Updates in computed tomography assessment of emphysema using computed tomography lung analysis

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Introduction Computed tomography (CT) lung analysis is a new CT technique that allows assessment of emphysema in a quantitative pattern to avoid subjective analysis.

Objective The aim of this study was to assess the role of a new CT lung analysis in quantitative assessment of pulmonary emphysema.

Patients and methods Totally, 30 patients with emphysema were included in this study who presented to the Chest Department of Ain Shams University for follow-up. All patients underwent full history taking, clinical examination, spirometry, and body plethysmography, and were then referred to the Radiology Department for noncontrast chest CT followed by lung volume analysis. Four patients among them were followed-up before and after medical volume reduction therapy.

Results There was a direct relationship between the CT lung volume, the percentage of low-attenuation area, as well as the total lung capacity measured by body plethysmography. Totally, 12 cases were found to be grade I by the Goddard score, with nine of them found to be GOLD I and three of them found to be GOLD II. Fifteen cases were found to be grade II by the Goddard score, with 12 of them found to be GOLD II and three of them found to be GOLD III/IV. Three cases were found to be grade III by the Goddard score with all of them found to be GOLD III/IV. The main site for distribution of the clusters according to their number was in the left upper lobe, whereas according to the cluster volume the main site was the right upper lobe. CT lung analysis guided the site of injection in four patients who underwent volume reduction therapy.

Conclusion CT lung analysis is a new technique that allows quantitative assessment of emphysema, which is important for categorization, follow-up, and treatment strategies. It must be added as a routine study accompanied by spirometric function.

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Keywords: air trapping, emphysema, low-attenuation area, lung analysis, quantitative computed tomography

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common daily health problem whose underlying pathogenesis is not fully recognized [1]. It is strongly associated with smoking, but multiple underlying genetic hypotheses are still under research [2]. It is defined as a chronic airflow obstruction [3,4]. The airflow limitation in COPD is produced by a combination of small airway remodeling [5] and emphysema [6] with varying distribution and severity. Subsequently, two main types can be identified according to the pathogenesis. The first type is the emphysema-predominant type where there is parenchymal destruction associated with reduction in the surface area available for gas exchange [6]. The second type is the airway-predominant type where there is inflammation, fibrosis, and abnormal thickening of the all the small airways [5–7]. The differentiation is important because different treatment strategies are provided for patients – in patients with emphysema-predominant COPD, lung volume reduction surgery may be effective, whereas in patients with airway-predominant COPD medical treatment is more appropriate [8]. Spirometry is the most commonly used technique to detect airway obstruction; it is characterized by being relatively simple, repeatable, noninvasive, and inexpensive that allows a global assessment of functional changes [8]. Many parameters are calculated during spirometry with forced expiratory volume in the first second in liters (FEV_1) and forced vital capacity (FVC) in liters being the most important parameters. The criterion for diagnosis of COPD is an FEV_1/FVC ratio of less than 70% [8]. However, this does not give any idea about the underlying pathology [9] and does not provide any information about the actual distribution of the emphysema [8]. Body plethysmography is widely used in obstructive air way diseases reflecting multiple functional and structural aspects [10]. Computed tomography (CT) lung analysis is not a part of the routine chest CT performed for patients with COPD. It provides nonsubjective information about the disease, which is not dependent on the radiologist's information and experience [1]. It provides information about the extent and severity of the

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disease process [11] and provides a continuous numerical score that is very important for follow-up [12]. Areas of the lung that are affected by emphysema have reduced CT attenuation coefficients [13]. CT densitometry can depict the distribution of the relative low-attenuation area (LAA) (i.e. the proportion of lung parenchyma with attenuation values lower than a predetermined threshold) [11,14–16]. This study aimed to assess the role of the new CT lung analysis in quantitative assessment of pulmonary emphysema.

Patients and methods

Totally, 30 patients known to have emphysema presented to the Chest Department of Ain Shams University for follow-up. Written consents were obtained from all patients to participate in this study according to the rules of the ethics committee in our institute. This was followed by full history taking and clinical examination. The study was conducted over the period from February 2014 to March 2016.

