Original Article

Associations Between Measurement RV, RV/TLC, and FRC/TLC with Clinical Symptoms in COPD Patients in Persahabatan Hospital

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Abstract

Background: This preliminary study to measure lung volume in patients with stable COPD in Persahabatan Central General Hospital Jakarta to determine the prevalence of the increasing value of lung volume in patients with stable COPD.

Methods: This study used a cross-sectional study design of outpatients with stable COPD who visited the asthma-COPD clinic at Persahabatan Central General Hospital Jakarta. The Lung volume test using a gas dilution Multiple Breath Nitrogen Washout (MBNW) was taken consecutively from February to March 2016.

Results: Tests of spirometry and Lung volumes were performed on 35 subjects. There were 3 subjects (8.6%) in COPD Group A, 9 subjects (25.7%) in COPD Group B, 9 subjects (25.7%) in COPD Group C, and 14 subjects (40%) in COPD Group D. At the age of 60 years, there were subjects (25.7%) and 60 years, 26 subjects (74.6%). Value Residual Volume/Total Lung Capacity (RV/TLC) has a significant relationship with the symptoms and a 6-minute walking test; however, Functional Residual Capacity/Total Lung Capacity (FRC/TLC) is significantly associated with the symptoms, a 6-minute walking test, and exacerbations within one year.

Conclusion: Value RV/TLC has a significant relationship with the symptoms and a 6-minute walking test; however, FRC/TLC is significantly associated with the symptoms, a 6-minute walking test, and exacerbations within one year.

Keywords: COPD, FRC/TLC, residual volume (RV), RV/TLC

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Submitted: May 30th, 2023
Accepted: July 20th, 2023
Published: October 31st, 2023

J Respirol Indones. 2023
Vol. 43 No. 4: 239–46
https://doi.org/10.36497/jri.v43i4.571

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as a chronic, progressive disease characterized by airflow obstruction that has no real change in its course. According to the 2014 Global Chronic Obstructive Lung Disease (GOLD) Report, COPD is a preventable and treatable lung disease characterized by persistent airflow barriers that are usually progressive and are associated with chronic inflammatory and respiratory tract responses to toxic or dangerous particles or gases. Exacerbations and comorbidities contribute to the disease severity.[1,2]

Changes in COPD pathology are complex and are associated with worsening respiratory physiology. Distal airways experience inflammation, airway wall fibrosis, smooth muscle hypertrophy, goblet cell hyperinflation, mucus hypersecretion, and pulmonary parenchymal destruction. The volume and number of submucosal glands and goblet cells increase, which results in chronic mucus hypersecretion in chronic bronchitis. In emphysema, the widening of the airways persists distally to the terminal bronchioles due to damage to the airway wall without fibrosis.[3,4]

Pulmonary function measurement has an important role in helping with the diagnosis and management of patients with respiratory disease. Pulmonary function tests that are often used are spirometry, Diffuse Lung Capacity (DLCO), lung volume, respiratory muscle strength, and the bronchial provocation test. Lung volume testing is mandatory to diagnose, manage, and prognosticate COPD. The importance of this test was shown by one of the studies by Talag et al, that for COPD patients who experience hyperinflation, it is necessary to have investigations such as spirometry or other static volume tests.[5]

However, it is different from the results of a study by Dykstra et al, who performed lung volume

examinations in 4,774 patients with obstructive pulmonary disease and found that there was little correlation between static volume and clinical symptoms.[6] But in Indonesia, there is no research data on the static volume test in clinical COPD patients. This study measures the relationship between RV, RV/TLC ratio, and the ratio of FRC/TLC to clinical symptoms in patients with stable COPD with influencing factors.

METHODS

This is a cross-sectional study of COPD-asthma outpatients in Persahabatan National Respiratory Referral Hospital using consecutive sampling. Inclusion criteria are all stable COPD outpatients in Asthma-COPD clinic willingly signed the informed consent form after a full explanation of the research procedure. Exclusion criteria are COPD patients suspected of having an acute pulmonary infectious disease characterized by the addition of symptoms of shortness of breath, sputum, and sputum discoloration; patients suffering from life-threatening infections; fatal terminal diseases; severe underlying diseases, including immunocompromise; COPD patients who are unable to complete a spirometry examination and measurement of lung volume; and former TB patients.

