### **Research Article**

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## Estimation of measured pulmonary artery to aorta ratio for prognosis of pulmonary hypertension in chronic obstructive pulmonary disease patients

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#### ABSTRACT

**Background:** Chronic obstructive pulmonary disease is a type of obstructive lung disease which is characterized by poor air flow to the lungs which worsens over time. Enlargement of the pulmonary artery is associated with the severe exacerbations of chronic obstructive pulmonary disease. Furthermore, it was indicated that MPA/AAo >1 could be an indicator to predict acute exacerbations of COPD. This study was thus undertaken to identify the association of MPA/AAo ratio and pulmonary hypertension by CT chest.

**Methods:** 157 patients with definite diagnosis of COPD and 50 patients without any cardiovascular disease or lung disease were included into the study. The patients were asked to lay down in left lateral position with calm breathing during the Doppler test for PH measurement; electrocardiogram and heart rate were also measured for all patients.

**Results:** Out of these 157 patients, 98 (62.4%) were males and 59 (37.6%) were females. Of the pulmonary artery diameter, the main, right and the left arterial diameter was considerably higher than that of the controls with 28.6, 21.8 and 21.5 mm respectively. There was no significant difference in the diameters of the ascending and the descending aorta between that of the patients and the controls. The ratio of MPA/AAo and MPA/DAo was higher in the patients that the controls. The MPA, LPA, RPA diameters were 30.3mm, 23.5mm and 23.2 mm in the patients with PH while they were significantly lesser in the COPD patients without PH. the most common comorbidities found was obesity, diabetes, dyslipidemia, stroke, abnormal CT findings, Emphysema, Fibrosis and Bronchiectasis with the MPA and AAo diameters significantly higher.

**Conclusions:** We conclude that a high MPA:AAo ratio correlated with increase in the MPA and AAo diameter and as a result, increased arterial pressure and presence of PH.

**Keywords:** Chronic obstructive pulmonary disorder, Main pulmonary artery diameter, Ascending aorta diameter, MPA/AAo ratio

#### **INTRODUCTION**

Chronic Obstructive Pulmonary Disease is a type of obstructive lung disease which is characterized by poor air flow to the lungs which worsens over time. The main symptoms are shortness of breath, cough and production of sputum.<sup>1</sup> Most people with chronic bronchitis are known to have COPD.<sup>2</sup>

COPD is associated with high morbidity and mortality, and is estimate to be the fifth leading cause of deaths in the world. It is also estimated that by 2030, COPD would become the third leading cause of deaths globally.<sup>3</sup> In the

United States, it is already the third leading cause of death.<sup>4,5</sup> One of the important factors of exacerbations for COPD is pulmonary hypertension, which increases the hospitalization rate and mortality among the patients with COPD.<sup>6</sup>

Pulmonary hypertension (PH) is a progressive disease of multifactorial etiology. A mean arterial pressure of >25 mmHg is considered to be pulmonary hypertension. Patients with PH have reduced quality of life, work ability and increased disability. If not detected early, the prognosis for the patients is very poor and can lead to progressive right ventricular failure with high mortality rate.<sup>7,8</sup>

Enlargement of the pulmonary artery is associated with the severe exacerbations of chronic obstructive pulmonary disease (COPD).<sup>9,10</sup> The PA diameter, the cross-sectional area, the ratio of the diameter to the bronchus, the ratio of the diameter to the pulmonary vein, the ratio of diameter to the aortic diameter, and multiple regression methods assessing dimension of the main and branching pulmonary arteries have been investigated to assess the association with PH.<sup>11-15</sup>

The accurate diagnosis of PH is very challenging as the diagnostic process is complex and requires high index of clinical suspicion.<sup>16</sup> Computed tomography (CT) chest scans have largely supported the diagnosis of PH, probably due to its ability to detect thromboembolism and identify any diffuse parenchymal lung disease that may not be identifiable in 15% of the chest x-rays.<sup>17,18</sup>

It was described in a study by Wells et al that MPA/AAo was associated with decline of FEV1 and this ratio increased in acute exacerbation of moderate to severe COPD.<sup>9</sup> Furthermore, it was indicated that MPA/AAo >1 could be an indicator to predict acute exacerbations of COPD. ON development of COPD, pulmonary vessels changed with the destruction of vascular bed and pulmonary vascular remodeling, causing PH.<sup>19</sup>

This study was thus undertaken to identify the association of MPA/AAo ratio and pulmonary hypertension by CT chest.

