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Quantitative assessment of emphysema distribution in smokers and patients with α_1-antitrypsin deficiency

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Summary
Introduction: Identification of upper lobe emphysema is mandatory before lung volume reduction surgery (LVRS). Here we introduce a CT-based objective model for describing the distribution of different types of emphysema.
Methods: Fifty COPD patients were included in the study. Half had α_1-antitrypsin deficiency (α_1-COPD) and the rest had smoking-induced emphysema (usual COPD). All patients were scanned 3 times. The relative area of emphysema in each CT slice was plotted against table position, and the cranio-caudal distribution was calculated as the slope of the regression line.
Results: The variation in slopes within a patient was much less than the variation in slopes between patients ($P<0.0001$). There was a significant difference between slopes in the α_1-COPD and the usual COPD groups ($P<0.0001$). In the α_1-COPD group, 24/25 patients had lower lobe emphysema. In the usual COPD group, 4 patients had upper lope predominance, 5 patients had heterogeneous distributions, and 16 patients had lower lobe predominance.
Conclusions: The majority of patients with smoking-related emphysema have a homogeneous distribution and lower lobe predominance although not as noticeable as in α_1-antitrypsin deficiency. An objective and quantitative method for determining the distribution of emphysema should be applied when selecting candidates for LVRS.

Introduction

Lung volume reduction surgery (LVRS) may kill patients, and the indication is delicate. The National Emphysema Treatment Trial (NETT)

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concludes that only a very well-defined subgroup of emphysema patients (i.e. upper lope emphysema) will benefit from surgery; most will experience no effect or even higher mortality with surgery compared to conservative therapy.[1] Despite the distribution of emphysema being crucial in patient selection, it is typically based on subjective judgement.

Emphysema is usually classified into 3 morphological subtypes: centrilobular emphysema (CLE), paraseptal emphysema (PSE) and panlobular emphysema (PLE) based on the portion of the pulmonary lobule that is involved. These subtypes have been described to have a characteristic distribution within the lung.[2] PLE is the predominant subtype in patients with α_1-antitrypsin deficiency, and is typically located in the lower lobes.[3] The commonest subtype of emphysema, which is the dominant type among cigarette smokers, is CLE. This subtype is reported to be most frequently distributed in the upper lung zones.[2,4–6] The imaging techniques and the definition of upper and lower lung zones vary among investigators, as does the description of findings. Precise evaluation of the distribution of emphysema has greatly improved with the introduction of computed tomography (CT) and the description of low attenuation areas (LAA) as the hallmark of parenchymal destruction in emphysema. To our knowledge this was first described in 1978 by Rosenblum et al.[7] who found that patients with emphysema have lower mean lung densities compared to healthy individuals, and even more striking, was the findings of large zones of extremely low density scattered throughout the lung. Quantitation of emphysema by CT can be based on either subjective (visual) or objective (computer) scoring. Visual scoring is both time-consuming and subject to observer variability.[8,9] Cederlund et al.[10] have described an interesting surgically orientated model for objective classification of emphysema heterogeneity using spiral CT. Their results show that 2/3 of the patients did not have clearly heterogeneous distribution (neither upper nor lower lobe predominance).

Before LVRS, the distribution of emphysema must be known. The NETT Research Group[1] has shown that surgical intervention improves survival only in patients with predominantly upper lobe emphysema and low exercise capacity. Here, we present an objective and quantitative method based on the Cederlund concept for describing the distribution of different types of emphysema; we also examine the reproducibility of this method.

Methods

Patient population

Fifty patients from outpatient clinic above 50 years of age with COPD were included in the study. Twenty-five patients had severe α_1-antitrypsin deficiency of PI*ZZ phenotype, verified by isoelectric focusing, and 25 patients had normal α_1-antitrypsin. The lung disease in the latter group is referred to as usual COPD, whereas the condition in patients with severe α_1-antitrypsin deficiency is referred to as α_1-COPD. The Ethics Committee of the County of Copenhagen approved the study, and all patients gave informed consent. Two patients with α_1-COPD were lifelong non-smokers and 23 were ex-smokers for at least 6 months before the

Table 1 Patient characteristics and lung function measurements in absolute and percent predicted.

Characteristic	Usual COPD		α_1-COPD	
	Measured	% Predicted	Measured	% Predicted
Sex (women/men)	18/7		13/12	
Age (y)	67 (7)		59 (7)	
Smoking (never/ex-/current)	0/0/25		2/23/0	
Height (cm)	165 (7)		171 (9)	
Weight (kg)	63 (11)		73 (16)	
FEV_1 (post β-2) (l)	1.19 (0.2)	52 (13) (29–74)*	1.26 (0.4)	44 (13) (28–72)*
FVC (post β-2) (l)	2.44 (0.5)	85 (15)	3.12 (1.0)	86 (16)
TLC (l)	5.86 (1.2)	108 (13)	7.51 (1.8)	122 (12)
RV (l)	3.28 (0.9)	153 (39)	4.08 (1.1)	188 (38)
DL_{CO} (mmol/kPa/min)	3.98 (0.9)	53 (13)	3.98 (1.5)	46 (19)
K_{CO} (mmol/kPa/min/l)	0.97 (0.3)	64 (18)	0.80 (0.3)	51 (18)

Numbers in parenthesis are standard deviations. *Range.