The latest chest X-ray was not performed; After anamnesis and physical examination, eligible subjects will be tested for spirometry and RV tests. FRC and TLC are calculated as tight scores based on mMRC and filled-out research worksheets. Recording of required data: general records, which include gender, age, smoking history, and the Brinkman Index. Record of measurements of the Body Mass Index, tightness score based on the criteria of the mMRC, 6-minute walking test, and exacerbation in the previous year.

RESULTS

The objectives of this study is to find the relationship between RV, RV/TTLC ratio, and the ratio of FRC/TTLC in asthma-COPD policlinic outpatient with clinical symptoms. The results of this study are based on primary data obtained from interviews, physical examinations, spirometry examinations, and lung volume tests. A total of 36 consecutive subjects were collected and interviewed, followed by a spirometry examination and lung volume test.

Table 1. Characteristics Of Research Subjects

Subject characteristics	N	%
Gender		
Man	35	100.0
Women	0	0.0
Age		
<60 years	9	25.7
≥60 years	26	74.3
History of COPD		
<5 years	28	80.0
≥5 years	7	20.0
COPD group		
Group A	3	8.6
Group B	9	25.7
Group C	9	25.7
Group D	14	40.0
Body Mass Index (BMI)		
Malnutrition	4	11.4
Normal	15	42.9
More nutrition	8	22.9
Obese	8	22.9
mMRC		
<2	10	28.6
≥2	25	71.4
Six-minute walking test		
>350	9	25.7
250-350	19	54.3
150-250	7	20.0
<150	0	0.0
Exacerbation		
<2	13	37.1
≥2	22	62.9
Smoking history		
Non-smoker	0	0.0
Former smoker	35	100
Brinkman Index		
Non-smoker	0	0.0
Mild	1	2.9
Moderate	20	57.1
Heavy	14	40.0
Symptoms		
Dyspnea	26	74.3
Chronic cough	9	25.7
Comorbid		
Without comorbid	16	45.7
With comorbid	19	54.4

A total of 35 study subjects consisted of 100% men. Subjects aged more than or equal to 60 years (74.3%) are the most common. Subjects who were diagnosed with COPD less than 5 years were 80.0% of subjects. COPD was divided into groups according the the latest GOLD criteria, Group A-B COPD was 34.3% and Group C-D COPD was 65.7%. As many as 42.9% of subjects with a normal BMI have the highest BMI.

The highest Modified Medical Research Council (MmRC) value is more or less equal to 2 or as much as 71.4%. The most successful six-minute walking test was at a distance of 250–350 meters by 54.3%. The history of exacerbations is more than or equal to 2 as many as 62.9% of subjects and exacerbations of less than 2 as many as 37.1%. The smoking history of the former smoker subject was 100.0%. Most subjects were moderate smokers about 57.1%, and 40% were heavy smokers. The most common symptoms are shortness of breath (74.3%) and chronic cough (25.7%). Most subjects in this studies have comorbidities (54.4%).

Table 2 shows the relationship between lung functions. There is no significant correlations between FEV_1 with RV, RV/TLC and FRC/TLC. The RV values that are smaller, RV/TLC and FRC/TLC are found in degrees III–IV compared to degrees I–II.

Table 2. The Relationship Between RV, RV/TLC and FRC/TLC Values with FEV_1 Values In Stable COPD Patients.

Category	FEV_1		Total (%)	*P*
	I-II (%)	III-IV (%)		
RV				
Normal	17 (51.5%)	16 (48.5%)	33 (100.0%)	0.227
Increase	2 (100.0%)	0 (0.0%)	2 (100.0%)	
RV/TLC				
Normal	1 (100.0%)	0 (0.0%)	1 (100.0%)	0.549
Increase	18 (52.9%)	16 (47.1%)	34 (100.0%)	
FRC/TLC				
Normal	9 (60.0%)	6 (40.0%)	15 (100.0%)	0.193
Increase	10 (50.0%)	10 (50.0%)	20 (100.0%)	

Table 3 shows the relationship between RV values, RV/TLC and FRC/TLC with clinical symptoms. There is no significant correlations between clinical symptoms and RV values. Increased RV values are found in symptoms of tightness. The value of RV/TLC when compared to clinical symptoms shows a significant relationship. The value of RV/TLC increased more in the symptoms of shortness of breath compared to symptoms of cough by 73.5%. There is a significant correlation between FRC/TLC with clinical symptoms. In shortness of breath, 85.0% increased FRC/TLC.