#### **METHODS**

The study was a retrospective analysis of first 23 this retrospective study was conducted by the Department of TB& Respiratory Medicine at Mallareddy institute of Medical sceices during a period of Three years. 157 patients with definite diagnosis of COPD and 50 patients without any cardiovascular disease or lung disease were included into the study. Patients with congenital heart disease, aortic aneurysm, other heart diseases, pulmonary hypertension etc were excluded from the study.

Pulmonary hypertension was diagnosed using colour Doppler ultra-sonic diagnostic apparatus. The patients

were asked to lay down in left lateral position with calm breathing during the Doppler test for PH measurement; electrocardiogram and heart rate were also measured for all patients. Systolic pulmonary artery was calculated according to the following formula:

 $sPAP = 4 Vmax^2+right$  arterial pressure, which was estimated by the reflux peak of systolic tricuspid regurgitation as per simplified Bernoulli equation. Pulmonary hypertension was diagnosed if the sPAP > 36mmHg.

CT- scans were performed with a 16-slice multidetector CT scanner, with patients in the supine position and breath at deep expiration. The parameters included Collimation  $64 \times 0.6$  mm, rotation time 0.5 s for mediastenum and 1.0 for lung paanchyma, pitch 1.0, tube voltage 120 kV, tube current dose modulated 50-200 mAs.

The following parameters were measured in triplicate,

- The widest part of Main PA diameter, before MPA bifurcation.
- Diameter of the right and left pulmonary artery: the widest portion after the bifurcation.
- Widest portion of the ascending aorta and the descending aorta at the same level of CT section used to measure the MPA. Based in this, the ratio of MPA/AAo and MPA/Dao were calculated.

Statistical analysis was calculated as mean, standard deviation and range where appropriate. T-test, chi-square tests were done for comparisons.

#### RESULTS

157 patients with confirmed COPD were included. The main indication for CT scan was dyspnea in all the patients. Out of these 157 patients, 98 (62.4%) were males and 59 (37.6%) were females (Figure 1).

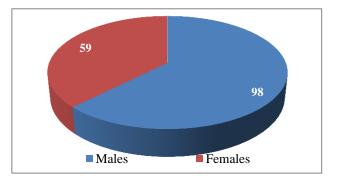


Figure 1: Sex wise distribution of patients.

The age of the patients and the controls were equivalent. More number of patients was males rather than females with COPD. Although the BME of the patients was slightly more than that pof the controls, it was not significant. More number of the patients was smokers compared to the controls. The CRP and the triglyceride levels were significantly higher than that of the controls. Of the pulmonary artery diameter, the main, right and the left arterial diameter was considerably higher than that of the controls with 28.6, 21.8 and 21.5 mm respectively. There was no significant difference in the diameters of the ascending and the descending aorta between that of the patients and the controls. The ratio of MPA/AAo and MPA/DAo was higher in the patients that the controls (Table 1).

 Table 1: Hemodynamic characteristics of patients and controls.

Variables	Patients	Controls
Age	55.1±3.2	53.2±4.1
Sex (M/F)	98/59	28/22
Height (cm)	169.4±7.2	154.9±5.1
Weight	68.1±2.1	54.8±5.1
BMI	25.1±3.1	22.8±2.9
SBP	127.9±4.1	111.6±4.7
DBP	84.6±4.6	76.2±2.5
Smoking		
Regularly	16 (10.2%)	1 (2%)
Occasionally	45 (28.7%)	6 (12%)
Never	96 (61.1%)	43 (86%)
Hypertension	63	0
Diabetes	61	0
Blood Sugar (mg/dL)	126.6±5.3	105.6±5.1
CRP (mg/L)	30.7±2.9*	15.6±5.2
TG (mg/dL	136.9±2.9*	129.9±3.2
MPA dia (mm)	28.6±2.1*	25.1±1.9
RPA Dia (mm)	21.8±1.7*	19.3±2.7
LPA dia (mm)	21.5±2.6*	18.3±2.4
Aortic dia (mm)	35.1±3.6	34.7±2.6
DAo dia (mm)	24.9±3.1	25.2±1.7
MPA/AAo	0.82±0.12*	0.73±0.16
MPA/DAo	1.13±0.28*	0.98±0.17

