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Computed Tomography Severity Grading of Chronic Obstructive Pulmonary Disease based on Volumetric Assessment of Inspiratory and Expiratory Scans

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Abstract

***Background & Aims*:** To determine attenuation threshold for detection and quantification of air trapping in obstructive airway disease. Quantify airway dysfunction in patients of obstructive airway disease & its correlation with pulmonary function tests.

Materials & Methods: Paired HRCT scans of 48 patients were done and correlated with Pulmonary Function Tests taken within 2 weeks of the study. Threshold attenuation value on expiratory scan that signifies air trapping was obtained by correlating relative volumes with PFT parameters (PEF 25-75% & RV/TLC). The lung volumes at this threshold were then correlated with PFT values signifying airway dysfunction (FEV1, FEV1/FVC and PEF 25-75%) and airway dysfunction was then quantified based on these volumes.

***Results*:** Maximum correlation of PFT parameters signifying air trapping is with relative volume of limited lung at -850HU (l850) ($p<0.005$) which was taken as the threshold for air trapping. Using this threshold (-850HU), we calculated the relative volume change of limited and whole lung (l850 & t850) and expiratory relative volume of limited and whole lung (ERV l850 & ERV t850). Significant correlation was seen between l850 and PFT parameters signifying airway dysfunction ($p<0.005$). A severity classification of obstructive airway disease was formulated based on l850 and classified patients into mild (l850<-30%), moderate (l850= -20 - -30%), severe (l850 =-10 - -20%), and very severe (l850 > -10%).

***Conclusion*:** l850 can be used as a CT parameter to quantify airway dysfunction irrespective of presence or absence of emphysema. Severity classification of obstructive airway disease was formulated based on l850.

***Keywords*:** FEV1 Forced Expiratory Volume in 1 sec, FVC Forced Vital Capacity, HRCT High-Resolution Computed Tomography, $PEF_{25-75\%}$ Peak Expiratory Flow (25 – 75 %), PFT Pulmonary Function Test, RV Residual Volume

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Introduction

Obstructive airway diseases are respiratory diseases characterized by airway obstruction. Although COPD shares similar characteristics with other obstructive lung diseases, such as the signs of coughing and wheezing, they are distinct conditions in terms of disease onset, frequency of symptoms, and reversibility of airway obstruction (1). Diagnosis of obstructive airway diseases requires several factors depending on the exact disease being diagnosed. However one common criterion is the FEV1/FVC ratio less than 0.7. COPD includes emphysema and chronic bronchitis which usually overlap in a given patient (2).

Smoking is a common patho-etiogenic factor in COPD. COPD has been classified based on PFT parameters into 4 grades: Mild-FEV1/FVC < 0.70, FEV1 ≥80% predicted; Moderate- FEV1/FVC < 0.70, FEV1 50-80% predicted; Severe- FEV1/FVC < 0.70, FEV1 30-50% predicted; Very Severe- FEV1/FVC < 0.70, FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure (3).

Inspiratory HRCT helps in evaluation of morphology of interstitium and lung parenchyma (4). In patients with small airway disease, an expiratory scan may provide additional information including functional assessment of airway obstruction (5).

On expiratory scans, a lack of increase in the lung attenuation is said to indicate air trapping which is one of the signs of airway obstruction (Fig 1). Thus expiratory scans can be useful in assessing air trapping in patients with normal or mildly deranged PFT as PFT. This is because PFT provides a global overview and maybe normal until large areas of both lungs are involved (6).

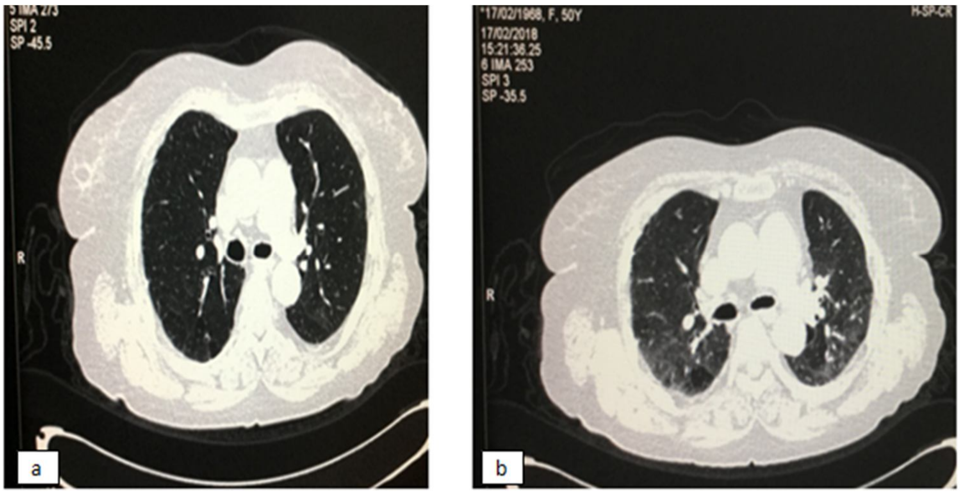

Figure 1. Paired inspiratory (a) and expiratory (b) CT showing air trapping. The normal lung increases in attenuation on expiration making areas of air trapping more conspicuous.

