Correlation between heart size and emphysema in patients with chronic obstructive pulmonary disease: CT-based analysis using inspiratory and expiratory scans

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Abstract

The objective of this study was to investigate the relationship between the extent of emphysema and heart size in patients with chronic obstructive pulmonary disease (COPD) using inspiratory and expiratory chest computed tomography (CT). This retrospective study was approved by the institutional review board and informed consent was waived. We measured lung volume (LV), low attenuation area percent (%LAA; less than or equal to -950 HU), maximum cardiac area, and maximum transverse cardiac diameter on inspiratory/expiratory chest CT in 60 patients with COPD. Spearman rank correlation analysis was used to determine the correlations between the heart and lung CT measurements, and the correlations between these measurements and spirometric values. On inspiratory CT, the maximum transverse cardiac diameter was negatively correlated with LV ($\rho = -0.42$; $p < 0.01$) and %LAA ($\rho = -0.43$; $p < 0.001$). Furthermore, on expiratory CT, the maximum cardiac area was negatively correlated with LV ($\rho = -0.35$; $p < 0.01$) and %LAA ($\rho = -0.37$; $p < 0.01$), and there was a negative correlation between transverse cardiac diameter and %LAA ($\rho = -0.34$; $p < 0.01$). Although inspiratory cardiac size was not correlated with any of the spirometric values, the maximum cardiac area and transverse diameter on expiratory scans were significantly correlated with the reduced airflow values on spirometry ($p < 0.01$). In patients with COPD, the transverse cardiac diameter decreased as the emphysema progressed. A smaller cardiac area on expiratory CT suggested the presence of large LVs, emphysema, and airflow limitation in COPD.

Keywords

Heart size, COPD, inspiratory, expiratory, CT

Background

Heart size is influenced by the cardiac and extra-cardiac components; the latter includes systemic blood volume, pulmonary vascular pressure, and ventilation. Preload and afterload affect pressure in the heart, and this can alter heart size. Also, the diaphragm that attaches to part of the pericardium changes the shapes of the thorax and heart.[1,2] During

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inspiration, the cardiac long axis moves from a transverse to a vertical direction with movement of the diaphragm, and the heart becomes elongated. In contrast, during expiration, the heart becomes wider, since the diaphragm elevates, and the cardiac long axis moves in a transverse direction.[1]

Chronic obstructive pulmonary disease (COPD) is considered a systemic disease that involves the pulmonary, cardiovascular, and musculoskeletal systems.[3] COPD results from obstruction and inflammation in the airways; it is characterized by airway limitations that cannot be reversed. Although right heart failure and hypertrophy occasionally occur in COPD patients due to increased pulmonary artery pressure and overload, a small heart size is frequently observed on chest radiography.[4] Thurlbeck et al. demonstrated that heart size on radiography decreased as the extent of emphysema progressed, since hyperinflation leads to flattened diaphragm.[4] However, to the best of our best knowledge, no previous research exists that quantitatively clarifies the association between heart size, the extent of emphysema, and spirometric values based on the measurements using computed tomography (CT).

With the development of chest CT, quantitative evaluations in patients with various obstructive diseases have demonstrated associations between CT-based measurements and pulmonary functional testing (PFT).[5,6] A previous study showed that both CT-based lung volume (LV) and the low attenuation area percent (%LAA) on chest CT is correlated with the results of PFT.[6] In addition, we have reported that changes in heart size on chest CT are affected by the phase of ventilation and the magnitude of inspiration/expiration.[1] Based on these observations, it can be predicted that heart size in COPD patients would be correlated with the extent of emphysema, and that respiratory changes in heart size would be correlated with spirometric values.

In this study, we, therefore, hypothesized that the measurement of heart size on inspiratory and expiratory CT would be correlated with %LAA and spirometric values. The aim of the current study is to determine the correlations among maximum cardiac area/transverse cardiac diameter, %LAA, and spirometric values.

Methods

This retrospective study was approved by our institutional review board, which waived the need for informed consent from patients.