Exclusion criteria

Pregnant women and patients with any other conditions that would interfere with breath-holding that was needed during CT examination were excluded.

Lung function

FEV_1, FEV_1/FVC ratio, and maximum mid-expiratory flow (MMEF) were measured using the spirometry system (Masterscreen 2001, version 4.5; Erich Jaeger GmbH, Germany). Readings were performed in triplicate, with the highest values recorded and expressed as percentages of the predicted value. The examination was carried out according to the guidelines of the American Thoracic Society [17].

Airways obstruction was defined as postbrochodilator FEV_1/FVC is 0.70 or less and FEV_1 less than 80% predicted. The patients were classified according to the severity using GOLD 2014 [3] into four categories.

Body plethysmography

Measurement was performed using a Master Lab–Body Plethysmography Unit (Body Box MasterScreen 2001, version 4.5; Erich Jaeger GmbH, Germany) according to the main principles of the American Thoracic Society/European Respiratory Society Task Force Guidelines [10,18].

Computed tomography chest without contrast

No special preparation was needed as the study was carried out without intravenous or oral contrast. The patient was supine with the arms elevated above the head.

CT machine: high-speed, 16-slice CT machine – General Electric (GE Healthcare, USA) was used.

Technique: the scan direction was craniocaudal in all patients. Scout was taken starting from 1 cm below the lowest costophrenic angle to 1 cm above the lung apices. Whole scans were taken during one breath hold with the patients instructed to exhale.

The CT parameters are illustrated in Table 1.

Image processing

The images were transferred to the work station where multiplanar reformatted images were obtained. All images were displayed with two different windows for interpretation (lung window '1500 width/600 level' and mediastinal window '400/40').

Computed tomography lung analysis

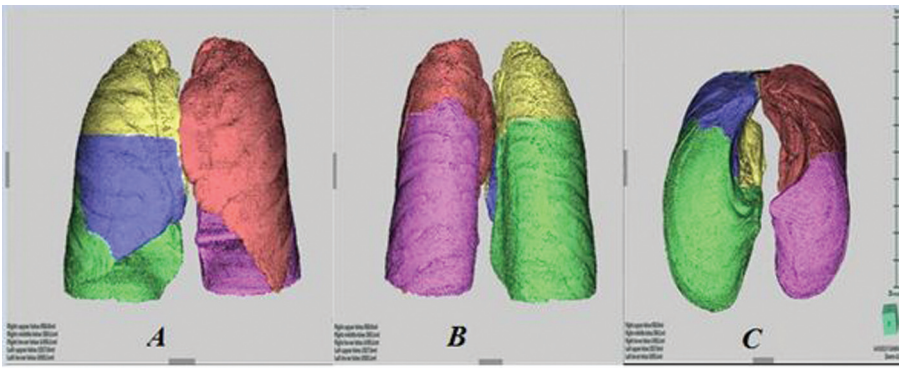
The analysis was performed using 3D synapse software.

(1) CT volumetry is an automated calculation of whole lung volume and the volume of each lobe separately. Color-coded 3D images for the lung were also available in any direction (Fig. 1).
(2) CT densitometry: it is an automated identification of the LAA, which is defined as an area with Hounsfield unit (HU) density less than 950, and is also defined as a cluster (Fig. 2).
(3) Goddard score calculation: it is the calculation of the percentage of LAA per surface area, and a specific scoring as shown in Table 2 was obtained to detect the severity degree. Each lung was divided into three zones: the upper zone, extending from the apices to the level of the aortic arch; the mid zone, extending to the level of tracheal bifurcation; and the lower zone, extending to the level of the diaphragm (Fig. 2).
(4) Cluster analysis: the clusters were classified according to their volumes as follow: class 1: 2–8 mm^3, class 2: 8–65 mm^3, class 3: 65–197 mm^3, and class 4: greater than 197 mm^3. Automated calculation of cluster number and