The presence of mosaic attenuation on HRCT remains an enigma, however, paired scans can help in the differential diagnosis as areas of air trapping will become more hypodense on expiratory scans suggestive of an airway disorder in comparison to vascular and infiltrative disorders [7, 8]. Air trapping needs to be differentiated from emphysema and architectural distortion and bullae may help in this regard being present in emphysema [9]. However, no objective measure has been sought to quantify air trapping which would be independent of the degree of associated emphysema. Also, there has been no definite consensus on the threshold density on expiratory CT that can be used to identify and quantify air trapping. Our study aims to enlighten these grey areas.

Methods

This study was an observational prospective study and was conducted in the Department of Radio-diagnosis and Imaging SKIMS Srinagar from October 2016 to June 2018.

CT Scanning Protocol:

All CT scans were done in the Department of Radio-diagnosis & Imaging SKIMS, Soura using CT SOMATOM SENSATION 64 with the following parameters:

Inspiratory and expiratory CT scans were obtained at the end of full inspiration and at the end of forced expiration. Images were reconstructed with a slice thickness of 1 mm and a reconstruction interval of 0.5 mm using a sharp kernel.

Interpretation of CT Scans:

We calculated the volume of entire lung by summing up voxels in the range of –500 to –1,024 HU and labeled it as volume of the whole lung (Fig 2). Lung volumes were then obtained between certain thresholds (–850, –870, –890, –910, –930, and –950 HU) with -950 HU as the lowest density in order to exclude emphysema which is usually taken as volume less than -950 HU. The relative volumes of the whole lung (volume of the whole lung at each of the above threshold divided by value of the whole lung multiplied by 100) were calculated both by inspiratory and expiratory scans (relative volume<a (%) = volume at each threshold/volume (–500 to –1024 HU) × 100. Relative volume was calculated in both inspiration (IRV < a) and expiration (ERV < a); a = attenuation threshold values between –850 and –950 HU).

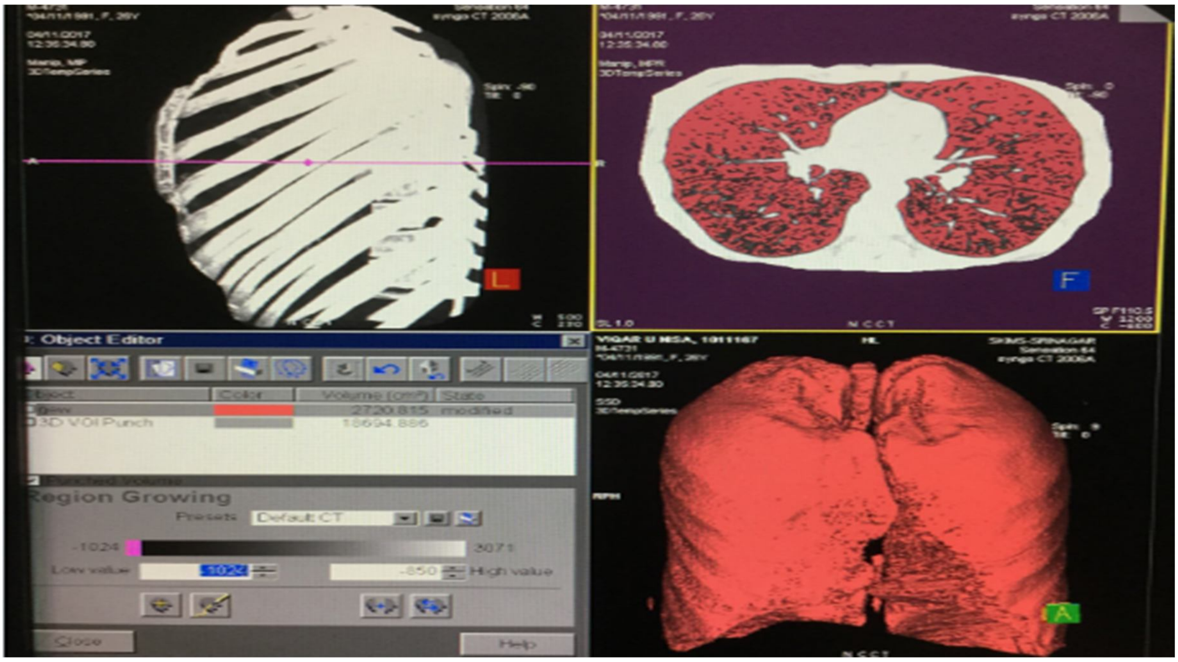

Figure 2. Calculation of volume of the whole lung at threshold level -850HU (-850HU - -1024HU) using 3D object editor. The volume in Red represents the voxels between -850HU and -1024HU, tracheal volume was excluded using object punching