Subjects

A total of 64 subjects with clinically stable COPD and a history of chest CT were initially identified by a radiologist (H.T., with 4 years of experience in thoracic radiology). These subjects underwent inspiratory and expiratory chest CT scans during a single visit to our institution from November 2012 to 2013. All subjects were current or former smokers (mean, 62.3 $\pm$ 34.8 pack-years). Patients who had huge bulla ($n = 2$), infectious pneumonia ($n = 1$), or interstitial pneumonia ($n = 1$) were excluded. The final study population included a total of 60 subjects. They were 52 males and 8 females (mean age, 73 years; range, 40–87 years). The body mass index (BMI) of all subjects was 22.6 $\pm$ 4.5 kg/m^2. These 60 subjects were classified into the following categories based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging: stage 1, $n = 16$; stage 2, $n = 30$; stage 3, $n = 14$; and stage 4, $n = 0$. Six subjects had a history of cardiac disease, including atrial fibrillation ($n = 4$), mitral regurgitation ($n = 1$), and old myocardial infarction ($n = 1$).

CT scanning

All patients were scanned with identical 64-row CT scanners (Aquilion 64, Toshiba Medical Systems, Otawara, Tochigi, Japan) at full inspiration and end-expiration with a breath hold. CT scanning settings for inspiratory scans were as follows: collimation, 64 mm $\times$ 0.5 mm; tube voltage, 120 kVp; tube current, 200 mA (inspiratory scan) or 80 mA (expiratory scan); gantry rotation time, 0.5 s; and beam pitch, 0.828 (helical pitch, 53). Inspiratory and expiratory scan data were converted to CT images using a soft tissue kernel (FC04) with a slice thickness of 0.5 mm without any overlap of serial sections. The imaging field of view was 320 mm $\times$ 320 mm and the pixel size was 0.625 mm $\times$ 0.625 mm.

Image analysis: Measurement of the lung on CT

CT-based inspiratory and expiratory LVs and %LAA (less than -950 HU) were automatically measured by a commercial workstation (NG 1 Ziostation ver. 1.17t; Ziosoft Inc., Tokyo, Japan). The software segmented the lung parenchyma after excluding the chest wall, hilum, and central airways. To evaluate changes in ventilation, the expiratory/inspiratory ratios of these lung measurements were calculated.

Table I. Lung and heart measurements on inspiratory and expiratory CT scans.

CT measurements		Mean $\pm$ SD		
		Inspiratory scan	Expiratory scan[a]	E/I ratio
Lung	LV (L)	5.0 $\pm$ 0.91	3.59 $\pm$ 0.86	0.71 $\pm$ 0.1
	%LAA (%)	26.1 $\pm$ 16.0	16.6 $\pm$ 13.6	0.62 $\pm$ 0.32
Heart	Maximum cardiac area (cm^2)	6.78 $\pm$ 1.34	7.71 $\pm$ 1.44	1.14 $\pm$ 0.1
	Maximum transverse cardiac area (cm)	10.5 $\pm$ 0.1	11.4 $\pm$ 1.2	1.1 $\pm$ 0.07

CT: computed tomography; SD: standard deviation; LV: lung volume; %LAA: low attenuation area percent; E/I: expiratory/inspiratory.
[a]Significantly different ($p < 0.0001$) from all inspiratory measurements.

Image analysis: Measurement of the heart on CT

We have previously investigated heart size on chest CT.[1] Thus, the same method was used in this study. The measurements of cardiac areas were performed using free open-source software (Image J, version 1.47, Bethesda, MD, USA). In brief, cardiac area on an axial CT image was measured as follows: (1) the slice that demonstrated the maximum cardiac area was selected; (2) using a threshold setting to exclude the pericardial fat pad (from 0 HU to 300 HU), the cardiac boundary was determined; and (3) cardiac area was extracted using another threshold setting (from -100 HU to 300 HU) to include fat tissues or low-density artifacts inside the heart.

The maximum transverse cardiac diameter was manually measured at the same level of cardiac area on an axial CT image shown by the workstation.

Pulmonary function testing

All subjects underwent spirometry, including forced expiratory volume in 1 s (FEV$_1$) and forced vital capacity (FVC). Both FEV$_1$/FVC and the predicted values for FEV$_1$ were obtained.

Statistical analysis

All statistical analyses were performed using JMP 10.0.2 software (SAS Institute, Cary, NC, USA). Data were expressed as the mean $\pm$ standard deviation. Spearman's rank correlation analysis was performed to evaluate the associations between the lung and heart indices; the spirometric values and the lung/heart indices; and the BMI and the lung/heart indices. Comparisons between inspiratory and expiratory measurements on CT were evaluated by the Wilcoxon signed-rank test. Allvalues of $p < 0.05$ were considered significant.