Table 1 The different parameters used in the computed tomography technique

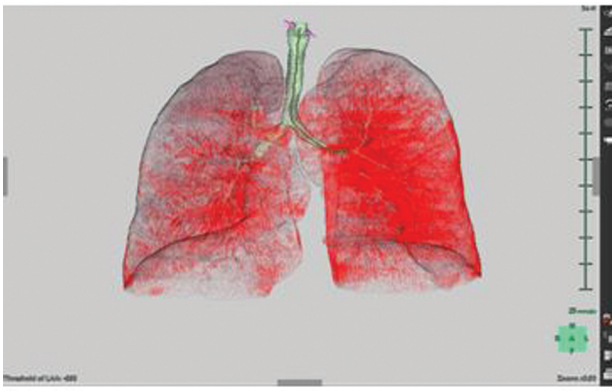
Thickness[a] (mm)	Interval[a] (mm)	Matrix	Pitch number	Speed	Rotation time	kV[b]	mA[c]	Field of view
1.25	0.625	512×512	1.75 : 1	35 mm/rotation	0.5 s	120	200	Large

Figure 1



One of our patients, a male of 55 years, who was a smoker presented for follow-up of emphysema. 3D color-coded images of the lung using CT volumetry with each lobe having a specific color. The lung can be visualized in different axis planes, for example, (a) anterior view, (b) posterior view, and (c) inferior (caudal) oblique view. The volume of each lobe is calculated automatically.

Figure 2



Goddard score:

Right lung	Area(cm^2)	LAA(%)	Score
Upper	94.5	2.0	0
Middle	124.4	2.8	0
Lower	175.5	5.4	1

Left lung	Area(cm^2)	LAA(%)	Score
Upper	121.5	7.6	1
Middle	149.8	9.3	1
Lower	139.4	9.3	1

Total score	4 (Mild)

The same patient with computed tomography densitometry showing automated red coloring of the low-attenuation area (LAA) less than –950 HU. Each area of the LAA is defined as a cluster. The percentage of LAA per surface area can be calculated. The table at the bottom of the image shows Goddard score calculation. In this patient, the Goddard score was 4 (mild), and this was consistent with the spirometric results classified as GOLD I.

cluster volume for each class inside each lobe was available (Fig. 3).

Data analysis

The results were collected and compared together. Data analysis was performed using IBM statistical program for social science, version 22.0 (SPSS, 2013; IBM Corp., USA). Quantitative and qualitative data are expressed as mean±SD, frequencies, and percentages. In addition, the relationship between total lung capacity (TLC), CT lung volume, and percentage LAA was assessed and considered significant when the *P*-value was less than 0.05.

Table 2 The method of Goddard score calculation

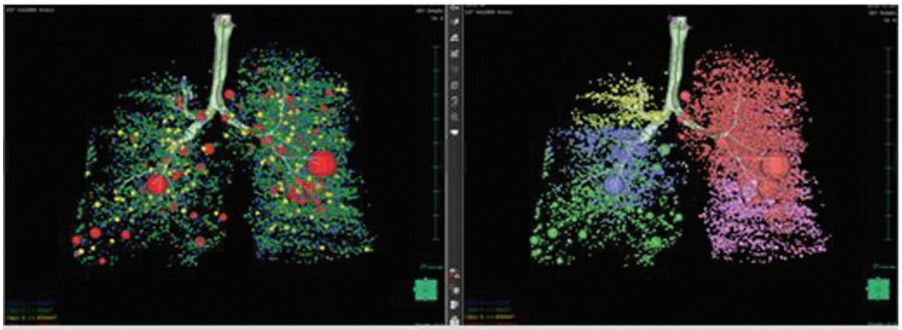
Percentage of LAA	Score	Grading
0–5	0	Normal=0
5–25	1	Mild=1–7
25–50	2	Moderate=8–15
50–75	3	Severe=16–24
75–100	4	

The percentage of low-attenuation area in the upper, middle, and lower zones of the right and left lungs is calculated and gives a specific score with its sum giving the final Goddard scoring. LAA, low-attenuation area.

