiography abnormalities findings ($p < 0.05$) except in left ventricular dysfunction (p 0.241).

Conclusion: Echocardiographic examination in COPD patients can identify cardiovascular complications in severe COPD patients (GOLD III and IV).

INTISARI

Latar Belakang: Komplikasi kardiovaskular yang disebabkan oleh PPOK akan mengubah fungsi normal dan bentuk anatomi dari jantung. Studi ini bertujuan untuk menilai hubungan antara derajat keparahan PPOK dan temuan patologis jantung melalui pemeriksaan ekokardiografi.

Metode: Penelitian ini merupakan studi analitik potong lintang untuk menilai hubungan derajat keparahan PPOK terhadap perubahan patologis pada jantung melalui ekokardiografi di unit rawat jalan Pusat jantung Terpadu Rumah Sakit H. Adam Malik Medan. Penderita PPOK dikelompokkan berdasarkan kriteria GOLD dari pemeriksaan spirometri, kemudian dibagi dalam 2 kelompok besar derajat keparahan penyakitnya yaitu kelompok penderita PPOK ringan-sedang (GOLD I - II) dan penderita PPOK berat (GOLD III – IV). Subyek kemudian dilakukan pemeriksaan ekokardiografi untuk menilai perubahan patologis pada jantung.

Hasil: Hipertensi pulmonal dijumpai pada 17% kasus. Temuan patologis jantung yang banyak dijumpai adalah hipertrofi ventrikel kanan sebesar 64.8%, gangguan fungsi diastolik ventrikel kiri sebesar 52.3% dan regurgitasi trikuspid sebesar 35.2%. Temuan patologis pada ekokardiografi ini lebih

banyak ditemukan pada kelompok dengan GOLD III dan IV. Beratnya derajat keparahan PPOK berhubungan dengan temuan patologis ekokardiografi (p < 0.05) kecuali disfungsi ventrikel kiri. (p 0.241)

Kesimpulan: PPOK derajat berat berhubungan dengan temuan patologis pada pemeriksaan ekokardiografi. Ekokardiografi memudahkan dalam deteksi awal komplikasi kardiovaskular pada pasien PPOK derajat berat (GOLD III dan IV).

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent, progressive airway obstructions and is associated with a chronic inflammatory response due to particles or toxic gases in the airways. Global initiatives for chronic obstructive lung disease (GOLD) estimated in 2020, this disease will increase its rank from the 6th to the 3rd cause of death worldwide.[1] Currently, COPD is known as one of the conditions that have a role in worsening heart function. Apart from having the same risk factors for cardiovascular disease, the course of the disease itself can also cause cardiovascular complications. Vice versa, the presence of cardiovascular abnormalities is undoubted as a contributor to morbidity and mortality in COPD.[2]

Heart complications caused by COPD include heart failure, atherosclerotic plaque deterioration, arrhythmias, and pulmonary hypertension.[3,4,5] COPD patients with heart failure will have a higher mortality rate (hazard ratio 1.24-1.7).[6] Additionally, patients with acute coronary heart disease (CHD) accompanied by COPD have poor short and long-term outcomes, higher mortality rates during hospitalization and higher rates of rehospitalization compared with patients without comorbid COPD. For complications of arrhythmia, Atrial fibrillation (AF) is an arrhythmia that is often found in COPD with prevalence reaching 4.7% to 15% in stable COPD.[7]

Another complication of COPD in the cardiovascular system is pulmonary hypertension. Increased pulmonary arterial pressure has been reported in 20% to 90% of COPD patients and each year increases by an average of 0.4 - 0.6mmHg.[8,9] Several previous studies have shown that pulmonary hypertension can determine the prognosis of COPD patients.[10]

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 patients, this examination has good sensitivity and specificity. Thus, this examination can be used in patients with COPD for screening, diagnosis, and evaluation of cardiovascular complications.[11] This assessment is very important to find out the changes that occur in the heart as early as possible so that the selection and administration of appropriate therapy can be started. In addition, the patient's prognosis in the future could be predicted and secondary precautions could be given as early as possible to improve the quality of life of patients.

Method

Design

This cross-sectional study was conducted at the Haji Adam Malik Medan General Hospital (RSUP HAM) with permission from the Research Ethics Committee of the Faculty of Medicine, University of Sumatera Utara (FK USU) -RSUPHAM since August 2018 until December 2018. The research subjects were male patients and women aged > 30 years who have been diagnosed with COPD from the Outpatient clinic of the Department of Pulmonology and Respiratory Medicine FK USU/RSUP HAM and have underwent spirometry examination using spirometry Chest Graph HI-701.