Limited lung volume was obtained by excluding the voxels with attenuation less than -950 HU i.e. volume with attenuation between -850 and -950 HU (Fig 3). -950 HU was validated by many previous studies as being the threshold for emphysema. We then calculated the relative volume of limited lung (volume of limited lung at each of the above threshold divided by value of limited lung multiplied by 100) on both inspiratory and expiratory scans (relative volume a –950 (%) = volume between any threshold (a) & –950 HU / volume between –500 to –950 HU × 100). Relative volumes were obtained in both inspiration (IRV -950) and expiration

(ERV -950); a = attenuation threshold value between –850 and –930 HU). We then calculated the change in the relative volumes that occurred between inspiratory and expiratory scans by subtracting the relative volumes in expiration from those in inspiration in both the whole lung (relative volume change <a) and the limited lung (relative volume change a–950).

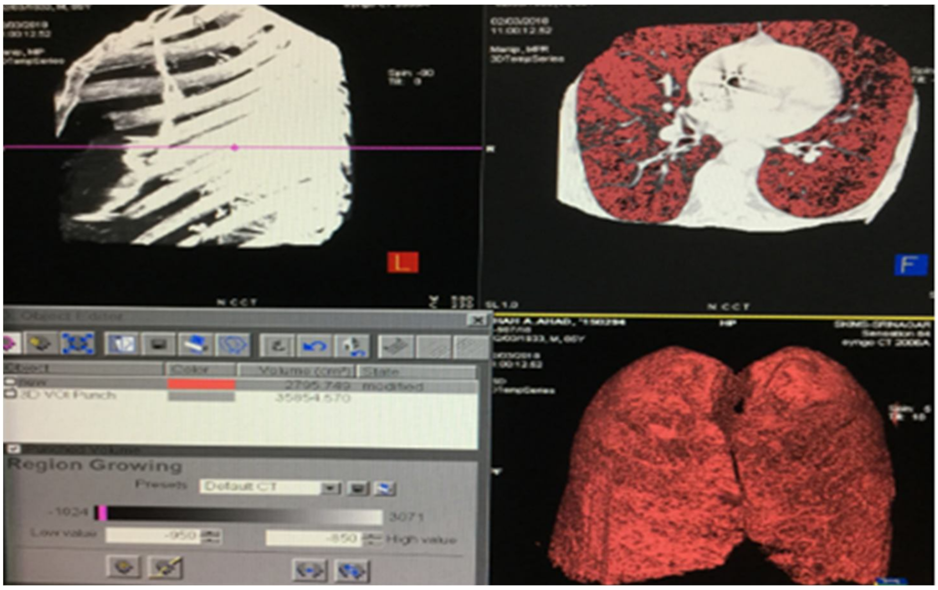

Figure 3. Calculation of volume of limited lung at threshold level of -850HU (-850HU - -950HU) excluding emphysematous voxels

Pulmonary Function Tests:

PFTs were performed within 2 weeks of obtaining CT scans using PC BASED MEDIKRO WINDOWS SPIROMETER WITH SOFTWARE VERSION 1.8 manufactured by MEDIKRO OY Finland**.** The spirometric parameters were recorded in accordance with the American Thoracic Society Guidelines 2005.

To obtain the attenuation threshold value for the detection of air trapping, Pearson's correlation coefficients were calculated between each relative volume change a–950 and the results of PFTs. We segregated our patients into mild and moderate-severe emphysema groups based on values of inspiratory relative volume <–950. Using the threshold value (-850HU) obtained in our study, Pearson's correlation coefficients between the expiratory relative volume <-850HU- -1024HU (ERV t850), expiratory relative volume -850HU – -950 HU (ERV l850), relative volume change< -850(t850), or relative volume change -850HU – -950HU (l850) and the results of PFTs in both groups were obtained. Comparisons of ERV t850, ERV l850, l850 and t850 between the moderate to severe emphysema group and mild emphysema group were done using the two-sample Independent t-test, one-way analysis of variance, and Pearson's correlation coefficient. p-value less than 0.05 was considered to be statistically significant.