Results

The present study was conducted on 30 COPD patients. The mean age of the selected population was 53±6.5 years SD. Totally, 25 patients were males, representing 83.3% of the study sample. Positive smoking history was found in all (100%) cases. There was a direct relationship between the CT lung volume and the TLC measured by body plethysmography. In addition, a direct relationship was observed with the percentage LAA (*P*=0.001) (Fig. 4). Totally, 12 (40%) cases were found to be grade I by the Goddard score, with nine (75%) of them found to be GOLD I and three (25%) of them found to be GOLD II. Totally, 15 (50%) cases were found to be grade II by the Goddard score, with 12 (80%) of them found to be GOLD II (Fig. 5) and three (20%) of them found to be GOLD III/IV. Three (10%) cases were found to be grade III by the Goddard score, with all of them found to be GOLD III/IV. The pulmonary functions tests in the form of GOLD score and the CT grading of emphysema using the Goddard score were equal in 24 cases, representing 80% of the cases. However, the Goddard score underestimated the degree of emphysema severity in six cases, representing 20% of cases in comparison with the GOLD scoring (Fig. 6).

Figure 3

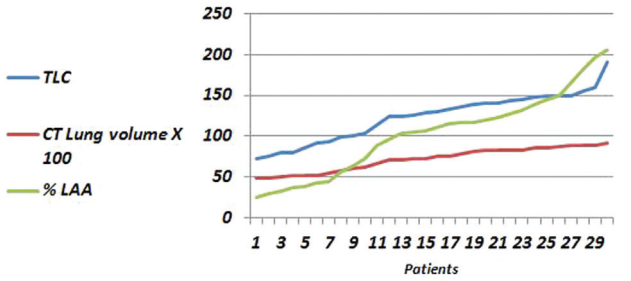


Cluster anlysis:

	D	K	Cluster number					Cluster volume(ml)				
			Class 1	Class 2	Class 3	Class 4	Total	Class 1	Class 2	Class 3	Class 4	Total
RUL	0.000	0	1175	218	9	3	1405	4.3	3.4	0.9	1.8	10.4
RML	0.000	0	1587	387	24	5	2003	6.0	6.9	2.6	8.4	23.8
RLL	0.000	0	3955	816	43	22	4836	14.5	13.7	4.5	9.8	42.5
LUL	0.000	0	7809	1767	87	33	9696	29.1	29.1	9.1	40.7	108.1
LLL	0.000	0	6078	1402	55	23	7558	22.7	23.5	6.1	30.5	82.8

The cluster analysis for the same patient in Figs 1 and 2, with the right upper image showing a 3D color-coded image for cluster distribution according to volume, with the blue color representing class 1, the green color representing class 2, the yellow color representing class 3, and the red color representing class 4. The left upper image shows a color-coded image of the clusters according to their anatomical distribution. The table shows an automated calculation of cluster volume and the number of each class of cluster inside each lobe of the lungs, giving a numerical nonsubjective distribution of emphysema. LLL, left lower lobe; LUL, left upper lobe; RLL, eight lower lobe; RML, right middle lode; RUL, right upper lobe.

Figure 4



The direct relationship between the total computed tomography lung volume and the total lung capacity measured with body plethysmography as well as the percentage low-attenuation area automatically calculated during the computed tomography lung analysis. CT, computed tomography; LAA, low-attenuation area; TLC, total lung capacity.

The main site for distribution of the clusters according to their number was in the left upper lobe (LUL), which was found in 15 cases, representing 50% of the cases, whereas according to the cluster volume the main site for distribution was the right upper lobe (RUL) (Fig. 7), which was found in 12 cases, representing 40% of the cases. The LUL was the lobe showing the maximum number of clusters (class 4), which was seen in 12 cases, followed by RUL, which was seen in eight cases (Fig. 8). The CT lung analysis gave us broad information about the actual distribution of the emphysema process as well as ample numerical information, which can be used in follow-up and selection of patients for lung volume reduction therapy (LVRT). CT lung analysis guided the site of injection in four patients (two patients with RUL distribution, one patient with LUL distribution, and another with RUL distribution) who underwent volume reduction therapy, with improvement of spirometric function in three of them (Table 3).