Patients diagnosed with bronchial asthma, lung cancer and pulmonary embolism with clear evidence before the study performed were excluded. In addition, patients with previously diagnosed coronary artery disease (history of angina, ischemia on electrocardiography, presence of ventricular wall motion abnormality on echocardiography or a documented history of myocardial infarction), patients with significant heart valve disorders (aortic valve stenosis/regurgitation, mitral valve stenosis/regurgitation, pulmonary valve stenosis and tricuspid valve stenosis) and congenital heart disease were also excluded from the study.

Data collection was carried out starting from clinical data which consisted of disease history, initial physical examination, ECG, chest X-ray, and spirometry results. The severity of COPD is determined by the GOLD criterion from spirometry results. In patients with Forced Expiratory Volume in 1 Second (FEV_1) divided with forced vital capacity (FVC) <0.70, the air flow resistance level is classified as GOLD I (FEV1 ≥ 80% prediction), GOLD II (50% ≤ FEV_1 <80% prediction), GOLD III (30% ≤ FEV_1 <50% prediction) and GOLD IV (FEV_1 <30% prediction).[1]

Echocardiography was performed in the left lateral decubitus position using GE Vivid S6 with a 3.2 MHz frequency heart probe. Examination with M-mode on the parasternal long axis view was performed to measure left ventricular ejection fraction by Teicholdz method, and assess left ventricular and right ventricular hypertrophy. A 2D technique of parasternal short axis view was performed to evaluate the presence/absence of inter-ventricular septal wall motion abnormality. An apical 4 chamber view examination was performed to measure right ventricular TAPSE (Tricuspid annular plane systolic excursion) with M-mode technique. Measurement of right ventricular basal diameter in major and minor axis with 2D technique, as

well as evaluation of tricuspid regurgitation using color and continuous wave Doppler was conducted. Left ventricular diastolic function is measured using the E and A wave ratio of pulse wave Doppler. Examination with subcostal view position was performed to measure RAP (right atrial pressure) from the inferior vena cava using M-mode.

Right atrial dilation was determined when the right atrial minor axis dimension was > 4.5 cm. Right ventricular dilatation was determined when basal diameter of right ventricle was > 41 mm. Right ventricular hypertrophy was determined when the lateral wall thickness of the right ventricle > 5 mm.[12] Right ventricular systolic dysfunction was determined if the tricuspid annular plane systolic excursion (TAPSE) value <17 mm.[13] Abnormal movement of the inter-ventricular septum was defined as movement of the ventricular septum to the left during systole and flatten (D shaped) during diastole. Left ventricular hypertrophy was calculated using the Cube formula:

$$LV\ Mass = 0.8 \times 1.4 \times [(IVS + LVID + PWT)^3 - LVID^3] + 0.6$$

IVS is the inter-ventricular septal wall diameter, LVID is the internal diameter of the left ventricle and PWT is the value of the posterior wall thickness of the left ventricle. Hypertrophy was defined when the left ventricular mass index value > 115 gr/m^2 in men and > 95 gr/m^2 in women. Left ventricular diastolic dysfunction was determined when mitral valve E / A ratio is <0.8 (Grade I), > 0.8 to < 2 (Grade II) and > 2 (Grade III).[14] Pulmonary hypertension was assessed by measuring pulmonary artery systolic pressure (PASP) from the peak velocity of tricuspid regurgitation (TV) in continuous wave Doppler using the following Bernoulli formula:

$$PASP = 4(TV)^2 + RAP$$

Pulmonary hypertension was determined when PASP> 40 mmHg. RAP was obtained through measurement of inferior cava vein diameter during inspiration and expiration period. Percentage of reduction of an inferior cava vein diameter would estimate RAP as follows: [13]

Inferior vena cava diameter during expiration	Percentage reduction of inferior vena cava	Estimated right atrial pressure
< 2.1 cm	> 50%	3 mmHg
> 2.1 cm	< 50%	15 mmHg
Not one of the above		8 mmHg

Echocardiography results were reviewed by two cardiology experts. Data were collected and analyzed. Patients was grouped into 4 groups based on GOLD criteria from spirometry examination, then grouped into 2 large groups: mild to moderate COPD (GOLD I-II) and severe COPD (GOLD III-IV).