Results

Patient profile:

We conducted paired HRCT scans of 48 patients and correlated them with PFT results. Of the 48 patients in our study, 20(42%) were males and 28(58%) were females. The mean age of patients in our study was 52.27 ± 13.30 yrs. The age range was 28 –80yrs.

Smoking history:

Among the 48 patients in our study, 43(90%) were smokers and 5(10%) were nonsmokers. A significant difference in PFT parameters and l850 between smokers and nonsmokers was found in our study (p<0.005).

Inspiratory relative volume -950 - -1024 HU (IRV <-950):

The mean value of IRV < -950 in our patients was 14.26%±6.22%.The patients were divided into two groups according to IRV < -950 values: mild emphysema group (IRV < -950 <15%, mean value=8.79%± 3.21%, mean age=50.12±13.3) and moderate to severe emphysema group (IRV<-950 >15%, mean value=19.72% ± 2.58%, mean age= 54.44±13.20). We had 24 (18 females and 6 males) patients in mild emphysema group and 24 (10 females & 14 males) patients in moderate-severe emphysema group.

We observed a significant difference (p-value< .0001) in the relative volumes of lung at threshold attenuation (t850, l850, ERV t850, ERV l850) between the mild emphysema group and moderate to severe emphysema group(Table 1).

Table 1. Differences in relative volume change in whole and limited lung at -850HU(t850,l850), expiratory relative volume at -850HU in whole and limited lung(ERV t850,ERV l850) among mild emphysema group and moderate to severe emphysema group and their significance

	emphysema group(IRV-950)	N	Mean	Std. Deviation	p-value
t850	Mild	24	-30.8308	7.66915	
	Moderate	24	-14.5179	6.77712	≤0.0001
l850	Mild	24	-27.3408	7.05915	
	Moderate	24	-17.5467	7.17964	≤0.0001
ERV t850	Mild	24	33.4758	4.85615	
	Moderate	24	53.2488	5.39691	≤0.0001
ERV l850	Mild	24	29.5816	7.17661	
	Moderate	24	47.2300	3.38957	≤0.0001

Correlation between relative volume change of limited lung at different attenuation levels and PFT parameters:

The maximum correlation between relative volume change and PFT parameters is observed at the attenuation value of -850 in the limited lung (l850). Relative volume change l850 showed significant correlation with PFT parameters signifying air trapping: RV/TLC(r=.861, p-value= <0.0001) and PEF 25-75% (r=-.829, p-value= <0.001) (Table 2, 3 and Fig. 4). -850 HU was thus taken as the threshold for air trapping.

Table 2. Correlation between relative volume change of limited lung at different attenuation levels and PFT parameters

		fev1(%P)	fvc(%P)	fev1_fvc(%P)	pef(%P)	rv_tlc(%P)
l850	Pearson Correlation	-.731**	-.420**	-.734**	-.829**	.861**
	p-value	<0.0001	.003	<0.0001	<0.0001	<0.0001
l870	Pearson Correlation	-.528**	-.246	-.619**	-.654**	.672**
	p- value	<0.0001	.093	<0.0001	<0.0001	<0.0001
l890	Pearson Correlation	-.556**	-.076	-.593**	-.548**	.570**
	p-value	<0.0001	.610	<0.0001	<0.0001	<0.0001
l910	Pearson Correlation	-.535**	-.049	-.545**	-.459**	.494**
	p-value	<0.0001	.742	<0.0001	.001	<0.0001
l930	Pearson Correlation	-.500**	-.052	-.483**	-.329*	.286*
	p-value	<0.0001	.724	<0.0001	.023	.049

Table 3. Correlation between relative volume change of whole lung at different attenuation levels and PFT parameters

		fev1(%P)	fvc(%P)	fev1_fvc(%P)	pef(%P)	rv_tlc(%P)
t850	Pearson Correlation	-.566**	-.218	-.588**	-.634**	.679**
	p-value	<0.0001	.137	<0.0001	<0.0001	<0.0001
t870	Pearson Correlation	-.565**	-.142	-.559**	-.597**	.636**
	p-value	<0.0001	.335	<0.0001	<0.0001	<0.0001
t890	Pearson Correlation	-.511**	-.064	-.510**	-.498**	.569**
	p-value	<0.0001	.665	<0.0001	<0.0001	<0.0001
t910	Pearson Correlation	-.518**	-.006	-.436**	-.413**	.409**
	p-value	<0.0001	.969	.002	.004	.004
t930	Pearson Correlation	-.324*	.064	-.402**	-.203	.184
	p-value	.025	.664	.005	.167	.210
t950	Pearson Correlation	-.158	.125	-.214	-.132	.008
	p-value	.284	.398	.145	.369	.957