Discussion

COPD is a very common disease in developing as well as developed countries secondary to high smoking rates as well as air pollution. The clinical as well as the spirometry results alone are not enough and do not reflect the actual distribution of the disease process. This is secondary to the underlying heterogenous pathogenesis, leading to a lot of mismatch between the clinical and the pulmonary function at one side and the actual degree of parenchymal destruction and pathology distribution from the other side [4,19]. These morphological changes can be characterized and quantified by multidetector CT [20]. Quantitative CT may be a highly interesting modality to detect these pathologies *in vivo*, because its separate analysis of disease components may allow morphological phenotyping and visual evaluation of CT images for pathology avoiding the dependence on radiologist experience [21].

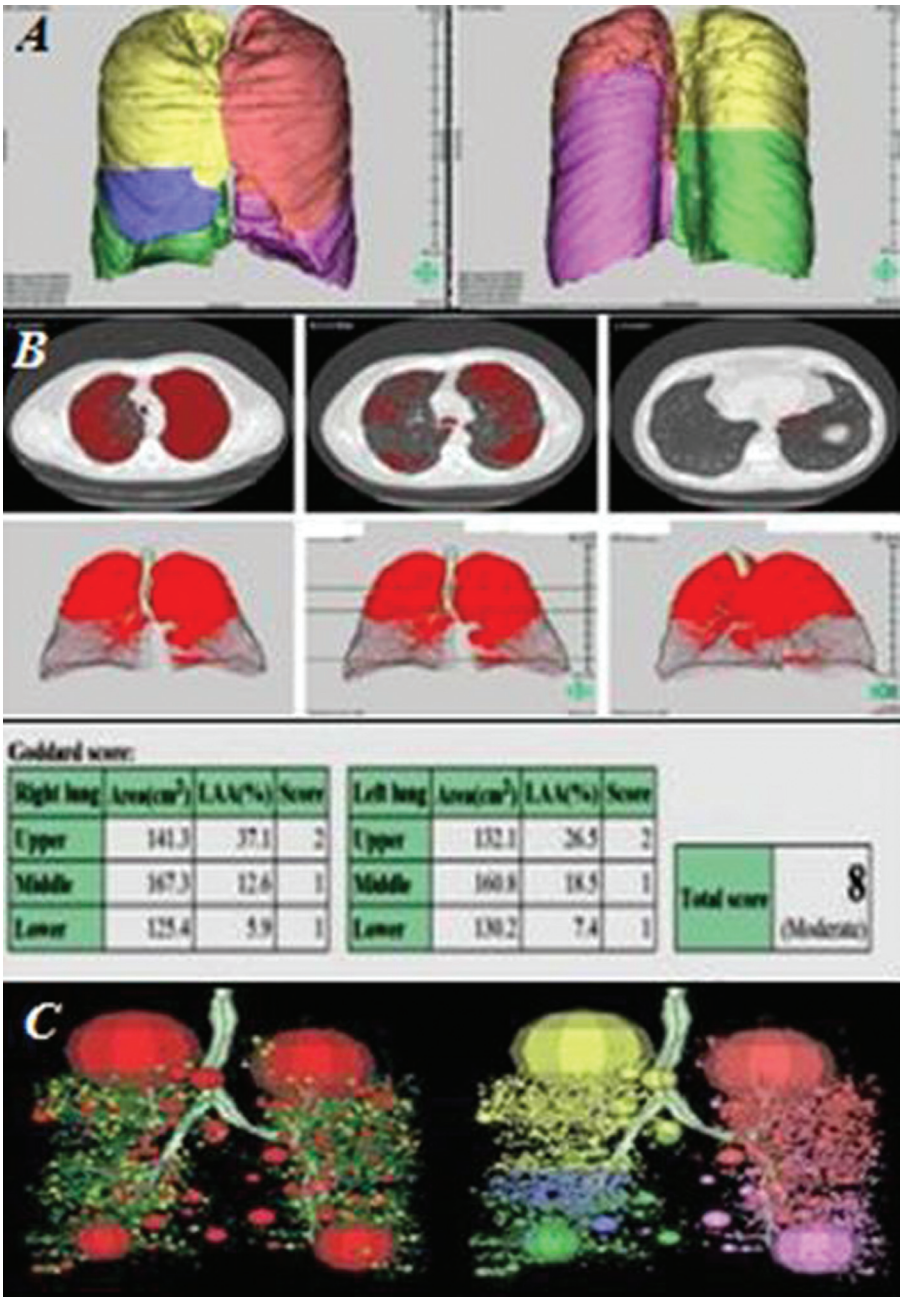
During image acquisition, in our study, we used 1.25-mm image thickness and 200 mA, and this is consistent with the study by Mishima *et al.* [22] , who compared the percentage of LAA obtained with several image thicknesses from 2 to 5 mm and different mA