Data analysis

All data were analyzed statistically using SPSS version 22. Categorical variables were presented as number or frequency (n) and percentage (%). Numerical variables were presented as mean and standard deviations for normally distributed data. The normality test for numerical variables in all subjects used the Kolmogorov-Smirnov test with n> 50. Cut-off points for numerical data were obtained through ROC curve. Comparisons between the two groups on categorical independent variables and categorical dependent variables was analyzed using Pearson Chi-Square test. If the Chi-Square test conditions were not met, then Kolmogorov Smirnov's 2K-Sample test was used. Comparison between two groups on numerical variables was analyzed using unpaired T-test. Variables were considered significant if the p-value is <0.05.

Results

Eighty eight COPD patients who have met the inclusion and exclusion criteria were included as subjects of the study which consisted of 22 people for each GOLD group. Of the total research subjects, 76 people (86.4%) COPD patients were men. Up to 45 people (51.1%) have a history of smoking for more than 20 years and most (61.4%) used a type of filter cigarette.

The following table shows the basic demographics of the study subjects with smoking history, hemodynamics, spirometry examination results and echocardiographic examination results to each GOLD group. From the table, we can observe that the group of subjects with GOLD I and GOLD II were younger compared to the group of severe COPD. The height, weight, blood pressure, and heart rate were not different between the four groups. Meanwhile, from the spirometry assessment, the average FEV1prediction was 51% and the predicted value was decreasing according to the increasing severity of COPD. Similar trend was seen in the predictive values of FVC and FEV1/FVC subjects of this study.

According to the right cardiac echocardiography examination (Table 2), most pathological changes in the heart were found in subjects with GOLD III and IV. Right atrial and ventricular dilation, right ventricular dysfunction, tricuspid regurgitation, inter-ventricular septal wall motion abnormality and pulmonary regurgitation was found. Right ventricular hypertrophy was found in the group GOLD I and II (40.9% and 45.5%), although it was more common in GOLD III and IV (81.8% and 90.9%).

According to measurement of right atrial pressure, all groups have pressures that were within normal limits, but this value was higher in line with the increasing severity of COPD. All groups have greater mean pulmonary arterial pressure (MPAP) than normal and this value increase in line with increasing severity of COPD. Meanwhile, only subjects in the GOLD I group have pulmonary artery systolic pressure (PASP) within the normal range.

Table 1.
Baseline Demographic Data of Subjects Based on COPD Severity

VARIABLE	NORMAL VALUE	TOTAL N = 88	GOLD 1 N = 22	GOLD 2 N = 22	GOLD 3 N = 22	GOLD 4 N = 22
Male (N,%)	-	76 (86.4)	17 (77.3)	17 (77.3)	21 (95.5)	21 (95.5)
Age (Years)	-	56. ± 14	45 ± 12	54 ± 16	65 ± 9	62 ± 8
Body weight (Kg)	-	62 ± 11	64 ± 9	61 ± 9	62 ± 12	60 ± 15
Body height (cm)	-	161 ± 6	163 ± 6	163 ± 6	161 ± 5	160 ± 8
Systolic blood pressure (mmHg)	100-130	124 ± 14	122 ± 8	123 ± 14	129 ± 17	123 ± 14
Diastolic blood pressure (mmHg)	60-90	77 ± 8	78 ± 5	74 ± 7	79 ± 10	78 ± 8
Heart rate (times/minute)	60-100	77 ± 11	77 ± 7	77 ± 11	74 ± 11	81 ± 12
FEV_1 (%)	80-120	51 ± 24	81 ± 0.9	65 ± 8	39 ± 6	20 ± 6
FVC (%)	≥70	57 ± 23	83 ± 8	68 ± 14	51 ± 11	28 ± 8
FEV_1 / FVC (%)	70-85	61 ± 18	68 ± 15	67 ± 9	63 ± 11	56 ± 18
Smoking duration (N,%)		43 (48.9)	18 (81.8)	20 (90.9)	4 (18.2)	1 (4.5)
< 20 years	-	45 (51.1)	4 (18.2)	2 (9.1)	18 (81.8)	21 (95.5)
>20 years						
Type of cigarette (N,%)		54 (61.4)	21 (95.5)	20 (90.9)	8 (36.4)	5 (22.7)
Filtered	-	34 (38.6)	1 (4.5)	2 (9.1)	14 (63.6)	17 (77.3)
Non filtered						
Mount of cigarette (N,%)		34 (38.6)	16 (72.7)	16 (72.7)	2 (9.1)	0 (0)
< 1 pack	-	45 (51.1)	6 (27.3)	6 (27.3)	16 (72.7)	17 (77.3)
1 -2 pack		9 (10.2)	0 (0)	0 (0)	4 (18.2)	5 (22.7)
> 2 pack						