\*p<0.001

# Table 2: Hemodynamics and CT comparisons in<br/>COPD patients with and without PH.

	COPD with PH N=63	COPD without PH N=94
Age	64.4±3.6	56.2±4.1
Sex (M/F)	42/21	55/39
CRP (mg/L)	30.4±4.1	27.4±3.6
TG (mg/dL	139.3±3.5	128±4.1
MPA dia (mm)	30.3±4.2	27.5±2.4*
RPA dia (mm)	23.5±2.3	20.4±1.9*
LPA dia (mm)	23.2±1.8	21.0±2.1*
Aortic dia (mm)	36.1±4.1	34.3±1.9 *
DAo dia (mm)	26.6±2.3	26.4±1.7
MPA/AAo	0.86±0.15	0.81±0.21*
MPA/DAo	1.15±0.19	1.06±0.22*
*p<0.001		

Among the COPD patients with pulmonary hypertension,  $2/3^{rds}$  were males and only  $1/3^{rd}$  was females. Although the CRP levels and the triglyceride levels were higher, they were not significant. The MPA, LPA, RPA diameters were 30.3 mm, 23.5 mm and 23.2 mm in the patients with PH while they were significantly lesser in the COPD patients without PH. Though there was not much difference in the descending aorta diameter, the ascending aorta was thicker in the COPD patients with PH (Table 2).

Among the patients, the most common comorbidities found were obesity, diabetes dyslipidemia. Few patients had stroke, abnormal CT findings, Emphysema, Fibrosis and Bronchiectasis. The MPA and AAo diameters and MPA/AAo ratio was significantly higher among the patients with the comorbidities than those without (Table 3).

#### DISCUSSION

COPD is a chronic inflammatory disease which not only affects the structure and the function of the lung but also influences the metabolism, hormone secretion and organ function of multiple systems all over the body.<sup>20</sup> As CRP is a marker for inflammation, it was found to be raised in many of the patients. The same was observed in a similar study by Chen, et al.<sup>20</sup>

Right-sided heart catheterization, an invasive procedure, is a gold standard for the diagnosis of PH. However, in some recent studies, it has been reported that PHC is necessary only for those patients who have to get lung transplantation or those attending clinical trials.

As CT is a non-invasive test, it is nowadays routinely performed for possible diagnosis of PH. It known to have the potential to be the first indicator towards the diagnosis of PH.<sup>11,14,21</sup> CT in conjunction with electrocardiographic measurements are strong correlates of MPA in patients especially those with underlying disorders. CT scan also provided a plausible mechanism for the development of relative enlargement of pulmonary artery in patients with severe COPD, which in turn has been linked with exacerbation.<sup>22,23</sup> A correlation of MPA/AAo ratio and PH is important due to the implications of comorbin COPD and PH on the exacerbation risk, exacerbation-related morality and all-cause mortality.<sup>24,25</sup> The MPA:AAo ratio is said to be better tool for diagnosing PH in patients with severe COPD than electrocadiography.<sup>26-29</sup>

In our study there was a predominance of male patients with COPD and PH. While the lipid levels of the patients were not much different than those of the controls, the triglyceride levels were considerably higher. This was similar to a study by Lee et al, who found MPA and AAo diameters to be more in males than in females, in obese patients and those with hypertension.<sup>30</sup>