Results

Lung and heart measurements on CT

Table 1 shows the lung and heart measurements on CT. The LV and %LAA were significantly larger on inspiration than on expiration ($p < 0.0001$, respectively). The maximum cardiac area and the maximum transverse cardiac diameter were significantly smaller on inspiration than on expiration ($p < 0.0001$ for both).

Spirometric values

FEV$_1$% predicted and FEV$_1$/FVC were 67.2 $\pm$ 21% and 51.2 $\pm$ 11.9%, respectively.

Lung and heart measurements on CT and their correlations with spirometric values

The correlations between CT-based measurements and spirometric values are shown in Table 2. The LV and %LAA at expiration were correlated with FEV$_1$% predicted and FEV$_1$/FVC ($p < 0.0001$, for all), and the correlations were stronger at expiration than at inspiration. The maximum cardiac area and transverse cardiac diameter at inspiration were not correlated with FEV$_1$% predicted or FEV$_1$/FVC, whereas the maximum transverse cardiac diameter at expiration was significantly correlated with both FEV$_1$% predicted and FEV$_1$/FVC ($p < 0.01$ for both). In addition, the maximum cardiac area at expiration was correlated with FEV$_1$% predicted ($p < 0.01$).

Correlations between lung measurements and heart measurements

Table 3 shows the correlations between the lung and heart measurements. In brief, the maximum transverse cardiac diameter on inspiration was negatively correlated with LV and %LAA ($p < 0.01$). However, the maximum cardiac area at inspiration was not

Table 2. Lung and heart measurements on CT and correlations with PFT.

	Correlation coefficient (ρ)	
	FEV_1%predicted	FEV_1/FVC
Insp-LV	-0.09 (NS)	-0.41 ($p = 0.001$)
Exp-LV	-0.49 ($p < 0.0001$)	-0.71 ($p < 0.0001$)
E/I-LV	-0.61 ($p < 0.0001$)	-0.57 ($p < 0.0001$)
Insp-%LAA	-0.38 ($p < 0.01$)	-0.64 ($p < 0.0001$)
Exp-%LAA	-0.49 ($p < 0.0001$)	-0.7 ($p < 0.0001$)
E/I-%LAA	-0.39 ($p < 0.01$)	-0.36 ($p < 0.01$)
Insp-maximum cardiac area	0.2 (NS)	0.31 (NS)
Exp-maximum cardiac area	0.36 ($p < 0.01$)	0.32 (NS)
Insp-maximum transverse cardiac diameter	0.15 (NS)	0.24 (NS)
Exp-maximum transverse cardiac diameter	0.34 ($p < 0.01$)	0.4 ($p < 0.01$)

CT: computed tomography; PFT: pulmonary functional testing; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; Insp: inspiratory; Exp: expiratory; LV: lung volume; %LAA: % low attenuation area; E/I: expiratory/inspiratory; NS: not significant.

correlated with LV or %LAA. The maximum transverse cardiac diameter at expiration was significantly correlated with %LAA ($p < 0.01$). The cardiac area at expiration was correlated with LV and %LAA ($p < 0.01$) (Figures 1 and 2).

Correlations between body habitus and lung/ heart measurements

Significant correlations were found between BMI and the following lung and heart measurements: insp-LV ($\rho = -0.34$; $p < 0.01$); exp-LV ($\rho = -0.39$; $p < 0.01$); insp-%LAA ($\rho = -0.58$; $p < 0.0001$); exp-%LAA ($\rho = -0.49$; $p < 0.001$); insp-maximum cardiac area ($\rho = 0.44$; $p < 0.001$); exp-maximum cardiac area ($\rho = 0.48$; $p < 0.001$); insp-maximum transverse cardiac diameter ($\rho = 0.54$; $p < 0.0001$); and exp-maximum transverse cardiac diameter ($\rho = 0.30$; $p < 0.05$).

Discussion

In this study, we found that the maximum transverse cardiac diameter becomes shorter as LV and %LAA increase during inspiration, although the maximum cardiac area was not correlated with the lung parameters. Thus, the heart in COPD is compressed during inspiration in a transverse direction by hyperinflation.