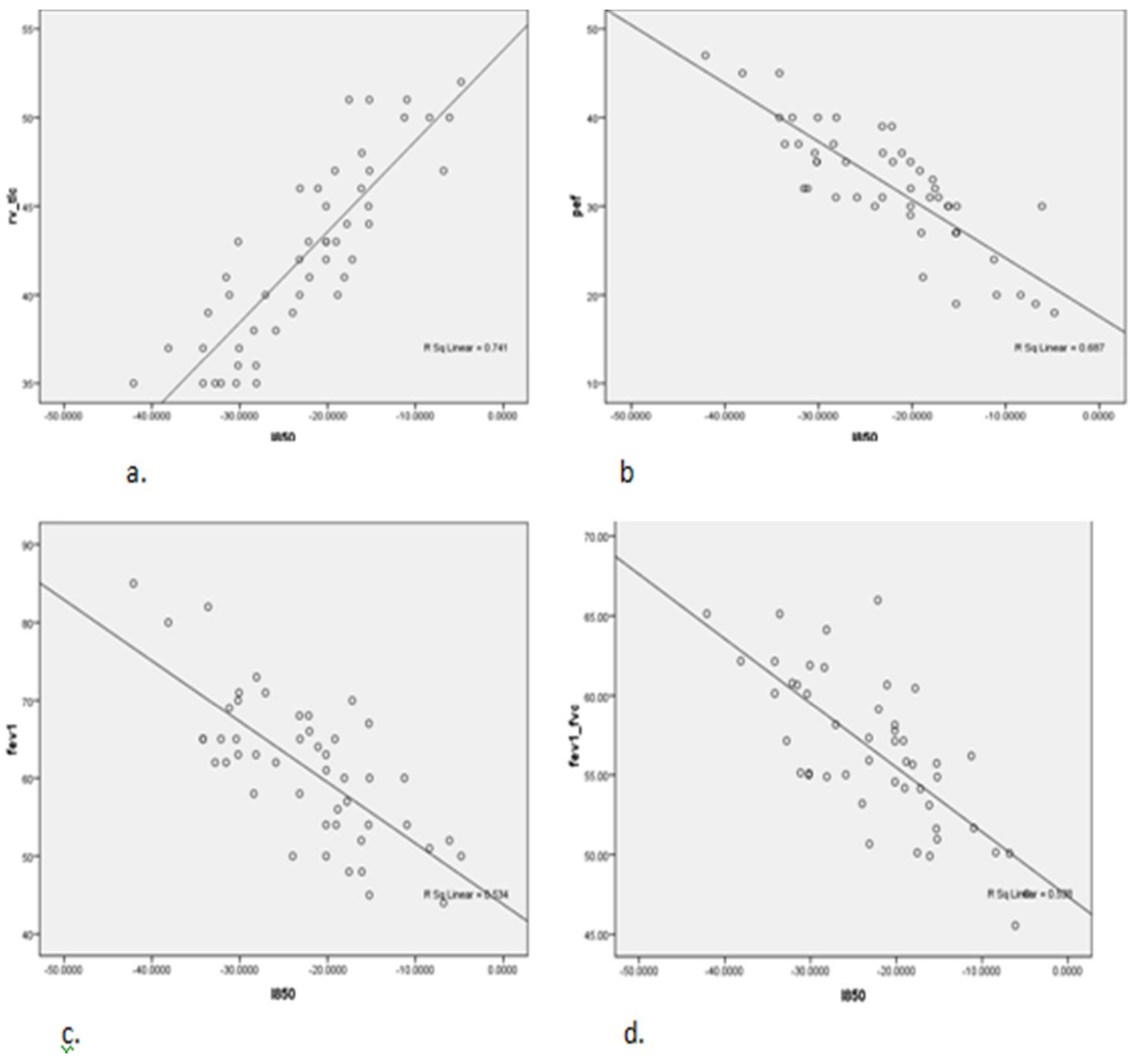

Figure 4. Simple scatter diagram showing significant correlation between l850 and a. rv_tlc, b. pef, c. fev1 and d.fev1_fvc

Severity classification of obstructive airway disease: The patients were classified based on the relative volume change of limited lung at threshold level (l850) and the classification was correlated with PFT parameters signifying airway dysfunction. A significant difference (p<0.001) was found between all the PFT parameters in the various proposed severity grades (Table 4). The airway dysfunction in obstructive airway disease was graded into four groups:

- mild(l850= less than-30%) ,
- moderate (l850 =-20% to -30%),
- severe (l850= -10% to -20%) and
- very severe (l850 = greater than -10%).