Table 3. The Relationship Between RV Values, RV/TLC and FRC/TLC With Clinical Symptoms in Stable COPD Patients.

Category	Symptoms		Total	*P*
	Cough	Dyspnoea		
RV				
Normal	9 (27.3%)	24 (72.7%)	33 (100.0%)	0.073
Increase	0 (0.0%)	2 (100.0%)	2 (100.0%)	
RV/TLC				
Normal	0 (0.0%)	1 (100.0%)	1 (100.0%)	0.030
Increase	9 (26.5%)	25 (73.5%)	34 (100.0%)	
FRC/TLC				
Normal	6 (40.0%)	9 (60.0%)	15 (100.0%)	0.001
Increase	3 (15.0%)	17 (85.0%)	20 (100.0%)	

Table 4 shows the relationship between RV, RV/TLC and FRC/TLC values with the mMRC scale. There is no significant correlations between mMRC scale and RV, RV/TLC and FRC/TLC values. RV/TLC values increased more on the mMRC scale ≥2 compared to the mMRC <2 scale of 70.6% or as many as 24 subjects. The value of FRC/TLC increased more on the mMRC scale ≥2 compared to the MmRC <2 scale of 85.0% or as many as 17 subjects.

Table 4. The Relationship Between RV, RV/TLC Values and FRC/TLC On The mMRC Scale In Stable COPD Patients

Category	MmRC		Total	*P*
	<2	≥2		
RV				
Normal	9 (27.3%)	24 (72.7%)	33 (100.0%)	0.351
Increase	1 (50.0%)	1 (50.0%)	2 (100.0%)	
RV/TLC				
Normal	0 (0.0%)	1 (100)	1 (100.0%)	0.385
Increase	10 (29.4%)	24 (70.6%)	34 (100.0%)	
FRC/TLC				
Normal	7 (46.7%)	8 (53.3%)	15 (100.0%)	0.085
Increase	3 (15.0%)	17 (85.0%)	20 (100.0%)	

Table 5 shows the relationship between RV, RV/TLC and FRC/TLC with a 6-minute walking test. There was no significant relationship between the 6-minute walking test scale and RV value. The value of RV/TLC when compared with the 6-minute walking test shows a significant correlation. The value of RV/TLC increased more in the 6-minute walking test

less than 350 meters. The relationship between the value of FRC/TLC with the 6-minute walking test showed a significant relationship but the FRC/TLC value increased more in the 6-minute <350 meters.

Table 5. The Relationship Between RV, RV/TLC and FRC/TLC Values on The 6-Minute Walking Test In Stable COPD Patients.?"

Category	6-minute walking test		Total	*P*
	<350	≥350		
RV				
Normal	24 (72.7%)	9 (27.3%)	33 (100.0%)	0.137
Increase	2 (100.0%)	0 (0.0%)	2 (100.0%)	
RV/TLC				
Normal	1 (100.0%)	0 (0.0%)	1 (100.0%)	0.004
Increase	25 (73.5%)	9 (26.5%)	34 (100.0%)	
FRC/TLC				
Normal	9 (60.0%)	6 (40.0%)	15 (100.0%)	0.003
Increase	17 (85.0%)	3 (15.0%)	20 (100.0%)	

Table 6 shows the relationship between RV, RV/TLC and FRC/TLC with exacerbations in 1 year. There was no significant relationship between exacerbations in 1 year and RV values. RV values that increased significantly were found in exacerbations in 1 year ≥2 compared to exacerbations in 1 year <2. The value of RV/TLC when compared to exacerbations in 1 year shows no significant relationship. The value of RV/TLC increased more in exacerbations in 1 year ≥2 compared to exacerbations in 1 year <2 by 64.7% or as many as 22 subjects. The relationship between the value of FRC/TLC and exacerbations in 1 year showed a significant relationship but the value of FRC/TLC increased more in exacerbations in 1 year ≥2 compared to exacerbations in 1 year <2 by 75.0% or as many as 15 subjects.