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

VARIABLE	NORMAL VALUE	TOTAL N = 88	GOLD 1 N = 22	GOLD 2 N = 22	GOLD 3 N = 22	GOLD 4 N = 22
Right atrial dilatation (N,%)	-	25 (28.4)	0 (0)	1 (4.5)	10 (45.5)	14 (63.6)
Right atrial major axis (mm)	34-52	40 ± 7	34 ± 2	37 ± 4	45 ± 6	47 ± 7
Right atrial minor axis (mm)	26-44	35 ± 8	29 ± 3	30 ± 4	41 ± 6	43 ± 6
Right atrial dilatation (N,%)	-	22 (25)	0 (0)	0 (0)	8 (36.4)	14 (63.6)
Linear dimension of right ventricle (mm)	24-41	37 ± 6	35 ± 4	33 ± 4	40 ± 4	42 ± 5
Right ventricle dysfunction (N,%)	-	13 (14.8)	0 (0)	0 (0)	3 (13.6)	10 (45.5)
TAPSE (mm)	16-30	20 ± 3	22 ± 1	22 ± 2	19 ± 3	18 ± 4
Tricuspid regurgitation (N,%)	-	31 (35.2)	2 (9.1)	3 (13.6)	12 (54.6)	14 (63.6)
mild		21 (23.8)	2 (9.1)	3 (13.6)	10 (45.5)	6 (27.3)
moderate		7 (8)	0 (0)	0 (0)	2 (9.1)	5 (22.7)
severe		3 (3.4)	0 (0)	0 (0)	0 (0)	3 (13.6)
Tricuspid regurgitation velocity (m/s)	1.9-2.5	2.5 ± 0. 6	2.0 ± 0.2	2.03 ± 0.3	2.4 ± 0.6	2.7 ± 0.8
Tricuspid regurgitation gradient (mmHg)	< 30	25 ± 3	16 ± 1	16.5 ± 2	23 ± 3	29 ± 3
Right ventricle hypertrophy (N,%)	-	57 (64.8)	9 (40.9)	10 (45.5)	18 (81.8)	20 (90.9)
Right ventricular thickness (mm)	2-5	6 ± 1	5.1 ± 1	5.4 ± 1	6 ± 1	6 ± 1
Inter-ventricular septal wall motion abnormality (N,%)	-	17 (19.3)	0 (0)	0 (0)	6 (27.3)	11 (50)
Pulmonary regurgitation (N,%)	-	27 (30.7)	1 (4.5)	1 (4.5)	11 (50)	14 (63.6)
Pulmonary Pressure half time (msec)	-	432 ± 7	525 ± 0.9	487 ± 0.9	431 ± 6	422 ± 8
RAP (mmHg)	3-15	5 ± 3	3 ± 1	4 ± 2	6 ± 3	8 ± 3
PASP (mmHg)	18-25	30 ± 7	19± 0.8	21 ± 1	30 ± 7	37 ± 10
MPAP (mmHg)	12-16	25 ± 6	20 ± 3	24 ± 2	26 ± 5	31 ± 4
Pulmonary hypertension (N,%)	-	15 (17)	0 (0)	0 (0)	3 (13.6)	12 (54.5)

Table 3
Basic Demographic Data of]Subjects Based on Left Heart Echocardiography

VARIABLE	NORMAL VALUE	TOTAL N = 88	GOLD 1 N = 22	GOLD 2 N = 22	GOLD 3 N = 22	GOLD 4 N = 22
Left ventricular diastolic dysfunction (N,%)	-	46 (52.3)	2 (9.1)	4 (18.2)	20 (90.9)	20 (90.9)
E/A	0.9-2.1	0.9 ± 0.2	1.08 ± 0.1	1.06 ± 0.2	0.80 ± 0.3	0.79 ± 0.3
Left ventricle hypertrophy (N,%)	-	15 (17)	1 (4.5)	3 (13.6)	5 (22.7)	6 (27.3)
Left ventricle mass index (gr/m^2)	49-115 (male) 43-95 (female)	92 ± 26	84 ± 18	90 ± 26	99 ± 30	97 ± 29
Left ventricle systolic dysfunction (N,%)	-	3 (3.4)	0 (0)	0 (0)	2 (9.1)	1 (4.5)
Left ventricle ejection fraction (%)	55-72	63 ± 7	66 ± 5	65 ± 6	63 ± 7	61 ± 6