At expiration, the maximum transverse cardiac diameter and area were correlated with %LAA and the spirometric values. Worsening emphysema and reduced airflow led to increased residual volume in COPD at expiration. These observations suggested that the transverse cardiac diameter and area decrease as COPD progresses and that this pattern is easier to observe on expiratory, rather than inspiratory, CT scans.

Intrathoracic pressure during ventilation is related to cardiopulmonary hemodynamics. During inspiration, negative intrathoracic pressure leads to dilatation of the right ventricle due to increased venous return. Intrathoracic pressure rises during expiration, which causes a reduction of right ventricular volume. Since hyperinflation of the lung leads to elevated intrathoracic pressure and reduced venous return, right ventricular volume becomes decreased as emphysema progresses.[7–9] However, vascular remodeling in COPD that results from inflammation and endothelial dysfunction causes primary pulmonary hypertension and cor pulmonale.[10] Increased pulmonary vascular pressure and pulmonary vascular resistance leads to right ventricular pressure overload and right ventricular hypertrophy, with subsequent right ventricular dysfunction.[11–13] In the left heart, previous studies demonstrated that left ventricular filling in COPD is affected by right ventricular loading due to ventricular interdependence.[9,13] Left ventricular volume in COPD decreases, since right ventricular overload displaces the interventricular septum toward the left side.[8,9,14] Also, Vonk Noordegraaf et al. demonstrated that the right ventricular wall is significantly thicker in patients with emphysema than without emphysema, but the left ventricular wall is not thickened.[15] Although the ventricular chambers and myocardium have been evaluated in previous studies, there is little information about changes in whole heart size including the four chambers and myocardium based on chest CT in COPD patients.

It would be easy to understand the phenomenon that hyperinflation of the lungs moves the diaphragm downward, since the diaphragm is partially attached to the pericardium. The heart would be displaced vertically in more patients with more severe COPD. In the current study, the transverse cardiac diameter at inspiration was shortened by emphysema. However, the cardiac area at inspiration did not decrease as %LAA and spirometric values became worsen. The difference may be related to the difference in the effect of lung hyperinflation between the

Table 3. Correlations between lung measurements and heart measurements.

CT measurements	Correlation coefficient (ρ)			
	Insp-LV	Exp-LV	Insp-%LAA	Exp-%LAA
Insp-maximum cardiac area (cm^2)	−0.29 (NS)	−0.34 ($p < 0.01$)	−0.32 (NS)	−0.2 (NS)
Exp-maximum cardiac area (cm^2)	−0.32 (NS)	−0.35 ($p < 0.01$)	−0.43 ($p < 0.001$)	−0.37 ($p < 0.01$)
Insp-maximum transverse cardiac diameter (cm)	−0.42 ($p = 0.001$)	−0.2 (NS)	−0.43 ($p < 0.001$)	−0.3 (NS)
Exp-maximum transverse cardiac diameter (cm)	−0.19 (NS)	−0.29 (NS)	−0.34 ($p < 0.01$)	−0.34 ($p < 0.01$)