Table 3 The Goddard score, forced expiratory volume in the first second, and percentage low-attenuation area of the four selected patients for lung volume reduction therapy before and after the interventional process

Patients	Site of maximum affection	Goddard score		FEV_1%		% LAA	
		Pre-LVRT	Post-LVRT	Pre-LVRT	Post-LVRT	Pre-LVRT	Post-LVRT
1	RUL (right upper lobe)	6	4	75	98	78	62
2	LUL (left upper lobe)	8	5	72	95	162	85
3	RLL (right lower lobe)	8	9	68	69	170	160
4	RUL (right upper lobe)	10	8	74	89	206	170

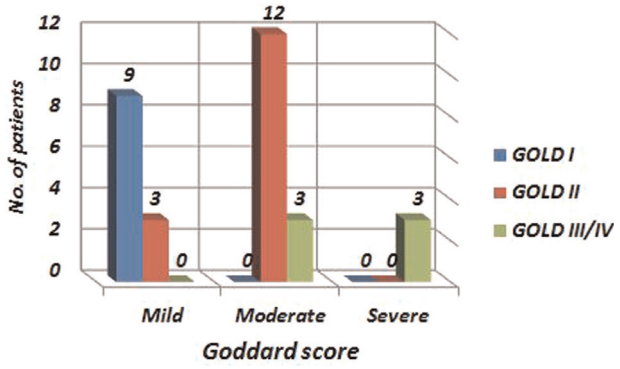
FEV_1%, forced expiratory volume in the first second; LAA, low-attenuation area; LVRT, lung volume reduction therapy.

Figure 5



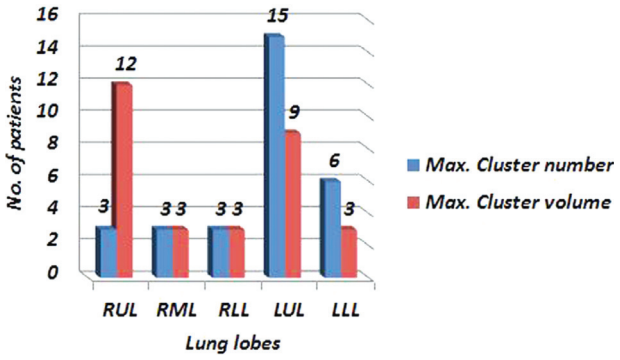
A final computed tomography (CT) result sheet for one of our cases, a 49-year-old male who presented for follow-up. (a) The CT volumetry with a total lung volume of 75, 41 l. (b) CT densitometry as well as Goddard score calculation; the patient had a score of 8 and was classified as having moderate-degree emphysema consistent with the spirometry results showing forced expiratory volume in the first second is 52 and forced expiratory volume in the first second and forced vital capacity ratio is 0.62 and classified as GOLD II. (c) The cluster analysis with bilateral upper lobe predominance.