Overall, 17% (15 people) of the study subjects have pulmonary hypertension. In line with the pathological results and anatomical changes of echocardiography that were found in many groups of subjects with GOLD III and IV, pulmonary hypertension was only found in that respective group.

According to the left heart echocardiographic examination (Table 3) 52.3% of COPD patients have left ventricular diastolic dysfunction and the proportions were most common in the GOLD III and IV groups. From this table, it can also be observed that the more severe the degree of COPD, the E/A value decreases. However, the left ventricular mass index value increases with the severity of the disease.

Table 4 presented the results of the bivariate analysis of the relationship between the severity of COPD and the categorical variables of echocardiography. It can be seen that all variables have a relationship that was statistically significant (p <0.001), except for left ventricular systolic dysfunction (p 0.241).

This study also searched for a new cut off points (Table 5) for each anatomical and right heart pressure value which was expected to be used as a reference, so we could ensure that the right heart changes was due to increasing severity of COPD. The new cut off points was obtained using the ROC curve.

Numerical variables analysis was performed to obtain changes in the anatomical and physiological functions measurement of the heart through echocardiography. In Table 6, it can be seen that the major axis, minor axis and right ventricular linear dimension in the severe degree group of COPD, as well as the thickness of the right ventricle, RAP, PASP, and MPAP were above the cut off value,

Table 4.
Bivariate Analysis Between the Degree of COPD Severity an Pathological Changes in Echocardiography

Pathological echocardiographic findings (N, %)	Severity of COPD		P VALUE
	Mild-moderate N = 44	Severe N = 44	
Right atrial dilatation	1 (2.3)	24 (54.5)	< 0.001
Right ventricle dilatation	0 (0)	22 (50)	< 0.001
Right ventricular dysfunction	0 (0)	13 (29.5)	< 0.001
Tricuspid regurgitation	5 (11.4)	26 (59.1)	< 0.001
Inter-ventricular wall motion abnormality	0 (0)	17 (38.6)	< 0.001
Pulmonary regurgitation	2 (4.5)	25 (56.8)	< 0.001
Right ventricle hypertrophy	19 (43.2)	38 (86.4)	< 0.001
Left ventricular diastolic dysfunction	6 (13.6)	40 (90.9)	< 0.001
Left ventricle hypertrophy	4 (9.1)	11 (25)	0.047
Left ventricle systolic dysfunction	0 (0)	3 (6.8)	0.241
Pulmonary hypertension	0 (0)	15 (34.1)	< 0.001

Table 5.
Cut off Points for Anatomical measurement and Right Heart Pressure in Severe COPD

Variable	Cut off point	Sensitivity	Specificity	AUC	P value
Major axis of right ventricle (mm)	38.5	84.1	86.4	93.7%	<0.001
Minor axis of right ventricle (mm)	34.5	86.4	97.7	96.7%	<0.001
Right ventricle linear dimension (mm)	36.5	79.5%	79.5%	89.3%	<0.001
TAPSE (mm)	16.5	70.5%	99%	80%	<0.001
Right ventricular thickness (mm)	5.5	84.1%	56.8%	73.2%	<0.001
RAP (mmHg)	6.5	68.2%	86.4%	77%	<0.001
PASP (mmHg)	28.5	50%	97.7%	74.8%	<0.001
MPAP (mmHg)	25.5	93.2%	93%	96.5%	<0.001
Tricuspid regurgitation velocity (m/s)	1.96	56.8%	95.5%	76.8%	<0.001
Tricuspid regurgitation gradient (mmHg)	25	47.7%	97.7%	76.2%	<0.001

Table 6.
Bivariate Analysis of COPD Severity with Measurement Values of Anatomic and Physiological Functions of the Hear Through Echocardiography