CT: computed tomography; Insp: inspiratory; Exp: expiratory; LV: lung volume; %LAA: % low attenuation area; E/I: expiratory/inspiratory; NS: not significant.
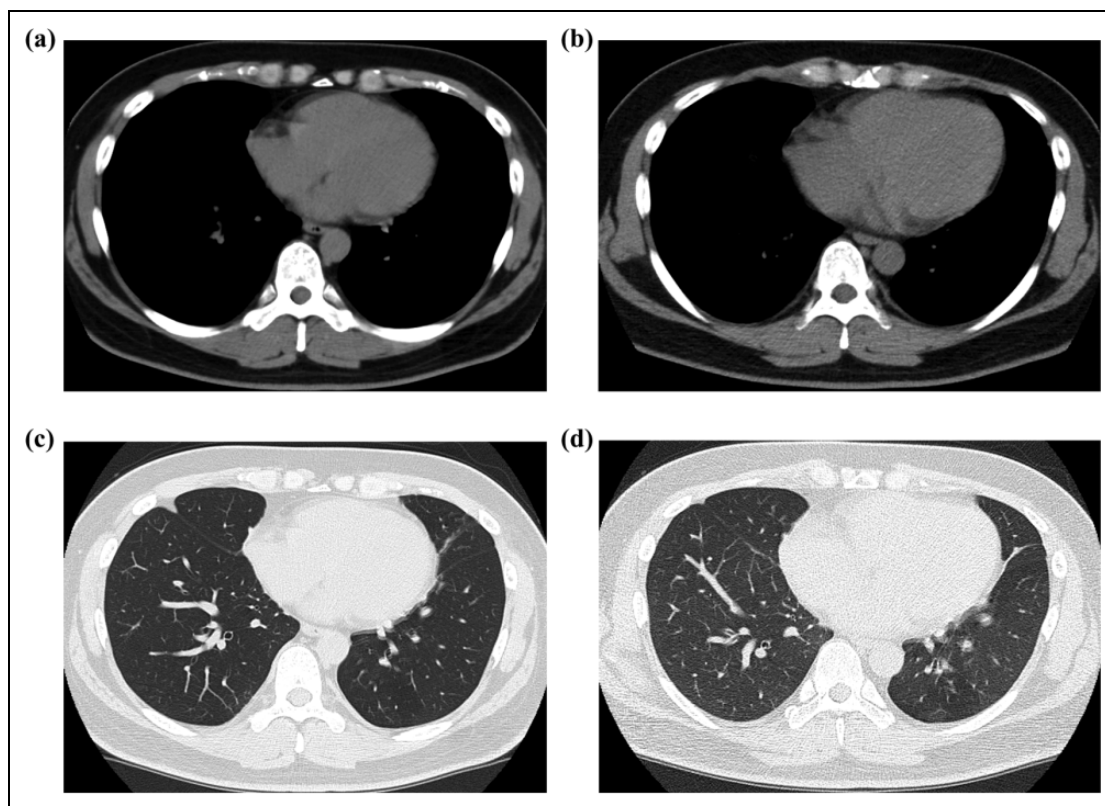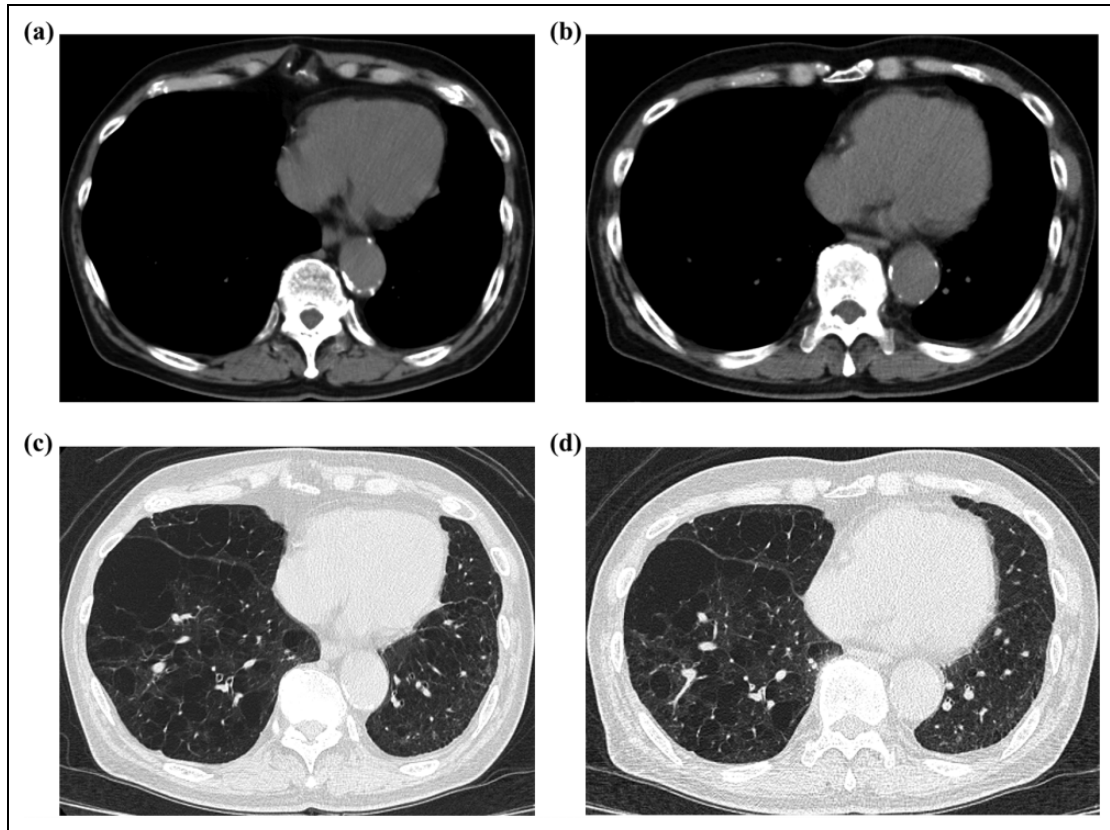