Table 6. Relationship Between RV, RV/TLC Values and FRC/TLC Against Exacerbations In 1 Year in Stable COPD Patients

Category	Exacerbation 1 years		Total	*P*
	<2	≥2		
RV				
Normal	13 (39.4%)	20 (60.6%)	33 (100.0%)	0.364
Increase	0 (0.0%)	2 (100.0%)	2 (100.0%)	
RV/TLC				
Normal	1 (100.0%)	0 (0.0%)	1 (100.0%)	0.404
Increase	12 (35.3%)	22 (64.7%)	34 (100.0%)	
FRC/TLC				
Normal	8 (53.3%)	7 (46.7%)	15 (100.0%)	0.009
Increase	5 (25.0%)	15 (75.0%)	20 (100.0%)	

DISCUSSION

A total of 35 study subjects (100.0%) were men. This is similar to the research from Ismail in the Persahabatan Hospital showing that most subjects are male (92.3%). Other studies from Travers et al and O'Donnell et al showed that most subjects are male (72.0% and 64.0% respectively).[7–9] In contrast to the study by Stroband et al in Leiden, there were fewer male gender categories (28.0%).[10]

Most of the study subjects' ages are over 60 years old (74.3%). The study from Ismail shows similar results, with 64,6% of subjects age 60-90 years old. Similar results were also reported by Travers et al mean age of the study subjects was 60 years, and in the study of O'Donnell et al, the mean age of the study subjects was 66 years.[8,9]

Subject nutritional status based on BMI in this study showed 42.9% of subjects with normal BMI, 22.9% with overnutrition, and 22.9% with obesity. Similar to Ismail's research, in the normal BMI category 61.5%. Results differ from Travers' study getting a BMI average of 26.8, which is also similar to O'Donnell et al's study getting an average BMI of 25.8, and research from Stroband et al.[8–10] with an average BMI of 26.2. The three studies that obtained obesity nutritional status had the highest average BMI.

In this case, the scale of tightness is the mMRC scale; in this study, the highest mMRC score is mMRC more than or equal to 2, as much as 71.4%, while the mMRC scale of less than 2 was 28.6%. This result is similar to Stroband et al's study in Leiden, which got the highest MmRC scale of more than 3.[10]

The value of the most 6-minute walking test in this study is a distance of 250–350 meters, as much as 54.3%, followed by a distance of more than 350 meters, as much as 25.7%, and a distance of 150–250 meters, as much as 20%. Similar to the study by Hartman et al getting a mean 6-minute road test in 91 COPD subjects of 319.2±97.5 meters, but different from the study of Balcells et al in Spain who received a midpoint test of the 6-minute road test on COPD subjects in the study, this is 440 meters.[11,12] This is also similar to the research by Nizet et al in the

Netherlands, who also got a mean test score of 6 minutes of 410 meters.[13]

The smoking history of the former smoker subject was 100.0%. Similar to the study of Balcells et al, the subjects who had and were smoking were 94.0% but different studies from Nizet et al, in their study of smoking with the subject smokers were 29.8%.[12,13] In this study, the severity of smoking is measured with the Brinkman Index. Most subjects were moderate smokers (57.0%), in contrast to Travers et al study and Stroband et al study which most subjects were heavy smokers.[8,10]

Symptoms in COPD subjects in this study were dominated by symptoms of 74.3% shortness of breath, while symptoms of chronic cough affected 25.7% of subjects. Slightly different from the study conducted by Kitaguchi et al, the most common clinical symptoms in subjects with COPD were symptoms of shortness of breath, which was 36.5%, while chronic cough was 28.2%.[14]