Of 48 patients, 13(27%) were graded as mild, 16 (33%) as moderate, 15 as severe (31%), and 4(8%) as very severe. There was a clear and significant difference (p<0.001) in the mean values of different PFT parameters among the severity grading groups we have proposed, giving credence to our severity grading model (Fig. 5-8).

Table 4. Correlation of PFT parameters among the severity grading groups showing significant (p<0.001) differences in the parameters

		N	Mean	Std. Deviation	p-value
fev1(%P)	Below -10	4	49.2500	3.59398	
	-10to-20	15	56.6667	7.15808	
	-20to-30	16	62.1250	6.78110	
	-30 to -40 (Above -30)	13	69.5385	7.88052	
	Total	48	61.3542	9.21028	<0.0001
fvc(%P)	Below -10	4	84.5000	4.93288	
	-10to-20	15	91.2667	7.33355	
	-20to-30	16	93.3125	6.95432	
	-30 to -40 (Above -30)	13	96.4615	7.77405	
	Total	48	92.7917	7.67133	0.034
fev1_fvc(%P)	Below -10	4	48.3350	2.20638	
	-10to-20	15	54.1033	2.91457	
	-20to-30	16	57.7744	3.96464	
	-30 to -40 (Above -30)	13	60.0392	3.50596	
	Total	48	56.4540	4.74534	<0.0001
pef(%P)	Below -10	4	48.3350	5.56028	
	-10to-20	15	54.1033	4.67822	
	-20to-30	16	57.7744	3.59398	
	-30 to -40 (Above -30)	13	60.0392	4.85825	
	Total	48	32.3125	6.81724	<0.0001
rv_tlc(%P)	Below -10	4	49.7500	2.06155	
	-10to-20	15	46.0000	3.70328	
	-20to-30	16	41.0625	3.31600	
	-30 to -40 (Above -30)	13	37.3077	2.65784	
	Total	48	42.3125	5.11633	<0.0001