Figure 1. Forty-year-old man with 4.3% and 1.6% of %LAA at inspiration and expiration, respectively. Axial CT images with mediastinal and lung windows at full inspiration ((a) and (c)) and at full expiration ((b) and (d)). The cardiac CSA and transverse cardiac diameter of CT images ((b) and (d)) are larger than those of CT images ((a) and (c)). %LAA: low attenuation area percent; CT: computed tomography.

anteroposterior direction and the transverse direction. Since the heart is sandwiched between the right and left lungs, it is easy to see how hyperinflated lungs caused by COPD can compress the heart, mainly in the transverse direction rather than the anteroposterior direction. It is our hypothesis that the small heart diameter on inspiratory CT scans or radiographs in COPD patients is caused by both caudal dislocation of the diaphragm and transverse compression of the heart by hyperinflated lungs. However, since this study only evaluated CT-based lung parameters and heart size/diameter, further studies are needed to examine the validity of our hypothesis.

In this study, body habitus, as measured by BMI, correlated with several lung and heart measurements. Progression of COPD generally causes weight loss

Figure 2. Seventy-seven-year-old man with 54.3% and 45.7% of %LAA at inspiration and expiration, respectively. Axial CT images with mediastinal and lung windows at full inspiration ((a) and (c)) and at full expiration ((b) and (d)). The cardiac CSA and transverse cardiac diameter of CT images ((b) and (d)) are as large as those of CT images ((a) and (c)). %LAA: low attenuation area percent; CT: computed tomography.

and hyperinflated lung with large LV. On the contrary, many obese people who have high abdominal pressure and elevated diaphragms demonstrated small LV and large heart size, particularly at expiration. Although it is difficult to decide which between emphysema severity and body habitus has a greater influence on heart size and its corresponding respiratory changes, we think that both factors significantly affect heart size.

In our study, the transverse cardiac diameter and cardiac area decreased as COPD progressed. The cardiac measurements at expiration were correlated with the spirometric values but not inspiration. Several studies have demonstrated that lung measurements obtained from expiratory CT better reflect peripheral airway dysfunction and correlate with spirometric parameters than those obtained from inspiratory CT in patients with COPD.[16,17] Also, our previous study demonstrated that changes in heart size between inspiratory and expiratory CT scans were correlated with changes in LV in subjects without COPD, and

that larger expiratory heart size and diameter were observed at smaller expiratory LVs.[1] Although the correlation between expiratory cardiac area or diameter and reduced airflow in the present study is difficult to explain, we believed that a larger LV on expiration in patients with more severe COPD may have resulted in compression of the heart by the hyperinflated lungs and in sustained downward stretching of the heart toward the diaphragm.

This study has several limitations. First, we did not evaluate cardiac function. Hypertrophy and enlargement of the heart can change its shape and dimensions. However, it is difficult to exclude any cardiac component, because the heart interacts closely with the lungs. Second, the radiation dose on expiratory CT was lower than that on inspiratory CT. A decrease in the radiation dose reduces image quality. The increased image noise might be associated with an underestimation of %LAA on expiratory CT. Third, there might be a selection bias, since the study did not include any patients with GOLD stage 4. To

investigate the changes in cardiac size with pulmonary hypertension or right heart failure, an additional study will be needed with more patients. Although systole and diastole could influence measurements of heart size on CT, this study did not assess the cardiac cycle or heartbeat to measure heart size. In addition, the end-expiratory scans might not have been obtained at true full expiration in all patients because of variations in expiratory effort, particularly in COPD patients with prolonged expiration. Therefore, future studies will need to investigate lung and cardiac measures on CT scans using the electrocardiographic gating and breath-triggering techniques.

Conclusion

We showed that cardiac compression by lung hyperinflation could explain the small transverse cardiac diameter in patients with COPD. Cardiac area and diameter measured on expiratory CT reflect airflow limitation better than those measured on inspiratory CT.

Declaration of conflicting interests

Funding

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