COPD patients in this study were mostly accompanied by 54.4% of comorbidities. In contrast to the research conducted by Nizet et al in the Netherlands, which obtained COPD subjects with comorbidities only 38.3% of whom had cardiovascular comorbidities 17%, diabetes mellitus 14.9%, hypertension 8.5%.[13]

There is no significant correlations between FEV_1 and RV, RV/TLC and FRC/TLC values. The residual volume is ≥120%, RV/TLC >30.0% and FRC/TLC >55.0% is smaller in degrees III-IV compared to degrees I-II. This is possible because the predicted RV values used are taken from European subjects. In contrast to the study of Dykstra et al in Rochester in 4774 subjects using a body plethysmograph and also predictive values used using predictions with the same race. There was a negative relationship between RV, RV/TLC and FRC/TLC with FEV_1 which means that the higher RV, RV/TLC and FRC/TLC in COPD patients the lower the FEV_1 value obtained. Weaknesses in the Dykstra et al study was that some patients did not remember the diagnosis of previous pulmonary disease that was told by their doctor.[6] In line with the study of Papaioannou et al in Greece 49 male subjects had a significant relationship (P<0.003) between an increase in the value of FRC/TLC with a decrease in FEV_1 value, the percentage of the relationship was 64%.[15]

The RV values increased more with symptoms of tightness, but there was no significant relationship with clinical symptoms. Similarly, the value of RV/TLC when compared with clinical symptoms showed a significant relationship, but the value of RV/TLC that increased in this study was more on the symptoms of shortness of breath compared to the symptoms of cough, (73.5%). In contrast to the study by Stroband et al, which examined 114 COPD patients who were divided into two groups, with and without chronic bronchitis, comparing the RV/TLC values showed that there were no significant differences (P=0.61) between events with chronic bronchitis and without chronic bronchitis, with 46.6% and 47.8%, respectively.[10]

The correlations between the value of FRC/TLC and clinical symptoms also showed a statistically significant relationship, but the value of FRC/TLC increased more in the symptoms of shortness of breath compared to the symptoms of chronic cough, which was 85.0%. In line with Parker et al's study in 20 patients with a prospective cohort method of five times observation, it was found that there was an increase in symptoms of shortness of breath compared to chronic cough associated with an increase in lung volume values in both RV, RV/TLC and FRC/TLC values. In the Parker et al study, there was an increase in trapped air and pulmonary hyperinflation, so symptoms of breathlessness were more dominant than chronic cough.[16]

This study obtained the result that there was no significant relationship between the mMRC scale and the RV value. This study found RV values increased in mMRC 2 by 50.0% (P=0.351). The higher the RV value, the higher the value of the mMRC obtained; this is because the RV prediction that is used to produce RV-predicted values does not use the value of Indonesian fiction. In contrast to the research from Gompertz et al in Germany conducted with a prospective cohort, they obtained a positive

relationship between the value of mMRC and the volume of residue, so that the higher the residual volume value, the higher the value of mMRC, with the relationship obtained at *P*=0.02.[17]

RV and TLC values increased more on the mMRC scale 2 compared to the mMRC <2 scale (70.6%). However, there is no significant correlation between RV/TLC and mmRC scale (*P*=0.385). In contrast to the study by Shin et al that divides the two groups, namely RV/TLC group ≥ 40.0% and RV/TLC value group <40.0% when linked to the mMRC scale, it is statistically significant so that the higher the RV/TLC value of a person, the more likely there will be pulmonary hyperinflation, and the higher the value of mMRC obtained.[18]

This study also tried to connect the value of FRC/TLC to the mMRC scale. This study found no significant relationship between FRC/TLC values that increased more on the mMRC scale 2 than the mMRC <2 scale of 17 subjects (85.0%). In contrast to the research by Parker et al showing a tendency to increase the mMRC scale with an increase in the value of FRC/TLC, with the increasing value of FRC/TLC in COPD patients, the mMRC scale also increased.[16] The tendency for an increase was also shown in the results of the study by Papaioannou et al, who obtained an increase in the value of FRC/TLC in the emphysema group, followed by an increase in the value of mMRC in the emphysema patient.[15]