Variables	Numbers	MPA	AAo	MPA/AAo
Obesity				
Yes	41	30.1±2.1*	34.1±4.1*	0.88±0.41*
No	116	25.1±3.7	29.8±3.1	0.83±0.64
Hypertension				
Yes	63	29.4±2.6*	33.6±3.1*	$0.89 \pm 2.5*$
No	94	26.1±1.9	30.5±2.8	$0.87 \pm 2.9$
Diabetes				
Yes	61	30.3±2.1*	34.2±3.3*	0.90±2.6*
No	96	25.4±3.1	30.1±2.9	$0.85 \pm 1.8$
Dyslipidemia				
Yes	58	31.4±2.4*	$34.1 \pm 3.9*$	0.91±2.8*
No	99	$26.5 \pm 2.5$	$30.5\pm3.1$	$0.88 \pm 2.9$
Stroke				
Yes	12	28.6±2.1	$32.2 \pm 2.7$	$0.87 \pm 2.5$
No	145	26.1±2.6	$30.4 \pm 3.1$	0.86±2.6
OLD (FEV1/FCV (%) <70				
Yes	17	27.5±2.1	$32.4 \pm 2.5$	0.86±3.1
No	140	26.1±1.6	$31.9\pm2.5$	$0.84{\pm}1.9$
Abnormal CT findings				
Yes	24	28.7±2.4	$34.1 \pm 3.2$	0.85±1.9
No	133	26.5±3.1	$31.4 \pm 3.2$	0.83±2.5
Emphysema				
Yes	6	28.1±2.6	$33.5 \pm 3.1$	0.85±2.7
No	151	26.7±1.7	$32.1\pm3.6$	$0.84{\pm}1.6$
Fibrosis				
Yes	8	28.2±2.1	$34.2 \pm 3.7*$	0.84±2.3
No	149	26.2±2.5	$31.3\pm2.6$	0.83±1.9
Bronchiectasis				
Yes	6	28.5±2.3	34.1±2.5 *	$0.86 \pm 2.8$
No	151	26.4±2.7	31.5±2.6	0.83±2.3

Table 3: MPA, AAo and MPA/AAo	values in patients with and	without underlying diseases.

\*p<0.001

The MOA in the controls in our study was 25.2mm while the AAo was 34.3mm. MPA/AAo was 0.98. IN other studies, the mean MPA ranged from 24.2 to 27.2mm, AAo was around 31.9-34.1 mm.<sup>31-35</sup>

Although very few of our patients were smokers, most of them had mild to severe COPD. It has been shown that there is a slight vascular alteration in smokers with normal pulmonary function also.<sup>6,4,36</sup>

MPA, AAo and MPA/AAo ratio was easily obtained by Chest CT. They are known to clinically correlate with underlying cardiopulmonary diseases.<sup>23,37</sup> In the present study, the diameters of main pulmonary artery, right pulmonary artery and left pulmonary artery were significant higher than those of the controls, though there was not much of difference in the ascending aorta and descending aorta diameters between the two sets of patients. As a result the MPA/AAo and MPA/DAo ration was larger in the patients with regards to the controls. The prevalence of PH in the COPD patients was 40%. It has been estimated in other studies that the prevalence may vary for 10% to as high as 85% depending on the severity of the underlying diseases.<sup>26,38-40</sup> This was in concordance to a study by Iyer, et al who found a prevalence of 40%.<sup>41</sup>

Number of studies has been performed to investigate the correlation between CT measurements of the PA and the presence and severity of PH.

We had very few cases of an MPA/AAo ratio >1. In other studies, a ration>1 was associated with future exacerbations of COPD, particularly in those patients who required hospitalization.<sup>23</sup> Association between pulmonary hypertension, MPA:AAo ratio and acute exacerbations of COPD was found in other studies also.<sup>42-45</sup>

Blum et al reported that COPD patients had a more dialated brachial artery and smaller change in post-hyperemia arterial diameter.<sup>46</sup> Iyer, et al also reported a

MPA/AAo ratio >1 was better by CT than ECG for predicting PH in patients with severe COPD, suggesting a correlation between impaired lung function and arterial diameter.<sup>41</sup>

The limitation in this study was the sample size. More number of patients needs to be investigated before any conclusion can make.

#### CONCLUSION

We conclude that a high MPA:AAo ratio correlated with increase in the MPA and AAo diameter and as a result, increased arterial pressure and presence of PH. These measurements are easy to obtain require minimal training and can be performed in the hospital easily. Therefore, CT can be used to measure the diameters of the main, right and left pulmonary artery and calculate the ratio of MPA:AAo.

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