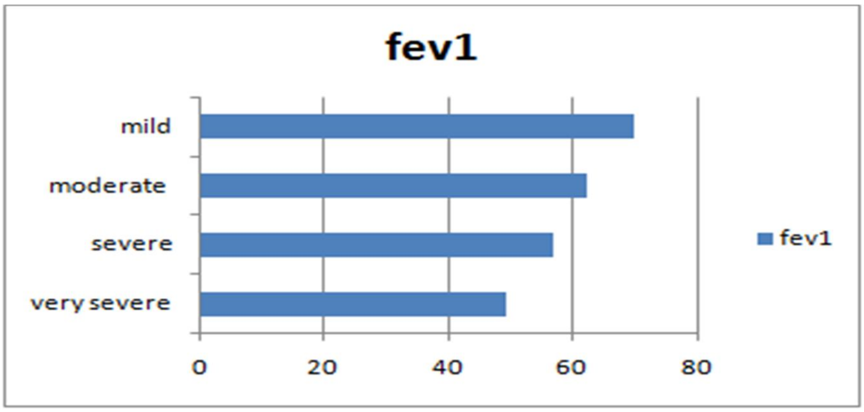

Figure 5. Mean values of fev1 in the severity grading groups

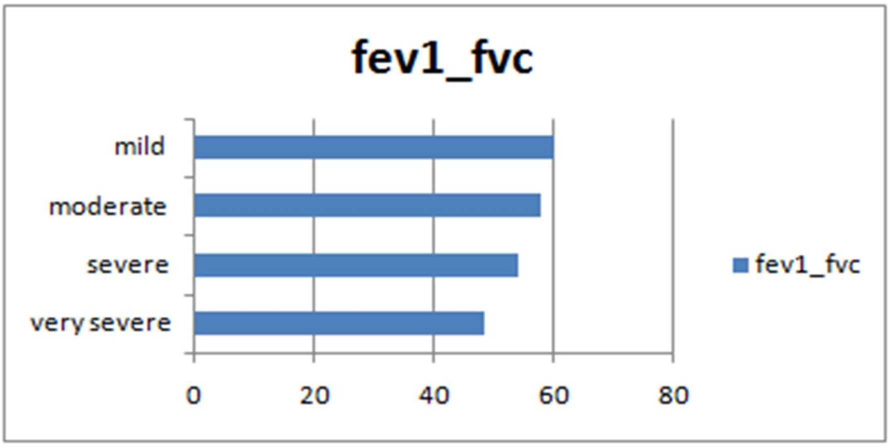

Figure 6. Mean values of fev1_fvc in the severity grading groups

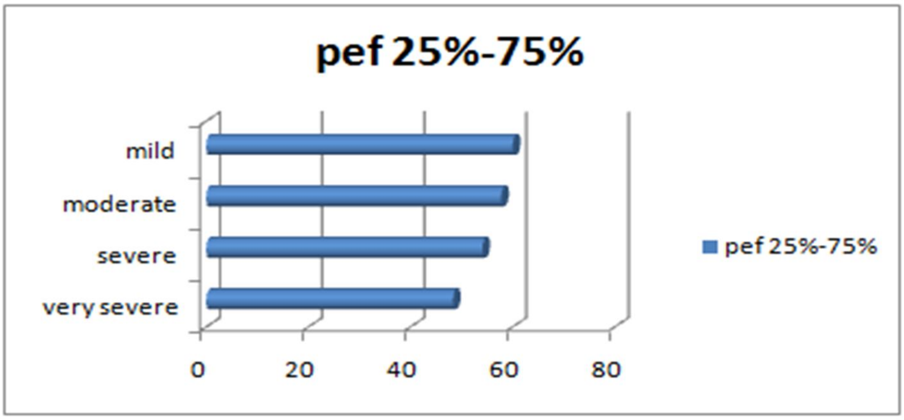

Figure 7. Mean values of pef 25%-75% in the severity grading groups

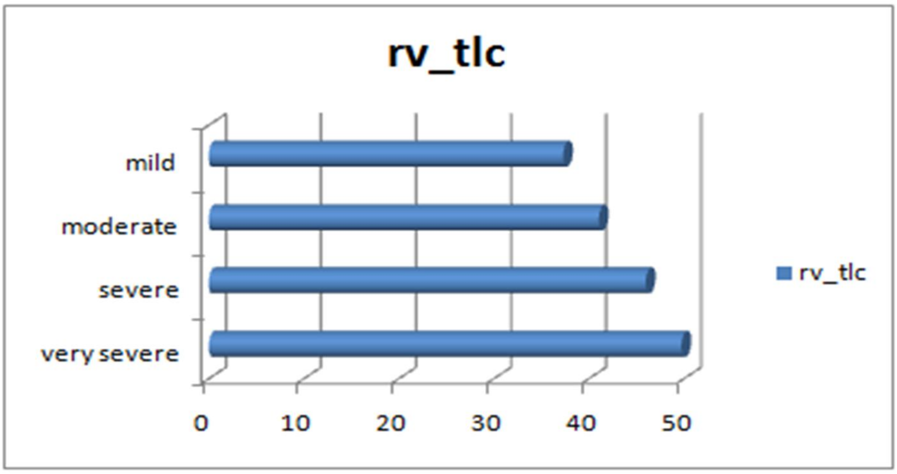

Figure 8. Mean values of rv_tlc in the severity grading groups

Discussion

This study was done to evaluate the role of paired HRCT in quantifying airway dysfunction in patients with obstructive airway disease. Threshold CT attenuation on expiratory scan below which air-trapping could be established was also sought in our study. The mean age of patients was 52.27 ± 13.30 yrs. The age range was 28 – 80 yrs. 48 subjects (28 females and 20 males) participated in our study. This number is comparable to the study conducted by Matsouka et al. (10) who included 36 patients in their study with 31 males and 5 females. The mean age of patients in this study was however 71 yrs (range 57-80).

In our study, we attempted to exclude emphysema by not including lung voxels with attenuation less than -950HU in the limited lung. We calculated the relative volume change for whole and limited lung at different threshold levels and compared them to the PFT parameters. The maximum significant correlation was seen between the relative volume change of limited lung at -850HU (l850) and fev1(r=-0.731, p-value= <0.0001), fev1_fvc (r= -0.734, p-value= <0.0001), pef25%-75 %(r= -0.829, p-value= <0.0001), RV_TLC(r=0.861, p-value= <0.0001) and fvc (r= -0.420, p-value=0.003) (Table 2 and 3). As l850 showed the maximum correlation with pef25%-75% and RV_TLC which signify air trapping, we took l850 as the threshold attenuation for identifying and quantifying air trapping. Significant correlations with PFT parameters were seen at attenuation values from -850HU - -910HU in the limited lung (-850,-870,-890 and -910), however maximum correlation was noted at -850HU. In their study Matsouka et al. (10) found that the maximum correlation between PFT parameters and relative volume of limited lung was at -860 HU. In another study, Hersh et al (11) found maximum correlation of PFT parameters with relative volume change in limited lung at -856HU. The correlation at different attenuation values could be due to the different attenuation levels selected and different CT acquisition and reconstruction techniques. Thus the attenuation threshold for air trapping varies from -850HU - -910 HU, however -850 HU seems to be the best value according to our study.