Numerical Variable	NORMAL VALUE	CUT OFF	Severity of COPD		P VALUE
			Mild-moderat	severe	
Major axis of right ventricle (mm)	34-52	38.5	35 ± 4	46 ± 6	< 0.001
Minor axis of right ventricle (mm)	26-44	34.5	30 ± 4	42 ± 6	< 0.001
Right ventricular linear dimension (mm)	24-41	36.5	33 ± 4	41 ± 5	< 0.001
TAPSE (mm)	17-30	16.5	22 ± 2	19 ± 3	< 0.001
Right ventricular thickness (mm)	2-5	5.5	5 ± 1	6 ± 1	< 0.001
Tricuspid regurgitation velocity (m/s)	1.9-2.5	1.96	2.3 ± 0.3	2.9 ± 0.6	< 0.001
Tricuspid regurgitation gradient (mmHg)	< 30	25	21 ± 4	34 ± 9	< 0.001
Pulmonary Pressure half time (msec)	<100 (severe)	-	573 ± 23	436 ± 89	< 0.001
PASP (mmHg)	18-25	28.5	25 ± 1	41 ± 9	< 0.001
MPAP (mmHg)	12-16	25.5	22 ± 3	31 ± 5	< 0.001
E/A	0.9-2.1	-	1.05 ± 0.2	0.8 ± 0.3	< 0.001
Left ventricular mass index (gr/m^2)	49-115 (male) 43-95 (female)	-	87 ± 22	98 ± 29	0.058
Left ventricle ejection fraction (%)	55-72	-	66 ± 6	60 ± 7	<0.001

Discussion

It was found that male and older age were only a small portion of several risk factors for COPD. Both of these are also risk factors for cardiovascular disease. The proportion of male COPD patients was 61.5% and women only 38.5% with an average age of 60 + 11 years were obtained in this study. It was in accordance with the results of the study performed by Maula et al (2015) in Pakistan which most of the research subjects were male (86.4%) and only 13.6% were women with an average age of 56 + 14 years. The average age was not much different from the present study and also Rawy (2015) and Agrawal (2017) which reported an average age of 53 + 9 years and 58 + 10 years, respectively. Moreover, severe COPD (GOLD III and IV) was found more often in subjects within the 6th decade of life.

Table 7.
Comparison of Echocardiographic Findings with Previous Studies

Echocardiographic findings	Present study	Venkateswara (2016)	Jatav (2017)
Right atrial dilatation	28.4 %	48.38 %	43 %
Right ventricular dilatation	25 %	46.77 %	
Right ventricular dysfunction	14.8 %	-	14 %
Tricuspid regurgitation	35.2 %	45.16 %	-
Inter-ventricular septal wall motion abnormality	19.3 %	17.74 %	-
Left ventricular diastolic dysfunction	52.3 %	6.45 %	46 %
Right ventricular hypertrophy	64.8 %	11.29 %	42 %
Pulmonary regurgitation	30.7 %	-	-
Left ventricular hypertrophy	17 %	-	11 %
Left ventricular systolic dysfunction	3.4 %	-	-
Pulmonary hypertension	17 %	56.45 %	44 %

The results of this study are not much different from the previous study conducted by Jatav et al which performed on 100 COPD patients consisting of 28 subjects with GOLD I/II and 73 subjects with GOLD III/IV. They obtained right atrial and ventricular enlargement 43%, right ventricular dysfunction 14%, hypertrophy right ventricle 42%, left ventricular diastolic dysfunction 46%, 11% left ventricular hypertrophy and 44% pulmonary hypertension.[15] Meanwhile, a study conducted by Venkateswara Rao et al. on 62 COPD patients consisting of 23 subjects GOLD II and 39 subjects GOLD III/IV had found that the pathological outcome of echocardiography was 48.38% right atrial enlargement, 46.77% ventricular enlargement, 45.16% tricuspid regurgitation, 35.48% ventricular hypertrophy, 17.74% abnormal motion of inter-ventricular septum, 6.45% ventricle systolic dysfunction, 11.29% left ventricular hypertrophy and 56.45% pulmonary hypertension.[16] The greater number difference in the studies conducted by Jatav and Venkateswara is due to the greater number of subjects with GOLD III / IV compared with the present study.