This study found no significant relationship between the 6-minute walking test and RV value because of the limited subjects and the prediction used by Europeans. In addition, this study between FRC/TLC with a 6-minute walking test also showed a significant relationship, but FRC/TLC increased more in the 6-minute <350-meter walking test compared to the 6-minute >350-meter road test by 85.7%. In line with the Wijkstra et al study in 40 subjects, this study did not connect directly but obtained an increase in RV, FRC/TLC with a decrease of 6 minutes of walking test so that the RV value increased and FRC/TLC on COPD subjects decreased test values. Six-minute walking is obtained in COPD patients. This is explained by the occurrence of dynamic hyperinflation during activities.[19]

The value of RV/TLC when compared with the 6-minute walking test shows a significant correlation. The value of RV/TLC increased more in the 6-minute walking test less than 350 meters compared to the road test 6 minutes >350 meters at 74.3%. In line with research by Shin et al, which showed the difference between the value of RV/TLC more or less equal to 40% and less than 40% with a 6-minute walking test, this study found that there was a significant difference with decreased of 6MWT while hyperinflation occurred (*P*=0.045).[18]

There was no significant relationship between exacerbations in 1 year and RV values, but RV values did increase in subjects with lesser exacerbations. The relationship between the value of FRC and TLC and exacerbations in 1 year was also significant, but the value of FRC and TLC increased more in exacerbations by 75.0%. The study from Kim et al divided the COPD subjects with and without chronic bronchitis with 290 and 771 Subjects, respectively.[20] In this study, there is no significant relationship between lung volume and the number of exacerbations a year. The patient also underwent a thoracic CT examination to confirm existing abnormalities in the lungs. The results showed a significant relationship between RV values and FRC/TLC in the group without chronic bronchitis, and exacerbations were also statistically significant can see the tendency to increase lung volume with a 1-year exacerbation in the group without chronic bronchitis.

The value of RV and TLC when compared to exacerbations in a year shows a significant correlation. Subjects with exacerbations more than twice a year show an increase in RV and TLC by 64.7%. In line with the research of Shin et al which also looked at the relationship between RV and TLC values and the occurrence of exacerbations. Study by Shin et al also found a significant relationship between the value of RV and TLC and the occurrence of exacerbations. The more frequent exacerbations in COPD patients, the higher the RV/TLC value in those patients, with *P*=0.012.[18]

In contrast to research from Birmingham by Gompertz et al, conducted on 70 subjects with a retrospective cohort method, Gompertz et al looked at the relationship between exacerbations the prior year, three times or less with lung volumes such as RV and TLC.[17] There were no significant differences between exacerbations in the previous year (118.8% and 124.8%, respectively), but there was an increase in lung volume values in this case if the exacerbation was ≥3.

LIMITATION

This study has limitations in several ways, namely that it did not carry out an FRC examination using a body plethysmograph as a gold standard check and was most accurate in determining functional residual capacity. There was outnumbered female subjects in this study. This study also did not perform chest X-ray examinations, so it could not confirm spirometry results. Predictive values used for residual volume still use European predictions because Indonesia does not yet have a standard predicted residual volume value.

CONCLUSION

The mean value of RV in milliliters is 1490.61 (150-3470). The mean RV% prediction value is 64.11% (6-141). The mean RV/TLC value is 36.90% (6-57). The average value of FRC/TLC is 57.23% (37-79). There is no relationship between FEV_1 values and lung volume with clinical symptoms in stable COPD patients. There is no relationship between RV values, RV/TLC and FRC/TLC with FEV_1 values in stable COPD patients. There is no relationship between RV values with mMRC scale and the CAT scale. There is a significant relationship between the value of RV/TLC and the value of FRC/TLC with the mMRC scale, but only the value of FRC/TLC has a meaningful relationship with the CAT scale. There is no relationship between RV values and FRC/TLC with a 6-minute walking test and exacerbation within 1 year. There is a significant relationship between the value of RV/TLC with the 6-minute walking test. The higher the value of RV/TLC, the lower the value of the 6-minute walking test and the increase in exacerbation of 1 year in COPD patients. There is no relationship between RV values, RV/TLC and FRC/TLC with the Brinkman Index and COPD group.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None.

FUNDING

None.

REFFERENCE

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