Figure 6



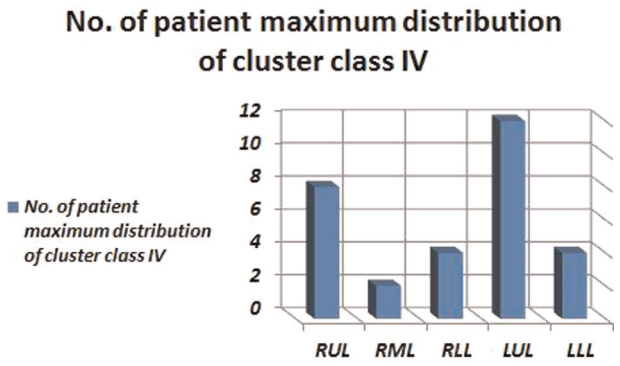
The results of the Goddard score in comparison with GOLD scoring.

Figure 7



The pulmonary distribution of the maximum cluster number and the maximum cluster volume. LLL, left lower lobe; LUL, left upper lobe; RLL, eight lower lobe; RML, right middle lode; RUL, right upper lobe.

Figure 8



The pulmonary distribution of cluster class IV, which is the largest cluster by volume. LLL, left lower lobe; LUL, left upper lobe; RLL, eight lower lobe; RML, right middle lode; RUL, right upper lobe.

parameters from 50 to 250 mA and found that 2-mm-thickness images or less using 200 mA were the most appropriate parameters to assess pulmonary emphysema. In addition, image acquisition in our study was carried out after forced expiration. This is consistent with many studies that have proved that CT results obtained with forced expiration are more accurate than during full inspiration in correlation to respiratory function results [23,24]. In contrast, Nishimura *et al.* [25] showed that expiratory CT underestimates the degree of emphysema as compared with inspiratory CT scans.

The present study found a direct relationship between the TLC and the lung volume obtained by CT volumetry as well as the percentage of LAA, and this consistent with many previous studies [26,27].

Hayhurst *et al.* [28] conducted the first study using CT as a method to quantify the degree of emphysema severity using HU frequency distribution. Percentage LAA is well established as the backbone parameter used in CT lung analysis to study the extent and degree of the disease [14]. It is defined as areas with low HU densities, with several studies being performed to assess the accurate value of HU density [8,11,29,30]; most of the studies found the value to be less than −950 which is the cutoff value used to calculate the LAA and is the same value used in our study.

In this study, the CT lung analysis gave almost the same results regarding detection of emphysema severity in comparison with GOLD scoring, with only six cases showing different underestimated results. Three of them showed mild-degree Goddard scores with GOLD type II, and the other three showed moderate-degree Goddard scores with GOLD type III. These six patients' spirometry showed indexes suggestive of underlying airway disease in the form of sever affection of small airways detected with forced expiratory flow at 25–75% in liters/second (FEF 25–75). These results suggest the need and the importance of performing CT airway assessment to determine the degree of airway narrowing, which in turn affects the degree of disease severity. By addition of airway assessment, CT lung analysis can be used for the categorization of COPD patients into emphysema-predominance or airway-predominance or even mixed types as noted in many previous clinical trials. Nakano *et al.* [20] found that the airway dimensions and the degree of parenchymal destruction distribution are independent to the lung function. In addition, Makita *et al.* [31] showed that multiple variations occurred within the same patient as the disease progressed.The CT lung analysis gave us broad information about the actual distribution of the emphysema process as well as a lot of numerical information, which were used in follow-up and selection of patients for LVRT. Our study showed the anatomical distribution of the disease process using CT densitometry as well as cluster analysis applications, with the LUL (15 patients) being the most involved lobe followed by the RUL (12 patients).

According to these results, four patients were selected for LVRT with improvement in spirometeric function in three of them; all of them had upper lobe distribution.

Selection of patients with intractable emphysema for LVRT as a treatment option is one of the main clinical applications of the CT lung analysis, as it reflects the actual distribution of the LAA, which cannot be interpreted by spirometry or by body plesyhthmography [32]. Nakano and colleagues found that patients with emphysema distribution involving the upper lung lobes had better outcome compared with patients with lower lobe distribution, who had higher postoperative morbidity and mortality [33–35], and this was consistent with our results.

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Conflicts of interest
There are no conflicts of interest.

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