To study the effect of emphysema on quantitative CT volumes, we divided the patients into mild emphysema group (IRV<15%) and moderate to severe emphysema group (IRV>15%). We found that in moderate to severe emphysema group, it was only l850 that correlated significantly with PFT parameters (fev1 r=-0.555, p-value<0.005, fev1_fvc r=-0.612, p-value<0.001, pef25%-75% r=-0.771, p-value<0.0001 and rv_tlc r=0.790, p-value<0.0001). In the mild emphysema group also l850 showed significant correlation with PFT parameters signifying airway dysfunction (fev1 r=-0.769, p-value<0.0001, fev1_fvc r=-0.714, p-value<0.0001, pef25%-75% r=-0.808, p-value<0.0001 and rv_tlc r=0.809, p-value<0.0001). Matsouka et al. (10) in their study found that the relative volume of limited lung at -860 HU correlated with PFT parameters in both mild and moderate to severe emphysema groups. Therefore, it can be concluded that l850 is a quantitative indicator of airway dysfunction in patients with obstructive airway disease irrespective of the degree of emphysema.

In our study, we classified severity of airway dysfunction in patients with obstructive airway disease according to l850. We classified patients into four groups: mild (l850 greater than -10%), moderate (l850 -10% to -20%), severe (l850 -20% to -30%), and very severe (l850 less than -30%). We correlated this classification with PFT parameters that signify airway dysfunction and found significant correlation (fev1 p-value<0.0001, fev1_fvc p-value<0.0001, fvc p-value=0.034, pef25%-75% p-value<0.0001 and rv_tlc p-value<0.017) (Table 4). This classification can only be applied to patients with known obstructive airway disease as all of our patients had deranged PFT parameters and no controls were taken in our study to see the volume of the limited lung at -850HU towards the normal spectrum. This classification would require further studies in normal subjects and those with near-normal or mildly deranged PFT parameters to be applied as a complete classification system for obstructive airway disease. To the best of our knowledge, there has been no such attempt to classify obstructive airway disease on the basis of relative volume change of limited lung at a certain threshold level that correlated significantly with PFT parameters.

In our study we found that PFT parameters, as well as relative volume of limited lung at the threshold level (l850), were significantly affected by smoking status of the patients. In patients who were smokers a significant correlation was present (fev1 p-value<0.0001, fev1_fvc p-value = 0.001, pef25%-75% p-value =0.002 and rv_tlc p-value =0.007 and l850 p value<0.0001). Our results are quite similar to those of Mistry et al.(12) who found significant differences in the PFT parameters between smokers and nonsmokers (Fev1 p-value<0.05, fev1_fvc p-value<0.05, fvc p-value< 0.05, and pef 25%-75% p-value<0.05). Similar results were also obtained by Lee et al. (13) who found a significant correlation of smoking with air trapping on CT as compared to nonsmokers(p-value<0.05). Therefore, patients with obstructive airway disease who are also smokers have an additional insult to their airway which leads to significant airway dysfunction and air trapping. This is evident by markedly deranged PFT parameters and also l850 on CT indicating air trapping. However, in our study, we had only 5 nonsmokers which was a limitation. Also we were not able to classify the smokers on the basis of cigarettes per day or no. of pack years.

Our study had few limitations, first, the number of patients in our study may not be representative of varying degrees of emphysema in different obstructive airway disease patients. A larger sample may be required to be representative of varying degrees of airway dysfunction and emphysema. Second, we did not have controls in our study to complete the severity classification for obstructive airway disease that we have proposed. Correlation of CT densitometric values in normal subjects may help in putting forth a better severity classification. Third, we did not have the facility of spirometrically gated paired CT scans. The end inspiration and end expiration technique is an acceptable protocol, however, spirometric gating allows a more accurate assessment of the degree of inspiration and expiration which can directly affect the CT densitometric parameters.

Conclusion

Paired inspiratory and expiratory CT is essential for grading airway dysfunction in obstructive airway disease. -850 HU can be taken as the threshold attenuation for identification and quantification of air trapping. l850 is the best CT volumetric parameter for quantification and grading of airway dysfunction in obstructive airway disease irrespective of presence or absence of emphysema.

Based on our study we recommend the use of paired inspiratory and expiratory HRCT to quantify airway dysfunction in obstructive airway disease. We also suggest a grading system to grade the severity of airway dysfunction based on CT densitometric volume measurements, however, further studies in normal subjects may be required to have a complete holistic grading system.

CONFLICT OF INTEREST: None.
No contribution of any kind was received from any source.

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