Although the incidence of pulmonary hypertension was only 17% (15 people), many signs of the excess volume have been found in the right ventricle. This can be seen from the average measurement value of anatomical and physiological functions through echocardiography. In this study, we found that the major axis and the minor axis of right ventricle were still in the normal range, but as the increasing severity of COPD, the value of these measurements was increased too. The right ventricular linear dimensions are also still in the normal range, except in the GOLD IV group of subjects who have discharged of the normal range. Falk et al. stated that this phenomenon occurs as a result of cardiac compensation for pulmonary vascular pressure which increases due to vascular remodeling in COPD, thus the right ventricle must increase its contractility to drain the volume of blood inside it.[17]

Right ventricular thickness had increased from the group of COPD subjects with GOLD I and increasingly increases according to the ascending severity of the disease. This finding was in accordance with Vork-Noordegraaf et al. finding that the initial sign of increased pressure in the right ventricle from echocardiography was right ventricular hypertrophy without accompanying right or left ventricular dysfunction.[18] The mean left ventricular mass index was in the normal range for each GOLD group.

In the assessment of the physiological function of the heart such as right ventricular contractility, the average measurement value is still in the normal range, but the higher the severity of COPD, the lower the value. This was in line with the decrease in cardiac compensation ability against the increase of right ventricular pressure due to the worsening of COPD.[17] The mean left ventricular systolic function was in the normal range for all GOLD groups, but it was different for the mean of left ventricular diastolic function in the GOLD III and IV groups which experienced interference. This was not different from the results of a study performed by Gupta of 40 COPD patients which obtained 47.5% of patients experiencing left ventricular diastolic dysfunction. In measuring the pressure of both RAP, PASP and MPAP, it appeared that the heavier the severity of COPD, the higher the pressure, where the highest mean pressure value is in the group of GOLD IV subjects. This was in line with the increased velocity of tricuspid regurgitation which is increasingly aggravated according to the increase in disease severity.[11]

Bivariate analysis was conducted to find the relationship between the severity of COPD and pathological echocardiographic findings. When analyzing the data, the four GOLD groups were simplified into 2 large groups, namely subjects with the GOLD I and II groups were included in the mild to moderate COPD and subjects with the GOLD III and IV groups were included in the severe COPD. From the results of the analysis (Table 4), it was concluded that the degree of severe COPD was related to all the pathological findings of the echocardiography, except for left ventricular dysfunction (p 0.241). The studies conducted by Venkateswara and Jatav also mostly showed similar results, where they stated that right atrial dilation, right ventricular dilation, right ventricular hypertrophy, tricuspid regurgitation and inter-ventricular septal movement abnormality were pathological findings of echocardiography that correlated with severe COPD (p <0.05) except for left ventricular hypertrophy (p 0.133 and

p 0.09) and left ventricular diastolic disorders (p 0.135 and p 0.06).[15,16] This may be due to the greater proportion of COPD III and IV subjects in the two previous studies. However, the incidence of left ventricular hypertrophy and impaired left ventricular diastolic function remained higher in the severe COPD group (GOLD III and IV) in both studies.

In contrast to the results of studies conducted by Venkateswara and Jatav which were in line with the results of this study, Rawy et al. in their study of 49 COPD patients managed to draw the conclusion that the prevalence of left ventricular diastolic disorder was very high (73.3%) in COPD patients and was associated with increased disease severity (p 0.0001).[19] Similarly, Kubota et al. Studied 688 COPD patients, of which 11.3% of COPD patients have left ventricular diastolic dysfunction (p 0.009) and were associated with degrees of COPD (OR 5.81, 95% CI 2.13-15.89, p 0.001).[20]

There are several mechanisms that might cause disruption of left ventricular diastolic function in COPD patients. First, the presence of chronic hypoxemia causes intracellular calcium transport disorders which eventually result in abnormalities in myocardial relaxation.[21] Second, the presence of pulmonary hypertension with chronic right ventricular hypertrophy that occurs in COPD is followed by dilatation of the right ventricle. As a result, during the early diastolic period, the inter-ventricular septum shifted to the left ventricular cavity so that the left ventricle loses its circular configuration.[22] This also depends on differences in the transeptal pressure gradient. Third, the presence of emphysema and pulmonary hyperinflation in COPD is associated with failure of the left ventricular filling phase. The increase in intra-thoracic pressure will reduce both ventricular preload and increase left ventricular afterload.[23] Furthermore, Huang et al. explain the presence of atherosclerotic plaques which are more burdensome due to smoking and the aging process in COPD patients will lead to myocardial ischemia and ultimately cause left ventricular diastolic disorders in COPD.[24]

Conclusion

Echocardiographic examination in COPD patients can identify cardiovascular complications in severe COPD patients (GOLD III and IV).

Acknowledgments

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